Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

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ORIGINAL CONTRIBUTION

Comparison of PIRO, SOFA, and MEDS Scores for Predicting Mortality in Emergency Department Patients With Severe Sepsis and Septic Shock

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Abstract

Objectives: The Predisposition Insult Response and Organ failure (PIRO) scoring system has been developed for use in the emergency department (ED) to risk stratify sepsis cases, but has not been well studied among high-risk patients with severe sepsis and septic shock. The PIRO score was compared with the Sequential Organ Failure Assessment (SOFA) and Mortality in ED Sepsis (MEDS) scores to predict mortality in ED patients with features suggesting severe sepsis or septic shock in the ED.

Methods: This was an analysis of sepsis patients enrolled in a prospective observational ED study of patients presenting with evidence of shock, hypoxemia, or other organ failure. PIRO, MEDS, and SOFA scores were calculated from ED data. Analysis compared areas under the receiver operator characteristic (ROC) curves for 30-day mortality.

Results: Of 240 enrolled patients, final diagnoses were septic shock in 128 (53%), severe sepsis without shock in 70 (29%), and infection with no organ dysfunction in 42 (18%). Forty-eight (20%) patients died within 30 days of presentation. Area under the ROC curve (AUC) for mortality was 0.86 (95% confidence interval [CI] = 0.80 to 0.92) for PIRO, 0.81 (95% CI = 0.74 to 0.88) for MEDS, and 0.78 (95% CI = 0.71 to 0.87) for SOFA scores. Pairwise comparisons of the AUC were as follows: PIRO versus SOFA, $p = 0.01$; PIRO versus MEDS, $p = 0.064$; and MEDS versus SOFA; $p = 0.37$. Mortality increased with increasing PIRO scores: PIRO < 5, 0%; PIRO 5 to 9, 5%; PIRO 10 to 14, 5%; PIRO 15 to 19, 37%; and PIRO ≥ 20, 80% ($p < 0.001$). The MEDS score also showed increasing mortality with higher scores: MEDS < 5, 0%; MEDS 5 to 7, 12%; MEDS 8 to 11, 15%; MEDS 12 to 14, 48%; and MEDS > 15, 65% ($p < 0.001$).

Conclusions: The PIRO model, taking into account comorbidities and septic source as well as physiologic status, performed better than the SOFA score and similarly to the MEDS score for predicting mortality in ED patients with severe sepsis and septic shock. These findings have implications for identifying and managing high-risk patients and for the design of clinical trials in sepsis.

ACADEMIC EMERGENCY MEDICINE 2014;21:1257–1263 © 2014 by the Society for Academic Emergency Medicine

Sepsis remains a significant global health challenge and is increasing in incidence, due largely to an aging population being at greater risk of sepsis.[1] Sepsis accounts for a large proportion of admissions to the intensive care unit (ICU), and mortality rates remain significant despite optimal care.[2,3]

Most patients presenting to the hospital with sepsis are initially assessed in the emergency department (ED).

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Received March 27, 2014; revision received June 18, 2014; accepted July 2, 2014.

This work was presented at the SMACC Gold Conference, Gold Coast, Australia, March 2014.

This research was partially funded by a grant from the Medical Research Foundation, Royal Perth Hospital.

The authors have no potential conflicts to disclose.

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© 2014 by the Society for Academic Emergency Medicine
doi: 10.1111/acem.12515
ISSN 1069-6563
PII ISSN 1069-6563583

Those with established organ failure (severe sepsis) and/or septic shock are resuscitated according to established consensus guidelines.[4] For those not meeting severity criteria, disposition options include admission to a non–critical care hospital bed, discharge to the community, or an ambulatory care service. This decision is based on the likelihood of the patient developing complications, and a number of clinical tools have been developed to aid this process. Typically these combine clinical variables to estimate the risk of short-term mortality. They may be intended for a specific condition, such as the Pneumonia Severity Index[5] and the "CURB-65"[6] score for pulmonary infection or be designed to use for a range of conditions. The Acute Physiology and Chronic Health Evaluation (APACHE) system[7] is used to predict mortality among critically ill patients admitted to the ICU, but requires data that are not available in the ED. The Sequential Organ Failure Assessment (SOFA) and Mortality in Emergency Department Sepsis (MEDS) scores (Data Supplements S1 and S2, available as supporting information in the online version of this paper) use clinical and laboratory variables to grade the severity of organ failure and have been demonstrated to correlate with mortality among those admitted from the ED with sepsis.[8–11]

