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First-hour infection recognition and 24-hour sepsis classification in emergency resuscitation-room encounters: a retrospective cohort study

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Abstract

Background

During the first hour of emergency resuscitation, clinicians must decide whether critical illness is infectious and whether an infected patient has, or develops, infection-associated organ dysfunction. The first decision may be difficult in older or severely ill patients with atypical presentations; the second determines the urgency of monitoring and resuscitation. We assessed how first-hour information supported these linked clinical questions.

Methods

This single-centre retrospective cohort included 1,195 non-consecutive adult resuscitation-room encounters: 240 non-infectious critical illnesses, 218 infections without sepsis and 737 cases of sepsis. We compared age, sex and vital signs; their combination with complete blood-count indices; and the further addition of lactate and procalcitonin. Analyses developed in 2023–2024 were applied without refitting to a post hoc 2025 sample. Question 1 distinguished final physician-adjudicated infection from non-infectious illness; Question 2 classified 24-hour Sepsis-3 status among adjudicated infections.

Results

In the 2025 sample, 139 of 174 encounters involved infection. Vital signs and complete blood-count indices distinguished infection from non-infectious illness with an area under the receiver operating characteristic curve (AUROC) of 0.808 (95% confidence interval [CI], 0.733–0.877). Adding lactate and procalcitonin increased the AUROC to 0.868 (0.813–0.921; change, 0.060 [0.029–0.097]). At a high-sensitivity threshold, 127 of 139 infections were identified and 23 of 35 non-infectious encounters were also flagged. Among 139 infected encounters, 110 met the 24-hour sepsis definition. Clinical and complete blood-count information identified 103 cases and showed moderate discrimination (AUROC, 0.780 [0.682–0.865]). Adding lactate and procalcitonin did not improve discrimination (AUROC, 0.766 [0.665–0.856]; change, − 0.014 [− 0.090 to 0.060]).

Conclusions

In this selected emergency-resuscitation cohort, first-hour vital signs and complete blood-count indices discriminated final infection classification from non-infectious critical illness, and lactate plus procalcitonin improved that discrimination. Among infected patients, first-hour clinical and complete blood-count information also discriminated 24-hour sepsis status, but lactate and procalcitonin added no clear value. These findings support structured early assessment and reassessment; they do not establish a stand-alone treatment rule.

Background

The first hour in an emergency department resuscitation room involves two related but different diagnostic decisions. Clinicians must first decide whether a critically ill patient is likely to have an infection, because that judgement determines the need for microbiological sampling, source investigation and timely consideration of antimicrobial treatment. Once infection is suspected, the next question is whether infection-related organ dysfunction indicates sepsis and therefore requires more intensive monitoring, resuscitation and escalation of care [1, 2]. Current sepsis guidance similarly distinguishes patients who need immediate treatment from those who require rapid assessment of both infectious and non-infectious causes [3].

The first decision is not always straightforward. Fever, cough, dysuria or diarrhoea may make infection apparent, but older, immunocompromised or severely ill patients may present with hypothermia, altered consciousness, hypotension or non-specific deterioration. These features also occur in non-infectious critical illness. Prospective emergency-department data show that both missed and overcalled sepsis persist during the first hour and that missed recognition can delay antimicrobials [4]. Even among patients who meet operational Sepsis-3 criteria, the presumed infection diagnosis or source may differ from the final adjudicated diagnosis [5]. Early sepsis recognition therefore begins with a credible assessment of whether infection is present.

Routine vital signs and complete blood-count (CBC) indices are rapidly available in most resuscitation rooms. Procalcitonin (PCT) can increase or decrease the probability of bacterial infection, whereas lactate reflects physiological stress and impaired perfusion across infectious and non-infectious conditions. Their clinical roles are therefore not interchangeable. Previous emergency studies have evaluated biomarkers for infection, sepsis or deterioration, often as a single target or in differently selected populations [6–10]. A marker that helps distinguish infection from non-infectious illness may not necessarily distinguish sepsis from infection without organ dysfunction.

