Identifying adults with sepsis, bedside tools versus administrative data: a cohort study

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Abstract

Background

Our objective was to calculate how well the bedside severity scores qSOFA, NEWS, and SIRS predict 30-day mortality from onset of infection compared to the Sepsis-3 recommended diagnostic criteria of an increase in SOFA score of ≥ 2 as a consequence of infection. We then assessed the ability of routinely collected administrative data (ICD-10 codes and blood culture sampling) to identify patients with clinical sepsis. The overall purpose is to inform development of a robust proxy measure for sepsis surveillance at scale.

Methods

This single centre retrospective case note review was set in a district general hospital in Scotland. Adult admissions between 1 st October 2015 and 31 st March 2016 with a blood culture were matched to admissions without a blood culture. The performance characteristics of SOFA, qSOFA, NEWS and SIRS were calculated to predict 30 day mortality. The ability of routinely collected administrative data to identify people with sepsis was assessed using receiver operating characteristic curves.

Results

This cohort of 958 admissions comprised 479 patients with a blood culture sampled and 479 without. There were 269 (28%) patients with sepsis as per the Sepsis-3 definition, and 361 (37.7%) with infection. 30-day mortality from onset of infection was 19.0% and 7.2% in the sepsis and infection groups respectively ($p < 0.001$). NEWS ≥ 7 (AUROC 0.71) was a more accurate predictor of 30-day mortality from onset of infection compared to SOFA ≥ 2 (or $\Delta 2$) (AUROC 0.63), qSOFA ≥ 2 (AUROC 0.64) and SIRS ≥ 2 (AUROC 0.65). ICD-10 sepsis codes (A40, A41 & R57.2) were recorded in only 26 (9.4%) sepsis admissions. Blood culture sampling performed better at identifying patients with sepsis (AUROC 0.63) compared to ICD-10 sepsis codes (AUROC 0.54) or positive blood cultures (AUROC 0.53).

Conclusions

NEWS ≥ 7 was a better predictor of 30-day mortality in patients with infection than SIRS, qSOFA or SOFA. ICD-10 sepsis codes lack sensitivity for reliable sepsis surveillance. Blood culture sampling showed potential for inclusion as part of a clinically relevant proxy marker for sepsis surveillance.

Introduction

Sepsis, redefined in 2016 as “life-threatening organ dysfunction caused by a dysregulated host response to infection”,¹ is globally estimated to cause approximately 5.3 million deaths per year.² Survivors of sepsis are at increased risk of hospital readmission and long term functional sequelae.^{3,4} Sepsis related morbidity, mortality and consequent financial burden^{5,6} has ignited an international focus on improving

the prevention, recognition, and management of sepsis.⁷ Evaluating the impact of changes intended to improve practice requires accurate surveillance of sepsis incidence and outcomes which is stable over time.

Sepsis surveillance has been complicated by both changes in definition and the number of clinical tools used to screen for sepsis. The Sepsis-3¹ consensus guidelines set out diagnostic criteria for sepsis as organ dysfunction, defined as an acute increase in total Sequential [Sepsis-Related] Organ Failure Assessment (SOFA)⁸ score of at least two, as a consequence of infection. Using the Sepsis-3 definition in emergency departments and general wards is challenging since SOFA is not routinely used outside of critical care. Furthermore, SOFA is calculated only once per 24 hours which limits its ability to detect sepsis early, crucial to the improvement of patient outcomes.⁹

In recognition of the need for a bedside tool to identify patients with infection at risk of poor outcomes the Sepsis-3 guidelines recommend the use of qSOFA (quick SOFA).¹ Other severity scores commonly in use include the National Early Warning Score (NEWS & NEWS2)^{10,11} and Systemic Inflammatory Response Syndrome (SIRS) criteria.¹² However, these scores differ in their ability to predict mortality among people with infection^{13,14} so there is a need to establish how they compare to SOFA as the Sepsis-3¹ gold standard to inform a clinically relevant, reliable measure for sepsis surveillance at scale.