The SOFA score uses only physiologic and laboratory variables but does not consider host factors such as age, ethnicity, and comorbid disease burden, which are important drivers of mortality in sepsis.[12,13] The MEDS score requires a subjective assessment of likelihood of short-term mortality and may perform less accurately at higher illness severity.[14] Another issue relates to virulence of the infecting pathogen. In recognition of these factors, the Predisposition Insult Response and Organ failure (PIRO) model has been proposed to reflect each of these domains.[15] This model, however, requires knowledge of the infecting agent, information that is rarely available in the ED. Howell et al.[16] have developed a PIRO model based on the likely clinical source of infection (Data Supplement S3, available as supporting information in the online version of this paper), which gave a high predictive accuracy for short-term mortality in a large multicenter validation study.[17] However, this study included a broad range of illness severity and overall mortality rates were low. We therefore aimed to compare the PIRO, SOFA, and MEDS scores for predicting outcome in high-risk sepsis patients in an adult ED setting.

METHODS

Study Design

This was a planned subgroup analysis of data gathered in the Critical Illness and Shock Study (CISS). The human research ethics committees at each participating hospital approved the study. Patients gave written informed consent if capable of doing so. Patients whose clinical conditions precluded obtaining prospective consent were enrolled under an initial waiver of consent according to the provisions in paragraph 2.3.6 of the Australian National Health and Medical Research Council ethical conduct guidelines for low-risk observational research.

Study Setting and Population

We analyzed cases of sepsis enrolled in the CISS at two metropolitan hospitals in Perth, Western Australia, between March 2010 and July 2013. The methodology of the CISS study has previously been reported.[18] In brief, patients presenting to the ED with a range of critical illnesses and meeting physiologic criteria suggesting shock or organ failure undergo real-time clinical data collection and repeated blood sampling by trained research nurses over the initial 24 hours of their hospital stays. Patients are recruited during research nurse hours (07:00 to 22:00), 7 days per week.

After excluding CISS patients with clear nonsepsis diagnoses (e.g., trauma, myocardial infarction, pulmonary embolism), sepsis cases were defined as at least two systemic inflammatory response features (heart rate > 90 beats/min, respiratory rate > 20 breaths/min, temperature >38 or <36°C, total white cell count >12 × 10^9 or <4 × 10^9/L), along with a decision to administer intravenous (IV) antibiotics in ED. We further classified sepsis patients according to standard consensus definitions.[19] Septic shock was defined as associated hypotension (systolic blood pressure [sBP] < 90 mm Hg despite ≥ 1000 mL isotonic crystalloid bolus), and/or hypoperfusion (serum lactate ≥ 4 mmol/L). Severe sepsis was defined as associated organ dysfunction (SOFA score on admission ≥ 2) in the absence of shock, and uncomplicated sepsis, as admission SOFA score < 2 and no requirement for organ support (ventilation, inotropes, or dialysis). Cases that were transferred from other health care facilities were excluded.

Study Protocol

The PIRO, SOFA, and MEDS scores were calculated from the individual data elements collected in the ED and recorded in the chart. The most abnormal value recorded in the ED was used in the score calculations, with the exception of Glasgow Coma Scale score for the SOFA score, which was the best presedation value recorded (as per convention). Blood pressure following IV crystalloid bolus was used for the PIRO score. For the purposes of the PIRO and MEDS score calculations, we defined terms such as "shock," "respiratory failure," "terminal illness," etc., with reference to the relevant original papers.[10,17] All data were abstracted into a structured datasheet by a single investigator (SPJM). Because in the ED the majority of patients are not ventilated, a modification of the respiratory domain of the SOFA score was used based on the fraction of inspired oxygen (FiO_2)/peripheral capillary oxygen saturation (SpO_2) ratio, where FiO_2 was known.[20] Where the precise FiO_2 was not known, this was estimated from the inspired oxygen concentration and device, according to Data Supplement S4 (available as supporting information in the online version of this paper). For the MEDS score, neutrophil bands were excluded as described by Vorwerk et al.[21] since these are not reported by our laboratory. Finally, the PIRO model was modified to use blood urea > 8 mmol/L to replace blood urea nitrogen (BUN) > 20 mg/dL, and again neutrophil bands could not be included in the score. The primary outcome was mortality at 30 days following ED presentation.