We therefore examined two linked questions using information available during the first hour. Question 1 asked whether a resuscitation-room encounter was ultimately attributable to infection. Question 2 asked, among infected patients, whether the patient met Sepsis-3 criteria within 24 hours. For each question, we evaluated the discrimination provided by routine clinical information and CBC results and the additional contribution of lactate and PCT.

Methods

Study design and setting

We conducted a retrospective, single-centre cohort study in the emergency department resuscitation room of Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China. This area receives patients who require immediate high-acuity assessment and treatment. Source records covered emergency visits from 7 April 2023 to 5 May 2025, and index samples were collected from 9 April 2023

to 7 May 2025. Reporting was guided by the STROBE statement and, for the analytical procedures, relevant TRIPOD + AI recommendations [11, 12].

Participants and cohort assembly

Eligible encounters involved adults aged 18 years or older whose residual routine CBC sample had been retained for a separate blood-smear imaging project. No blood-smear image or morphology variable was used in the present study. Inclusion also required age, sex, first recorded vital signs, CBC results and sufficient information to determine the final clinical group. A calculable Sequential Organ Failure Assessment (SOFA) score was required for encounters classified as infection or sepsis. Sampling was non-consecutive. Some patients were not enrolled because they were transferred, declined blood sampling or did not have the required residual sample or clinical information. The total source denominator and a complete breakdown of non-enrolment could not be reconstructed.

Only the first eligible sample after entry to the resuscitation room was analysed for each encounter. Exact duplicate records were removed. Clinically distinct visits by the same patient were retained, with repeated encounters kept together during model development. During the final reference-standard audit, one encounter was excluded because SOFA could not be reconstructed from the available component data. The final dataset contained 1,195 encounters.

First-hour clinical and laboratory information

Age, sex, medical history, vital signs and laboratory results were extracted retrospectively from the electronic medical-record and laboratory information systems. Temperature, systolic blood pressure, pulse, respiratory rate and peripheral oxygen saturation were the first values recorded after entry to the resuscitation room. CBC, arterial lactate and PCT were the first results obtained within one hour. According to source abstraction, these measurements preceded antibiotics, intravenous fluid resuscitation and vasopressor treatment, although the available records did not permit a detailed audit of when each result became visible to the treating clinician.

CBC measurements were performed using the Sysmex XN-9000 haematology system. PCT was measured on the bioMérieux VIDAS platform with the VIDAS B·R·A·H·M·S PCT assay. Arterial lactate was measured using the Radiometer ABL90 FLEX blood-gas analyser. Equipment, reagents and reference ranges did not change during the study period.

Rule-based cleaning corrected clinically unambiguous formatting errors, including misplaced decimal points, and removed exact duplicates. Records requiring an inferred correction or showing an internal CBC inconsistency were flagged for audit.

Clinical review and reference classification

Two physicians—an associate chief physician and an attending physician—independently reviewed the complete record for each encounter. Disagreements were adjudicated by a third physician, who was a chief physician. Review was retrospective and non-blinded. Reviewers could see the clinical laboratory results, including CBC, lactate and PCT, but did not see model outputs. Infection was determined after considering the clinical presentation, imaging, microbiological findings and treatment course; the discharge diagnosis, infection assessment and SOFA score formed the primary basis for final grouping.

Sepsis was defined according to Sepsis-3 as infection accompanied by an infection-related increase of at least two SOFA points [1]. Baseline SOFA was assumed to be zero. Reviewers recalculated SOFA from the original clinical and laboratory data across all six organ-system domains and used the worst score during the first 24 hours. Infection without sepsis was defined as definite or strongly suspected infection with a SOFA increase below two points. The non-infectious critical-illness group comprised other acute or critical conditions for which the final clinical assessment excluded infection. Before analysis was finalised, an internal consistency audit identified five encounters whose exported group or SOFA summary conflicted with the prespecified rule. Repeat record review reclassified two encounters from sepsis to infection without sepsis and one from sepsis to non-infectious illness, corrected one SOFA summary from 1 to the documented score of 2, and excluded one encounter because SOFA could not be reconstructed. All five encounters occurred before 2025.

Two clinical research questions

Question 1 and Question 2 refer to clinical research questions, not questionnaire items. No questionnaires or survey instruments were used; data were retrospectively extracted from electronic medical records and laboratory systems.