The development of sepsis surveillance measures using clinical rather than administrative data is considered desirable¹⁵ however, the national use of electronic health records is not yet widespread even in high income countries. Meantime, there is a need for an objective and reliable method of identifying people with sepsis at scale. The most commonly used administrative data in tracking epidemiological trends are the International Classification of Diseases, Tenth Revision (ICD-10) codes.¹⁶ The use of ICD-10 codes to track sepsis is controversial due to changes in definition, trends in coding practice and the range of potentially appropriate codes.¹⁷ Recent data for NHS England reported a doubling in the use of sepsis codes (A40, streptococcal sepsis; A41, other sepsis; & R57.2, septic shock) between 2016/17 and 2017/2018.¹⁸ The sudden increase in use of these sepsis codes will be multifactorial but, such large changes in coding practice signals problems with using ICD-10 codes in isolation for sepsis surveillance and risks misinterpretation as an absolute rise in sepsis incidence.¹⁹ There is therefore a need for a clinically relevant, robust and resilient method to identify patients with sepsis which can be applied at scale, ideally from routinely collected administrative data.¹⁹

The aims of this paper are:

1. To calculate the performance characteristics of clinical severity scores (qSOFA, SOFA, NEWS, SIRS) in predicting the 30-day mortality of people with infection.
2. To calculate the performance characteristics of administrative data (ICD-10 codes and blood culture sampling) in identifying people with sepsis, as defined by Sepsis-3 criteria.

Methods

Ethical approval was obtained from the West of Scotland Ethics Committee (ref: 17/WS/0044).

The Caldicott Guardian gave permission for access to the data.

Patient population

This was a single-centre retrospective case note review of adult patients admitted to a large district general hospital in Greater Glasgow & Clyde, Scotland. We identified all adult (≥ 16 years) admissions, lasting at least 24hrs, between 1st October 2015 and 31st March 2016 inclusive from the hospital administration system. Blood culture data were extracted for all adult patients admitted during the study period from the hospital microbiology system. The blood culture data were linked to the hospital admission data. Patients admitted to maternity units were excluded.

Patients with a blood culture were matched 1:1 to patients who did not have a blood culture taken but were in the same ward within 24 hours of the blood culture sampling and had a similar length of stay (± 2 days). All matched critical care admissions were included. A random sample of matched ward patients was obtained using a computer generated list of random numbers.

Case note data collection and definitions

Physiological data, laboratory results and clinical notes were extracted from scanned clinical records on the hospital's Clinical Portal. Data were anonymised at point of collection and stored securely. Case notes were reviewed for evidence of infection over the whole course of the index admission and categorised as having no infection, infection, or sepsis. Infection was defined as a documented source of infection and administration of antibiotics. Sepsis was defined as per Sepsis-3¹: as infection plus a SOFA score of ≥ 2 for ward patients, and a change of 2 for critical care patients.

Physiological data were collected at two time points: onset of infection and time of highest NEWS score in the 48 hours prior to and 48 hours post onset of infection to identify the point of highest acuity. Onset of infection was defined as the date and time of first blood culture taken or first antibiotic dose, whichever was earliest. For patients admitted to critical care within 48 hours pre or post infection onset, the second time point was defined as highest SOFA score in that time frame.

Collection of Administrative Data

Administrative data was defined as data currently collected nationally which was relevant to sepsis and comprised: blood culture sampling, positive blood cultures and ICD-10 codes for infection and sepsis. The blood cultures were reviewed by a consultant in infectious disease (CM) and categorised as negative, positive or contaminated (Additional file 1).

All ICD-10 codes assigned for each admission were extracted from Trakcare®, the hospital administration system. A list of infection and sepsis codes (Additional file 2) was constructed, informed by the literature,²⁰ reviewed, and agreed by CM.