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Data Analysis

The method of analysis was to compare the area under the receiver operator characteristic (ROC) curves (AUC) for each of the three scoring systems. Descriptive statistics are presented, with the Wilcoxon rank-sum test used for continuous data comparisons, and chi-square test for categorical data. Statistical analyses were performed using Stata version 12.

RESULTS

A total of 240 participants with sepsis were included (Figure 1). Their clinical characteristics are summarized in Table 1. The majority had severe sepsis or septic shock, and overall mortality at 30 days was 20%. A total of 105 participants (44%) were admitted to ICU beds. Of the 135 not admitted to ICU beds, 101 received ward-level care (which included IV fluids, antibiotics, noninvasive ventilation, and dopamine infusion), 29 had treatment limitations precluding ICU admission, and two died in the ED prior to admission. The most frequent site of infection was respiratory tract (40%), followed by urinary tract (19%), skin or soft tissue (13%), abdominal (12%), bloodstream (7%), and others (2%). A clinical source was not identified in 7%. The infecting organism was identified in 54% of cases, with a slight predominance of Gram-negative organisms.

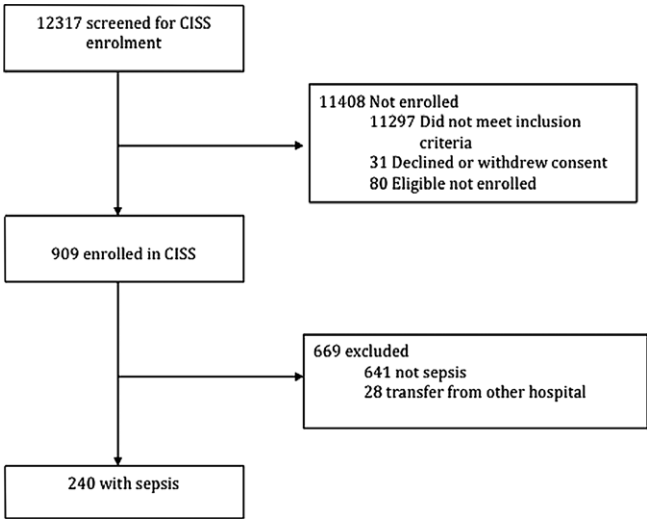

Figure 1. Study enrollment flowchart. CISS = Critical Illness and Shock Study.

Figure 2 shows the ROC curves for the PIRO, SOFA, and MEDS scores for 30-day mortality. Pairwise comparisons of the AUC were as follows: PIRO versus SOFA, p = 0.01; PIRO versus MEDS, p = 0.064; and MEDS versus SOFA, p = 0.37. A sensitivity analysis stratified by ICU admission showed similar performances of each of the scores. However, among patients admitted to the ICU (n = 105), the PIRO score was superior to the MEDS score: AUC 0.87 versus 0.75, p = 0.02. Full details are shown in Data Supplement S5, available as supporting information in the online version of this paper.

Table 2 compares the characteristics of those patients who died within 30 days versus survivors. Those who died were older; had higher comorbidity scores; and had significantly higher PIRO, SOFA, and MEDS scores. Table 3 shows the increasing mortality across increasing PIRO score and MEDS score quintile.

DISCUSSION

Severity scoring for sepsis has implications for patient disposition and outcomes. Although international consensus guidelines define sepsis as a systemic inflammatory response in the context of suspected or proven infection,[4] these criteria are neither sensitive nor specific.[19] This is particularly so in the dynamic setting of

Table 1
Participant Characteristics and Outcomes

Variable	Sepsis	Severe Sepsis	Septic Shock	All
n (%)	42 (18)	70 (29)	128 (53)	240 (100)
Age (yr)	55 (48–72)	71 (56–78)	67 (52–78)	67 (51–78)
% male	57	66	65	64
Vital signs				
Temperature (°C)	38.6 ± 0.9	37.9 ± 1.4	37.4 ± 1.7	37.8 ± 1.6
Pulse rate (beats/min)	115 ± 19	113 ± 23	110 ± 25	112 ± 23
Respiratory rate (breaths/min)	26 ± 8	31 ± 7	28 ± 8	29 ± 8
sBP (mm Hg)	113 ± 21	115 ± 21	84 ± 13	98 ± 23
GCS score	15 (15–15)	15 (14–15)	15 (14–15)	15 (14–15)
Lactate (mmol/L)	1.6 (1.1–2.1)	2.1 (1.3–2.9)	3.1 (1.6–5.0)	2.3 (1.4–3.8)
SOFA score	1 (0–1)	3 (3–5)	6 (5–9)	5 (2–7)
MEDS score	4 (3–6)	8 (5–10)	11 (8–13)	8 (6–11)
PIRO score	9 (5–11)	13 (11–15)	15 (12–18)	13 (10–17)
CCS	1 (0–2)	2 (1–4)	2 (1–4)	2 (1–4)
ICU admit, *n* (%)	4 (10)	16 (23)	85 (66)	105 (44)
Length of stay	5 (3–15)	7 (4–12)	7 (4–16)	7 (4–14)
Death within 30 days, *n* (%)	0 (0)	14 (20)	34 (26)	48 (20)