Question 1 included all encounters and asked whether the final physician-adjudicated diagnosis was infection—including both infection without sepsis and sepsis—rather than non-infectious critical illness. This corresponded to the early need to pursue an infectious source, obtain appropriate microbiological samples and reassess the indication for antimicrobials.

Question 2 included only encounters with adjudicated infection and asked whether the patient met the study definition of sepsis within the first 24 hours rather than infection without sepsis. This corresponded to the need to recognise infection-related organ dysfunction and prioritise monitoring and resuscitation. Because the reference classification used the worst SOFA score during the first 24 hours, Question 2 combined patients who met the definition on arrival and those who met it later during that period; it therefore evaluated classification of 24-hour sepsis status from first-hour information, not the timing of sepsis onset.

The two questions were analysed separately. Question 2 used the adjudicated infection group rather than the output of Question 1; the study therefore evaluated a two-stage clinical framework, not an implemented serial algorithm.

Statistical analysis

Continuous variables are reported as median and interquartile range (IQR), and categorical variables as number and percentage. Group comparisons used the Kruskal–Wallis test for continuous variables and chi-square or Fisher–Freeman–Halton tests for categorical variables. Full comparison statistics are provided in the supplementary material; the main table focuses on clinical characteristics.

For each question, first-hour information was examined at three successive levels. The clinical information set contained age, sex, temperature, systolic blood pressure, pulse, respiratory rate and peripheral oxygen saturation. The clinical-plus-CBC set additionally contained white blood cell count, neutrophil percentage, haemoglobin and the neutrophil-to-lymphocyte ratio. The full first-hour set further added arterial lactate and PCT as a combined block. Platelet count, which contributes to SOFA, was examined only in sensitivity analysis. White blood cell count, neutrophil-to-lymphocyte ratio, lactate and PCT were transformed using $\log(x + 1)$.

The contribution of each information level was quantified using L2-penalised logistic regression. Missing predictors were median-imputed and continuous predictors standardised using development-data parameters. The regularisation parameter was selected by stratified, patient-group-blocked five-fold cross-validation in 2023–2024. Patient groups appearing again in 2025 were removed from development. The fitted analysis was then applied without coefficient refitting to the 2025 sample. The calendar split was selected before performance was examined, but the two-stage framing and final information sets were settled after preliminary inspection that included 2025 results; the 2025 analysis is therefore described as a post hoc temporal evaluation rather than an independent validation.

Discrimination was summarised by the area under the receiver operating characteristic curve (AUROC). The main comparison for each question was the change after adding lactate and PCT to clinical and CBC information. Ninety-five per cent confidence intervals (CIs) for AUROC and paired AUROC changes were obtained from 2,500 stratified patient-group bootstrap samples. Thresholds were selected from out-of-fold development predictions to achieve approximately 90% sensitivity and then kept unchanged in the 2025 sample. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated with Wilson 95% CIs. Area under the precision–recall curve, Brier score and calibration were treated as secondary descriptive analyses.

Sensitivity analyses examined encounters with both lactate and PCT measured, restricted Question 1 to infection without sepsis versus non-infectious illness, excluded chronic kidney failure or cirrhosis from Question 2, and added platelet count. Biomarker missingness was described by final clinical group, and SOFA status was cross-tabulated against the final classification. Analyses used Python 3.12.13, NumPy 2.5.2, pandas 3.0.5, SciPy 1.16.1, statsmodels 0.14.6 and scikit-learn 1.7.1. The random seed was 20260829.

Use of generative artificial intelligence tools

OpenAI ChatGPT and Codex were used to assist with English-language editing, manuscript organisation, figure refinement and code-assisted consistency checks. They were not used to determine eligibility, assign clinical classifications or generate study data. All outputs were critically reviewed and verified by the authors, who take full responsibility for the accuracy and integrity of the manuscript. No generative-image model was used to create or alter scientific data or results.

Results

Clinical characteristics of patients with infection, sepsis and non-infectious critical illness

The study included 1,195 first-sample encounters: 362 from 2023, 659 from 2024 and 174 from 2025 (Fig. 1). Final clinical review classified 240 encounters as non-infectious critical illness, 218 as infection without sepsis and 737 as sepsis. Thus, 955 encounters were included in Question 2.