Score Calculation

Each patient with a suspected or confirmed source of infection plus antibiotic administration had the following scores calculated: qSOFA, SOFA, NEWS and SIRS. The scores were calculated as per the original tables published elsewhere.^{1, 8, 10, 12}

Baseline SOFA score for ward patients was assumed to be zero, as per Sepsis-3.¹ A SOFA score of ≥ 2 , consequent to infection, was considered to be indicative of sepsis in general ward patients whilst critical care patients required a change of SOFA score of ≥ 2 , consequent to infection. A clinical cut off score of ≥ 2 was applied to qSOFA and SIRS. Performance of NEWS was assessed using both the medium (NEWS ≥ 5) and high (NEWS ≥ 7) clinical risk thresholds.¹⁰

Statistical Analysis

The performance characteristics of the severity scores were assessed for their ability to predict 30-day mortality from the onset of infection using the clinically adopted cut off scores for each tool. Missing data were treated as normal values in score calculation. The area under the receiver operating characteristic curve (AUROC) and 95% confidence intervals were calculated for each severity score using both the clinically recommended cut-off values and across all values. The difference between the AUROCs across all values was assessed using DeLong's test.²¹

The ability of administrative data to identify people with sepsis was assessed by calculation of performance characteristics of variables singly and in combination, and plotting of AUROC against the Sepsis-3 definition of sepsis. It was also assessed against the best performing severity score in predicting mortality: infection plus NEWS ≥ 7 .

Descriptive statistics were used to compare differences between groups. Pearson Chi-Square was calculated for categorical variables. Mann-Whitney U was applied to assess differences between continuous variables in two groups. Kruskal-Wallis was used to assess differences among more than two groups, on a single continuous variable. A p value of less than 0.05 was considered significant.

Analyses were undertaken using SPSS v25.0 and SAS v9.4.

Results

During the study period there were 11207 adult admissions ≥ 24 hrs (Fig. 1). Of these, 1826 (16.3%) admissions had at least one blood culture sampled and 9381 (83.7%) admissions had no blood cultures. Admissions with a blood culture were matched to admissions without a blood culture by clinical area at

time of blood culture (+/- 24hrs) and length of stay (+/- 24hrs) to achieve a balanced cohort of patients with and without blood cultures. Due to the small number of critical care admissions the criteria were revised to matching by critical care area at time of blood culture (+/-96hrs) and length of stay (+/-48 hrs). We matched 898 ward admissions with a blood culture to 898 ward admissions without a blood culture (n = 1796). Within the critical care population, 35 blood culture admissions were matched to 35 admissions without a blood culture (n = 70).

A final cohort of 1000 admissions (500 with and 500 without a blood culture) comprised a simple random sample of 930 index ward admissions (465 with a blood culture and their matched 465 non-blood culture admissions) and all eligible index critical care admissions (n = 70). Twenty-one admissions were excluded due to missing or inaccessible case notes (n = 20) or misclassification (n = 1) of which 4 were matched as critical care admissions and 17 as ward admissions. Their matched admission was also excluded (n = 21), leaving a final cohort of 958 admissions (479 with and 479 without ≥ 1 blood culture).

Study population

The final cohort sample (n = 958) had a median age of 68 (IQR 52–79) and 54% were female. Of the total cohort, 630 were treated for infection and of those, 269 (42.7%) had sepsis as per Sepsis-3 criteria (see Table 1). People with sepsis were older ($p = < 0.001$), had a longer hospital stay ($p < 0.001$) and were more likely to die ($p < 0.001$) compared to those with infection or no infection. Only 35.3% (n = 95) patients meeting Sepsis-3 criteria had suspected or confirmed sepsis documented contemporaneously in their medical notes.