Unless otherwise stated data are median (IQR) or mean ± SD.
CCS = Charlson Comorbidity Score; GCS = Glasgow Coma Scale; ICU = intensive care unit; MEDS = Mortality in Emergency Department Sepsis; PIRO = Predisposition Insult Response and Organ failure; sBP = systolic blood pressure; SOFA = Sequential Organ Failure Assessment.

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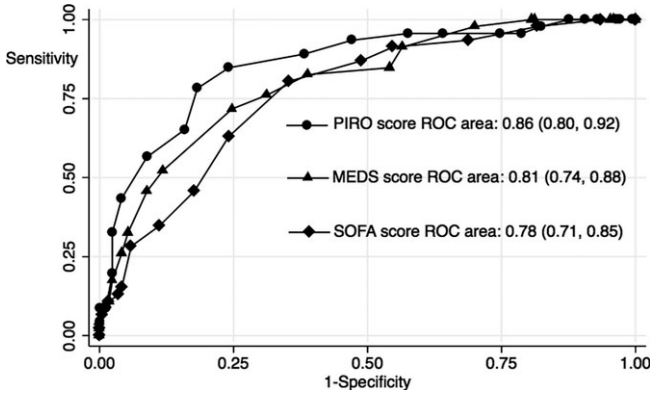

Figure 2. ROC curves for PIRO, MEDS, and SOFA scores for 30-day mortality ($n = 240$). MEDS = Mortality in Emergency Department Sepsis; PIRO = Predisposition Insult Response and Organ failure; ROC = receiver operator characteristic; SOFA = Sequential Organ Failure Assessment.

Table 2
Comparison of Participants Who Died Versus Survivors

Variable	Survived	Died	p-value
N	192	48	—
Age (yr)	67 (50–77)	71 (60–83)	0.013
% male	61	75	0.07
Lactate (mmol/L)	2.1 (1.2–3.3)	4.0 (2.3–6.4)	<0.001
CCS	2 (0–3)	3 (1–5)	0.002
SOFA score	4 (2–6)	7 (6–10)	<0.001
MEDS score	8 (5–10)	12 (10–15)	<0.001
PIRO score	12 (9–14)	18 (16–20)	<0.001

Unless stated otherwise data are median (IQR) values.
CCS = Charlson Comorbidity Score; MEDS = Mortality in Emergency Department Sepsis; PIRO = Predisposition Insult Response and Organ failure; SOFA = Sequential Organ Failure Assessment.

Table 3
30-day Mortality Rate for PIRO and MEDS Score Quintiles (see also Figure 3)

Score Quintile	Survived	Died	Mortality, % (95% CI)
PIRO score			
0–4	12	0	0 (—)
5–9	36	2	5 (0–12)
10–14	97	5	5 (1–9)
15–19	43	25	37 (25–48)
≥20	4	16	80 (62–98)
Total	192	48	
MEDS score			
0–4	38	0	0 (—)
5–7	49	7	12 (4–21)
8–11	84	15	15 (8–22)
12–14	14	13	48 (29–67)
≥15	7	13	65 (43–87)
Total	192	48	

MEDS = Mortality in Emergency Department Sepsis; PIRO = Predisposition Insult Response and Organ failure.

the ED, where microbiologic results are rarely available and diagnosis often requires clinical judgment. A recent systematic review of sepsis scoring systems in the ED found that case definitions and mortality rates varied considerably between studies, making valid comparisons problematic.[22] For example, the MEDS score, the most frequently studied model, used the clinical decision to draw a blood culture as the enrollment criteria in its derivation cohort.[10] While subsequently found to be predictive of mortality up to 1 year among ED patients with sepsis,[11] other authors found that among patients with septic shock undergoing early goal-directed therapy (EGDT) resuscitation, predictive performance of MEDS for outcome was poor.[14] An additional limitation of the MEDS score is that a large weighting is given to a subjective assessment of short-term mortality by the treating clinician.