After earlier encounters from patient groups represented in 2025 were removed, the development set contained 1,006 encounters for Question 1, including 802 infections. For Question 2, it contained 804 infected encounters, of which 617 met the sepsis definition. The 2025 temporal sample contained 174 encounters (139 infections) for Question 1 and 139 infected encounters (110 sepsis) for Question 2.

The median age was 65 years (IQR, 52–76), and 715 encounters (59.8%) involved male patients (Table 1). Patients with sepsis were older and had higher pulse and respiratory rates than patients with non-infectious critical illness. Median PCT concentrations increased across the three groups from 0.025 ng/mL in non-infectious illness to 0.190 ng/mL in infection without sepsis and 1.230 ng/mL in sepsis. Median neutrophil-to-lymphocyte ratios were 3.88, 6.71 and 8.58, respectively. Lactate differed less markedly, with corresponding medians of 1.21, 1.20 and 1.40 mmol/L. Median SOFA was 0 in both non-sepsis groups and 4 in the sepsis group, as expected from the reference definition.

Table 1
Clinical characteristics by final diagnostic group

Characteristic	Overall	Non-infectious critical illness	Infection without sepsis	Sepsis	Missing, %
Number of encounters	1,195	240	218	737	—
Age, years	65.0 (52.0–76.0)	59.0 (44.0–72.0)	65.0 (46.2–75.8)	67.0 (55.0–77.0)	0.0
Temperature, °C	36.6 (36.5–37.0)	36.6 (36.5–36.8)	36.7 (36.5–37.3)	36.7 (36.5–37.2)	0.2
Systolic blood pressure, mmHg	125.0 (110.0–142.0)	127.0 (112.0–144.0)	129.0 (115.0–141.0)	123.0 (108.0–140.0)	0.1
Pulse, beats/min	87.0 (77.0–101.0)	82.0 (72.0–93.5)	88.0 (78.0–100.0)	89.0 (78.0–105.0)	0.3
Respiratory rate, breaths/min	20.0 (17.0–23.0)	19.0 (16.0–20.0)	20.0 (17.0–22.2)	20.0 (18.0–24.0)	1.4
Peripheral oxygen saturation, %	98.0 (97.0–100.0)	98.0 (97.0–100.0)	98.0 (97.0–99.0)	98.0 (97.0–100.0)	1.5
White blood cells, $\times 10^9$/L	9.00 (6.26–12.76)	7.92 (6.14–10.43)	9.27 (6.10–12.54)	9.60 (6.38–13.75)	0.1
Neutrophils, %	79.3 (69.2–87.3)	72.0 (61.1–80.0)	78.7 (68.2–85.4)	82.1 (73.0–89.0)	0.3
Haemoglobin, g/L	103.0 (80.2–123.0)	114.0 (85.0–131.0)	107.0 (93.5–122.0)	98.0 (76.0–121.0)	0.1
Neutrophil-to-lymphocyte ratio	6.88 (3.56–13.88)	3.88 (2.31–6.95)	6.71 (3.57–11.52)	8.58 (4.55–17.24)	0.3
Lactate, mmol/L	1.30 (1.00–2.00)	1.21 (0.90–1.80)	1.20 (0.90–1.65)	1.40 (1.00–2.10)	16.8
Procalcitonin, ng/mL	0.440 (0.070–4.660)	0.025 (0.025–0.207)	0.190 (0.025–1.230)	1.230 (0.195–12.340)	7.9
SOFA score	2.0 (1.0–4.0)	0.0 (0.0–1.0)	0.0 (0.0–1.0)	4.0 (2.0–6.0)	0.1
Male sex	715 (59.8%)	145 (60.4%)	95 (43.6%)	475 (64.5%)	0.0

Note. Values are median (IQR) or n (%). Percentages for categorical variables use non-missing observations as the denominator. IQR, interquartile range; SOFA, Sequential Organ Failure Assessment.