Table 1
Demographics and clinical characteristics

	All Patients (n = 958)	Sepsis (n = 269)	Infection Only (n = 361)	No infection (n = 328)	p*
Age, Median (IQR)	68 (52–79)	72 (57–82)	67 (51–78)	66 (50–77)	< 0.001
Female, n (%)	517 (54%)	131 (48.7%)	208 (57.6%)	178 (54.8%)	0.08
Scottish Index of Multiple Deprivation (SIMD), n (%)					
1 (least affluent)	342 (36.5%)	94 (35.9%)	130 (37.1%)	118 (36.4%)	0.91
2	175 (18.7%)	54 (20.6%)	60 (17.1%)	61 (18.8%)	
3	195 (20.8%)	53 (20.2%)	76 (21.7%)	66 (20.4%)	
4	118 (12.6%)	36 (13.7%)	45 (12.8%)	37 (11.4%)	
5 (most affluent)	107 (11.4%)	25 (9.5%)	40 (11.4%)	42 (13.0%)	
Emergency Admission, n (%)	903 (94.3%)	258 (95.9%)	354 (98.1%)	291 (88.7%)	< 0.001
Median Length of Stay, days (IQR)	4.5 (2.6–7.7)	5.94 (3.6–10.0)	4.2 (2.6–7.5)	3.8 (2.2–6.5)	< 0.001
Critical Care Admission, n (%)	92 (9.6%)	50 (18.6%)	20 (5.5%)	22 (6.7%)	< 0.001
Critical Care Admission 48hrs pre/post Infection, n (%)	59 (6.2%)	46 (17.1%)	13 (3.6%)	-	< 0.001
Suspicion of Sepsis documented, n (%)	198 (20.7%)	95 (35.3%)	99 (27.4%)	4 (1.2%)	0.003
Antibiotics prescribed, n (%)	692 (72.2%)	269 (100%)	361 (100%)	62 (18.9%)	< 0.001
Oral antibiotics only, n (%)	113 (11.8%)	34 (12.6%)	67 (18.6%)	12 (3.7%)	< 0.001

*p values calculated from Kruskal-Wallis for continuous variables among more than two groups, Mann-Whitney U for continuous variables in two groups, and Chi square for categorical variables.

	All Patients (n = 958)	Sepsis (n = 269)	Infection Only (n = 361)	No infection (n = 328)	p*
Blood culture obtained, n (%)	479 (50%)	186 (69.1%)	242 (67.0%)	51 (15.5%)	< 0.001
Positive blood culture, n (%)	42 (4.4%)	24 (8.9%)	18 (5.0%)	0 (0.0%)	< 0.001
Died in Hospital, n (%)	72 (7.5%)	47 (17.5%)	16 (6.9%)	9 (2.7%)	< 0.001
30 Day Mortality from admission, n (%)	97 (10.1%)	56 (20.8%)	28 (7.8%)	13 (4.0%)	< 0.001
30 Day Mortality from onset of infection, n (%)	-	51 (19.0%)	26 (7.2%)	-	< 0.001
*p values calculated from Kruskal-Wallis for continuous variables among more than two groups, Mann-Whitney U for continuous variables in two groups, and Chi square for categorical variables.					

In addition to the 62 admissions matched by critical care area at time of blood culture 30 ward patients were admitted to critical care at some point during their stay (n = 92). Of the 92 critical care patients, 59 were admitted to critical care within 48 hours pre or post onset of infection.

There was no significant difference in the presence of SIRS ≥ 2 (p = 0.675) or NEWS ≥ 5 (p = 0.124) between sepsis and infection only admissions (Table 2). Compared to the infection group significantly more patients in the sepsis group had a NEWS ≥ 7 (p = 0.02) or qSOFA ≥ 2 (p < 0.001).

Table 2
Frequency of positive severity scores.

	Sepsis (n = 269)	Infection Only (n = 361)	p*
SIRS ≥ 2	175 (65.1%)	229 (63.4%)	0.675
NEWS ≥ 5	153 (56.9%)	183 (50.7%)	0.124
NEWS ≥ 7	103 (38.2%)	97 (26.9%)	0.002
qSOFA ≥ 2	50 (18.6%)	28 (7.8%)	< 0.001
*p values calculated from Mann Whitney U for continuous variables and Chi square for categorical variables.			

The respiratory component of the SOFA score had a high number of missing values (n = 546) due to ward patients rarely having an arterial blood gas obtained. Glasgow Coma Scale (GCS), used in qSOFA and

SOFA, also had a high number of missing values (n = 467).