The PIRO model for sepsis has been described by Marshall[23] as analogous to the Tumour Nodes Metastases staging system for cancer. The rationale is that clinical trials in sepsis should recognize the enormous clinical heterogeneity of the condition, and a severity scoring system is necessary to undertake meaningful comparisons between patient groups. The PIRO model has been adapted specifically for use in the ED and does not require knowledge of the infecting organism.[17] Patients were identified by the decision to give antibiotics in the ED, and overall mortality was 6.1%. The authors reported an AUC of 0.83 in the external validation of their PIRO model. In our study, which predominantly consisted of patients with severe sepsis and septic shock, with an associated higher mortality rate of 20%, performance of PIRO model was comparable with an AUC of 0.86.

Other studies have evaluated the utility of the PIRO model in ED sepsis.[24–26] De Groot et al.[24] compared the PIRO and MEDS with physician judgment to predict the need for ICU admission. They found that the PIRO did not perform better than physician judgment in predicting disposition from the ED to a ward bed or to the ICU. However, the analysis excluded 40% of patients who were admitted to the ward and deemed not suitable for ICU. Physician judgment alone resulted in one in six patients who required ICU care being erroneously admitted to the ward, although when PIRO and clinical judgment were combined (as would be the case in practice), the sensitivity for predicting ICU requirement improved. In a later study the same group compared the performance of the PIRO score to predict mortality in high- and low-risk ED sepsis populations. Among low-risk ED sepsis patients (mortality 6%), the PIRO performed well with an AUC of 0.83, similar to our findings, but only 0.68 in a higher risk cohort (mortality 22%) of ED sepsis patients. However, these two cohorts were recruited at different time points over a 5-year period and using different enrollment criteria, limiting direct comparisons. Finally in a recent Chinese study of ED sepsis patients, the PIRO model had an AUC of 0.82 for 28-day mortality. The authors stated that the "O" (organ failure) element of the score was as useful as the entire score, but they excluded patients with metastatic malignancy and liver disease, which are elements of the PIRO model. Clearly, differing case definitions and enrollment criteria between studies can affect results.

We found the MEDS score to also perform well, with an AUC of 0.81. This is in contrast to Jones et al.[14] who

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found the MEDS score to have an AUC of 0.61 among ED patients with septic shock. Similarly Nguyen et al.[27] found MEDS to have an AUC of 0.63 in a registry database of patients undergoing EGDT in the ED. Our results are similar to the AUC of 0.78 found among "all-comers" with sepsis in the original MEDS score validation study.[10] Again, patient selection may have accounted for these differing findings, because although our study represented a sicker group of patients, only around half the patients in our study were admitted to the ICU. Our study included patients in whom critical care admission was not deemed either necessary or appropriate or who died in the ED prior to transfer to the ICU. Although no statistical difference was found in the MEDS score AUC between those admitted to the ICU versus the ward, the MEDS score did underperform the PIRO score for the ICU-admitted patients. This may reflect the higher relative weighting in the MEDS score given for patients with terminal illness who were not suitable for ICU admission. Other authors have also examined the performance of the MEDS score. Sankoff et al.[28] studied 385 ED patients with systemic inflammatory response syndrome criteria who were admitted to the hospital and found an overall mortality rate of 9%, with a MEDS score AUC of 0.88. In a retrospective study of 276 patients with severe sepsis, Chen et al.[29] found that MEDS score calculated from ED data outperformed the APACHE II score for mortality prediction (AUC 0.75 vs. 0.62, $p < 0.01$).

For the admission SOFA score, we found a 30-day mortality AUC of 0.78. This is comparable to the AUC of 0.75 for admission SOFA score to predict in-hospital mortality found in a study of 248 ED patients with septic shock.[9] The SOFA, however, takes no account of age and comorbidity, known to be independent drivers of sepsis mortality.[12,13] While our data confirm that organ failure is important in predicting worse outcome, it is unsurprising that the PIRO, which takes into account age, comorbidity, and the source of infection, outperformed the SOFA for 30-day mortality prediction. We found the PIRO and MEDS scores to perform similarly overall, although the PIRO model may have better sensitivity for mortality. While the MEDS and PIRO do have some common variables, the PIRO model is more complex, requiring 13 variables compared to eight for the MEDS score. The clinical utility of a more complex model in practice remains to be demonstrated. Our findings are consistent with those of Howell et al.[17] in demonstrating a PIRO score of ≥15 is associated with particularly high mortality risk. Finally, the PIRO model may be a means of stratifying enrollment into clinical trials of interventions in sepsis so meaningful intergroup comparisons can be made.

Other PIRO models have been studied in sepsis assessment in the ED. Nguyen et al.[27] evaluated the original PIRO model[15] among sepsis patients undergoing EGDT in the ED. They found that PIRO performed similarly to APACHE II and outperformed the MEDS score; however, the PIRO model tended to overestimate mortality and the AUC was 0.71. The authors suggested the PIRO was most discriminatory in higher-risk patients. In a Portuguese study, Cardoso et al.[30] developed another risk prediction model for sepsis using the PIRO concept with good predictive value for mortality (AUC = 0.85), while Chen and Li[26] developed and validated a PIRO based model for ED assessment of community acquired pneumonia in China with AUC of 0.82 in the validation cohort (17% overall 28-day mortality).

LIMITATIONS

The main limitation relates to case selection. This was a planned subgroup analysis of sepsis patients within a broader study of ED patients presenting with critical illness and was not representative of the spectrum of severity of sepsis in the ED. Cases were selected using an objective and pragmatic case definition. All ED sepsis studies have patient selection issues to some extent, given the lack of a reliable case definition. To minimize bias, we calculated risk scores in a structured manner using predefined data elements by a single investigator. It was therefore impractical to assess interrater reliability or blind to outcome. The risk scores were not calculated in real time in the ED and not used to guide clinical care. None of the three scoring systems are used routinely in the participating EDs to guide patient management. Finally, we did not undertake formal calibration analysis to compare the predicted mortality rates with those actually observed for different levels of the scores, since this is heavily dependent on the overall risk profile of the cohort studied and beyond the aims of this study.

CONCLUSIONS

The Predisposition, Insult/Infection, Response, and Organ dysfunction model, taking into account comorbidities and septic source as well as physiologic status, performed better than the Sequential Organ Failure Assessment and Mortality in Emergency Department Sepsis scores for predicting mortality in ED patients with severe sepsis and septic shock. These findings have implications for identifying and managing high-risk patients, and for the design of clinical trials in sepsis.

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Supporting Information

The following supporting information is available in the online version of this paper:

Data Supplement S1. Sequential Organ Failure Assessment (SOFA) score with modification of respiratory component to include FiO_2/SpO_2 (Paraharipande et al.) or supplemental oxygen where the PaO_2 is not measured or patient not ventilated.

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Data Supplement S2. Mortality in ED Sepsis (MEDS) score with neutrophil bands >5% not included as these were not reported by the laboratory, giving maximal total score 24.

Data Supplement S3. The PIRO Score.

Data Supplement S4. Inspired oxygen conversion chart for estimation of fraction of inspired oxygen (FiO_2). LPM = liters per minute.

Data Supplement S5. Sensitivity analysis comparing AUC for PIRO, MEDS, and SOFA scores for patients admitted to ICU (n = 105) versus not admitted to ICU (n = 135).

Announcing Usus – A community website on usage

Usus (Latin for usage) is a new, independent, community-run website (http://www.usus.org.uk/) for all those interested in the usage of online content. It is designed to support a productive conversation among librarians, publishers, aggregators, and repository managers so that we can all get the best possible usage reports for our electronic resources.

The Usus website provides:

- A source of hints and tips on solving known problems
- A list of vendors with problems that are affecting the credibility and/or usefulness of the COUNTER reports
- A collection point for suggestions for new COUNTER usage reports and metrics

Supervisory Board

The Usus Supervisory Board will ensure that the website is editorially independent and will serve the needs of the community. Chaired by Anne Osterman, Deputy Director of VIVA (the Virtual Library of Virginia), the members of the Supervisory Board are:

Anne Osterman, VIVA, USA (Chair)
Simon Bevan, Cranfield University, UK
Melissa Blaney, ACS Publications, USA
Anna Creech, University of Richmond, USA
Lorraine Estelle, JISC, UK
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Travel Award

Thank you to Project COUNTER for the financial support needed to get Usus off the ground. COUNTER has also offered to provide a travel award worth £1,000/$1,500 to a librarian who contributes the best opinion piece for the News & Opinions section of the Usus site. The award can be used to travel to the Charleston Conference, UKSG Conference, or Electronic Resources & Libraries Conference. Please send your submissions of 1,000 words or less to usus.stats@gmail.com by December 31, 2014.

For more information, please contact Usus at: usus.stats@gmail.com

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