Performance characteristics of SOFA, qSOFA, NEWS and SIRS criteria

The performance characteristics of each severity score in predicting 30-day mortality from onset of infection were calculated using the usual clinical cut-off scores (Table 3). qSOFA had the lowest sensitivity (37.7%, 95%CI 26.9–49.4%), but the highest specificity (91.1%, 95%CI 88.5–93.4%). SIRS had the highest sensitivity (89.6%, 95%CI 80.5–95.4%) but lowest specificity (39.4%, 95%CI 35.3–43.6%).

NEWS performed best for prediction of 30-day mortality from onset of infection using both the high risk cut off of ≥ 7 (AUROC 0.71, 95% CI, 0.65–0.78) and across all values (AUROC 0.78, 95%CI 0.73–0.83) (Fig. 2). SOFA ≥ 2 had the poorest AUROC using the cut off of ≥ 2 (change of ≥ 2 for critical care patients) at 0.63 (95% CI, 0.57–0.70) but performed better when plotted across all values (AUROC 0.72, 95%CI 0.66–0.78). DeLong's method indicated that, when plotted across all values, NEWS was significantly better at predicting 30-day mortality than SIRS ($p = 0.001$), or qSOFA ($p = 0.03$), and no better than SOFA ($p = 0.12$).

Table 3
Performance of severity scores in the prediction of 30-day mortality

	Died within 30 days (n)	Mortality below cut off value	Sensitivity (95% CI)	Specificity (95% CI)	PPV* (95% CI)	NPV* (95% CI)	AUROC* (95% CI)
SOFA ≥ 2	51	7.2% (26/361)	66.2% (54.6– 76.6)	60.6% (56.4– 64.7)	19.0% (14.5– 24.2)	92.8% (89.6– 95.2)	0.63 (0.57– 0.70)
NEWS ≥ 5	65	4.1% (12/294)	84.4% (74.4– 94.7)	51.0% (46.7– 55.2)	19.4% (15.3– 24.0)	95.9% (93.0– 97.9)	0.68 (0.62– 0.74)
NEWS ≥ 7	53	5.6% (24/430)	68.8% (57.3– 78.9)	73.4% (69.5– 77.1)	26.5% (20.5– 33.2)	94.4% (91.8– 96.4)	0.71 (0.65– 0.78)
SIRS ≥ 2	69	3.5% (8/226)	89.6% (80.5– 95.4)	39.4% (35.3– 43.6)	17.1% (13.5– 21.1)	96.5% (93.1– 98.5)	0.65 (0.59– 0.7)
qSOFA ≥ 2	29	8.7% (48/552)	37.7% (26.9– 49.4)	91.1% (88.5– 93.4)	37.2% (26.5– 48.9)	37.2% (26.5– 48.9)	0.64 (0.57– 0.72)
*PPV: Positive Predictive Value; NPV: Negative Predictive Value; AUROC values calculated using cut-off points stated for each severity score.							

The performance characteristics of each tool were also calculated separately for ward and critical care patients. Of the 630 patients with either infection or sepsis, 571 were ward admissions and 59 were

admitted to critical care. For ward patients (n = 571) NEWS predicted 30-day mortality (AUROC 0.80) better across all values than the AUROCs for any other tool (SIRS, 0.71, p = 0.003; qSOFA, 0.71, p = 0.001; SOFA, 0.66, p < 0.001).

SOFA was the best predictor of 30-day mortality among the critical care patients (n = 59) with an AUROC across all values of 0.75, followed by NEWS (AUROC 0.64), qSOFA (AUROC 0.64), and SIRS (AUROC 0.52). Delong's test indicated that SOFA was statistically significantly better at predicting 30-day mortality than SIRS (p = 0.02) but no better than qSOFA (p = 0.2) or NEWS (p = 0.31).

Performance characteristics of routine data to identify people with sepsis

Only 26 (9.7%) sepsis admissions had a sepsis ICD-10 code (A40, A41 or R57.2) (Table 4). Coding for infection was more frequent with 65.1% of sepsis admissions being allocated at least one infection code. More than 80% of infection and sepsis codes allocated to infection and/or sepsis admissions were from three ICD-10 chapters: diseases of the respiratory system (J00-J99), certain infectious and parasitic diseases (A00-B99) and diseases of the genitourinary system (N00-N99).

Having a blood culture taken was better at identifying people with sepsis (AUROC 0.63, 95%CI 0.59–0.67) than having either, a positive blood culture result (AUROC 0.53, 95%CI 0.49–0.57), or sepsis codes (A40, A41 and R57.2) (AUROC 0.54, 95%CI 0.5–0.58) (Table 4). The best performing combination of administrative data was the presence of one of an infection code, sepsis code or a blood culture (AUROC 0.67, 95%CI 0.64–0.71).

Table 4
Performance characteristics of administrative data to identify people with sepsis

	n	Patient with sepsis but no administrative data variable	Sensitivity (95% CI)	Specificity (95% CI)	PPV* (95% CI)	NPV* (95% CI)	AUROC (95% CI)
Infection code	175	18% (94/521)	65.1% (59.0–70.8)	62.0% (58.2–65.6)	40% (35.4–44.8)	82.0% (78.4–85.2)	0.64 (0.6–0.67)
Sepsis code	26	26.5% (243/916)	9.7% (6.4–13.8)	97.7% (96.3–98.7)	61.9% (45.6–76.4)	73.5% (70.5–76.3)	0.54 (0.5–0.58)
Infection or sepsis code	191	15.9% (78/92)	71% (65.2–76.4)	60.1% (56.3–63.8)	41.0% (36.5–45.6)	84.1% (80.6–87.3)	0.66 (0.62–0.69)
Blood culture taken	186	17.3% (83/479)	69.1% (63.3–74.6)	44.4% (53.7–61.2)	38.6% (34.4–43.4)	91.6% (79.0–86.0)	0.63 (0.59–0.67)
Positive blood culture result	24	26.7% (245/916)	8.9% (5.8–13.0)	97.4% (95.9–98.4)	57.1% (41.0–72.3)	73.3% (70.3–76.1)	0.53 (0.49–0.57)
Infection or sepsis code or blood culture taken	241	8.4% (28/334)	89.6% (85.3–93.0)	44.4% (40.7–48.2)	38.6% (34.8–42.6)	91.6% (88.1–94.4)	0.67 (0.64–0.71)
Infection or sepsis code plus blood culture taken	136	20.9% (133/637)	50.6% (44.4–56.7)	73.1% (69.7–76.4)	42.4% (36.9–48)	79.1% (75.8–82.2)	0.62 (0.58–0.66)
*PPV: Positive Predictive Value; NPV: Negative Predictive Value.							

The performance of administrative data in identifying people with infection and NEWS ≥ 7 (Table 5) was similar to its ability in identifying people meeting the Sepsis-3 criteria (Table 4). Sepsis codes performed poorly in identifying both sepsis (AUROC 0.54, 95%CI 0.5–0.58) and people with infection and NEWS ≥ 7 (AUROC 0.51, 95%CI 0.47–0.56). Positive blood cultures were also poor at recognising people with sepsis (AUROC 0.53, 95%CI 0.49–0.57) or NEWS ≥ 7 (AUROC 0.52, 95%CI 0.47–0.57).

Table 5

Performance characteristics of administrative data to identify patients with infection & NEWS ≥ 7

	n	Infection + NEWS ≥ 7 but no administrative data variable	Sensitivity (95% CI)	Specificity (95% CI)	PPV* (95% CI)	NPV* (95% CI)	AUROC (95% CI)
Infection code	136	12.3% (64/521)	68% (61.1– 74.4)	60.3% (56.7– 63.8)	31.1% (26.8– 35.7)	87.7% (84.6– 90.4)	0.64 (0.6– 0.68)
Sepsis code	12	20.5% (188/916)	6% (3.1– 10.3)	96% (94.4– 97.3)	28.6% (15.7– 44.6)	79.5% (76.7– 82.1)	0.51 (0.47– 0.56)
Infection or sepsis code	144	11.4% (56/492)	72% (53.9– 61.1)	57.5% (53.9– 61.1)	30.9% (26.7– 35.3)	88.6% (85.5– 91.3)	0.65 (0.61– 0.69)
Blood culture	154	9.6% (46/479)	77% (70.5– 82.6)	57.1% (53.5– 60.7)	32.2% (28.0– 36.5)	90.4% (87.4– 92.9)	0.67 (0.63– 0.71)
Positive blood culture	15	20.2% (185/916)	7.5% (4.3– 12.1)	96.4% (94.9– 97.6)	35.7% (21.6– 52)	79.8% (77.1– 82.4)	0.52 (0.47– 0.57)
Infection or sepsis code or blood culture	185	4.5% (15/334)	92.5% (87.9– 95.7)	42.1 (38.5– 45.7)	29.6% (26.1– 33.4)	95.5% (92.7– 97.5)	0.67 (0.64– 0.71)
Infection or sepsis code and blood culture	113	13.7% (87/637)	56.5% (49.3– 63.5)	72.6% (69.2– 75.7)	35.2% (30.0– 40.7)	86.3% (83.4– 88.9)	0.65 (0.60– 0.69)
*PPV: Positive Predictive Value; NPV: Negative Predictive Value.							

Discussion

To the best of our knowledge this is the first study which investigates the performance of qSOFA, SIRS, NEWS and SOFA in predicting 30-day mortality of patients in a mixed hospital cohort. We found that the severity scores varied widely in their ability to identify people who met the Sepsis-3¹ criteria. NEWS ≥ 7 was a better predictor of 30-day mortality from onset of infection than SOFA, qSOFA or SIRS in patients with infection. When plotted across all values, however, it did not perform significantly better than SOFA.

Analysis of routinely collected administrative data revealed that only one in ten patients with clinical sepsis had an ICD-10 sepsis code allocated and consequent poor performance as a proxy measure for

sepsis surveillance. Positive blood cultures also performed poorly, however, blood culture sampling alone demonstrated potential as one component of a robust measure for sepsis surveillance.

While the results of this study are limited by its retrospective, single centre design, the review of infection across the whole hospital admission rather than only at admission, provides a complete picture of sepsis incidence within the cohort. The use of clinical data to identify people with sepsis also avoided the bias of selecting patients on the basis of their ICD-10 codes and also enabled assessment of coding patterns.

The high number of missing values for the respiratory component of SOFA, due to the absence of arterial blood gases in ward patients, and poor documentation of the Glasgow Coma Scale (GCS), used in qSOFA and SOFA, may have resulted in SOFA scores which under-represented the true acuity of the ward population. Other studies have also noted GCS as being frequently missing.²² We considered replacing GCS with AVPU (Alert, Verbal, Pain, Unresponsive), however, although AVPU was more complete, only 6 out of 17 patients identified as having a GCS ≤ 13 had an abnormal AVPU. The limitations of AVPU in identifying people with altered mentation is reflected in its amendment within NEWS2 to ACVPU to include 'new confusion or delirium'.¹¹

Our findings are consistent with the broader literature demonstrating superior performance of NEWS over qSOFA and SIRS in predicting mortality.^{13,23,24,25} Although other studies have reported SOFA as being superior to NEWS in predicting mortality,^{14,26} this was not replicated in our data. Indeed, SOFA had poorer performance characteristics in our cohort than reported in other retrospective studies.^{27,28} This may be explained by SOFA predicting sepsis-associated mortality less well in the ward population of our cohort and its high level of missing data.

The suboptimal performance of qSOFA in predicting mortality, particularly in terms of sensitivity, is similar to that reported elsewhere.^{29,30,31} Our study also found that, compared to NEWS, qSOFA did not perform well in identifying people who met the Sepsis-3 criteria. These findings add to the body of evidence which challenges the use of qSOFA over NEWS.¹³ Similar to other studies, SIRS had a high sensitivity but poor specificity and as such is a poor predictor of those patients with infection at an increased risk of a poor outcome.^{13,24}

In line with other studies,^{20,32} our research reported under coding for sepsis and consequent poor performance of the ICD-10 sepsis codes in identifying patients with sepsis. The growth in coding for sepsis observed in the literature has contributed to reporting of significant increases in documented sepsis incidence.^{18,34,35} Such changes compromise the use of sepsis codes as a robust and reliable measure of sepsis incidence and underline the need for accurate sepsis epidemiology based on a combined measure which is resistant to bias. Our finding of lack of sensitivity in sepsis codes and lack of specificity in infection codes, supports recent concerns about the quality of coding, its impact on epidemiological trends and potential for misinformed influence on policy and practice.³⁵

Although no one combination of administrative data variables had an AUROC of > 0.7 , the cut-off for acceptable discrimination, this study did identify nationally collected administrative data with better predictive accuracy for sepsis than the sepsis explicit ICD-10 codes currently used. Blood culture sampling, for example, performed significantly better than ICD-10 sepsis codes in identifying patients meeting the Sepsis-3 criteria. As an administrative data variable, blood culture sampling is unaffected by trends in diagnostic coding but is susceptible to changes in sampling practice. Further study is required to assess the effect that standardisation of blood culture sampling in sepsis has on its sensitivity and specificity as a measure. Positive blood cultures predictably performed poorly as a surrogate marker for sepsis and, as reported elsewhere, lacks the sensitivity required for sepsis surveillance.³⁶

The development of a stable measure to identify people with sepsis from administrative data would make a significant contribution to both sepsis surveillance and, more broadly, to the decisions policy makers make in relation to resource allocation in a fiscally pressured system. It would also address the concerns raised about potential for over-coding and over-diagnosis.³⁵ Further investigation and validation of a combined measure is required in a larger, multicentre cohort.

Conclusions

Our results support the use of $\text{NEWS} \geq 7$ to identify patients with infection at increased risk of death at 30 days. The use of sepsis explicit ICD-10 codes to identify people with sepsis performed poorly in this cohort. Although complete alignment between routinely stored data and clinical diagnosis is considered unachievable,³⁷ a measure which is stable and performs well should continue to be pursued. Blood cultures as clinical, but routinely stored data, demonstrated potential as one component of a robust surrogate marker for sepsis. This study provides an important insight into the ability of administrative data to identify people with sepsis at scale.

Abbreviations

ACVPU:Alert, Confused, Verbal, Pain, Unresponsive; AUROC:Area under the receiver operating characteristic curve; AVPU:Alert, Verbal, Pain, Unresponsive; GCS:Glasgow Coma Scale; ICD-10:International Classification of Diseases, Tenth Revision; NEWS:National Early Warning Score; NEWS2:National Early Warning Score 2; qSOFA:quick Sequential Organ Failure Assessment; SIRS:Systemic Inflammatory Response Syndrome; SOFA:Sequential Organ Failure Assessment

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the West of Scotland Ethics Committee (ref: 17/WS/0044).

The Caldicott Guardian gave permission for access to the data.

Availability of data and materials

The dataset generated during this study cannot be made publicly available as it contains data on individual patients.

Consent for publication

Not applicable.

Competing interests

MB: None; K.R. was the National Clinical Lead for Sepsis and the Deteriorating Patient workstream of the Scottish Patient Safety Programme between May 2012 and October 2017. As such, he was instrumental in the National Sepsis strategy and the recommendation and adoption of NEWS across Scotland; CM: None; ES: None; AP: None

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Authors' contributions

MB, CM & KR conceived, designed and coordinated the study. MB drafted the manuscript. ES & AP contributed to data analysis. KR, CM, AP & ES assisted in preparation and editing of the manuscript.

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Additional Files

Additional file 1. ICD-10 infection and sepsis codes

A list of ICD-10 infection and sepsis codes reported in the cohort.

Microsoft Word 2007-2013 (.docx)

Additional file 2. Blood Culture Organisms.docx

A list of the organisms grown from blood cultures obtained within the cohort.

Microsoft Word 2007-2013 (.docx)

Figures

Figure 1

Cohort selection flow diagram

Figure 2

Receiver operating characteristic curves for 30-day mortality per severity score

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [AdditionalFile2.BloodCultureOrganisms.docx](#)
- [AdditionalFile1.ICD10infectionandsepsiscodes.docx](#)