Characteristic	Overall	Non-infectious critical illness	Infection without sepsis	Sepsis	Missing, %
Hypertension	502 (42.3%)	88 (37.0%)	83 (38.2%)	331 (45.3%)	0.8
Diabetes mellitus	304 (25.6%)	48 (20.2%)	61 (28.1%)	195 (26.7%)	0.8
Cardiovascular disease	240 (20.2%)	33 (13.9%)	51 (23.5%)	156 (21.3%)	0.7
Chronic kidney failure	85 (7.2%)	1 (0.4%)	4 (1.8%)	80 (10.9%)	0.6
Cirrhosis	53 (4.5%)	3 (1.3%)	2 (0.9%)	48 (6.6%)	0.8
Malignancy	296 (25.0%)	42 (17.6%)	52 (24.0%)	202 (27.7%)	0.8

Note. Values are median (IQR) or n (%). Percentages for categorical variables use non-missing observations as the denominator. IQR, interquartile range; SOFA, Sequential Organ Failure Assessment.

First-hour information and infection classification

In the 2025 sample, age, sex and first vital signs alone provided modest separation of infection from non-infectious critical illness (AUROC, 0.706; 95% CI, 0.626–0.787). Adding CBC indices increased the AUROC to 0.808 (0.733–0.877). Adding lactate and PCT further increased the AUROC to 0.868 (0.813–0.921; Table 2; Fig. 2). The paired increase over clinical and CBC information was 0.060 (95% CI, 0.029–0.097).

Thus, routinely available first-hour information discriminated the final physician-adjudicated infection classification, and clinician-ordered lactate and PCT results added information in this cohort.

First-hour information and 24-hour sepsis classification

Among the 139 infected encounters in the 2025 sample, 110 met the 24-hour sepsis definition. Age, sex and vital signs alone yielded an AUROC of 0.709 (95% CI, 0.603–0.805). Adding CBC indices increased the AUROC to 0.780 (0.682–0.865), indicating moderate discrimination of 24-hour sepsis status from routine first-hour information.

The full first-hour information set, including lactate and PCT, had an AUROC of 0.766 (95% CI, 0.665–0.856). The paired change from adding these two biomarkers was − 0.014 (95% CI, − 0.090 to 0.060; Fig. 2). Thus, the combined clinical and laboratory assessment helped identify patients who met the 24-hour sepsis definition, but the observed separation was carried mainly by clinical and CBC information; lactate and PCT did not add clear discrimination for this second question.

Table 2
First-hour performance in the 2025 temporal sample

Clinical question	Information set	AUROC (95% CI)	TP/FP/TN/FN	Sensitivity (95% CI)	Specificity (95% CI)
Infection vs non-infectious critical illness	Age, sex and vital signs	0.706 (0.626–0.787)	126/30/5/13	0.906 (0.847–0.945)	0.143 (0.063–0.294)
Infection vs non-infectious critical illness	Clinical information + CBC	0.808 (0.733–0.877)	125/25/10/14	0.899 (0.838–0.939)	0.286 (0.163–0.451)
Infection vs non-infectious critical illness	Clinical information + CBC + lactate/PCT	0.868 (0.813–0.921)	127/23/12/12	0.914 (0.855–0.950)	0.343 (0.208–0.508)
Sepsis vs infection without sepsis	Age, sex and vital signs	0.709 (0.603–0.805)	103/26/3/7	0.936 (0.874–0.969)	0.103 (0.036–0.264)
Sepsis vs infection without sepsis	Clinical information + CBC	0.780 (0.682–0.865)	103/21/8/7	0.936 (0.874–0.969)	0.276 (0.147–0.457)
Sepsis vs infection without sepsis	Clinical information + CBC + lactate/PCT	0.766 (0.665–0.856)	104/19/10/6	0.945 (0.886–0.975)	0.345 (0.199–0.527)

Note. Question 1 included 174 encounters, of which 139 involved infection. Question 2 included 139 infected encounters, of which 110 met the 24-hour sepsis definition. Thresholds were fixed from out-of-fold development predictions to target approximately 90% sensitivity. AUROC, area under the receiver operating characteristic curve; CBC, complete blood count; CI, confidence interval; FN, false negative; FP, false positive; PCT, procalcitonin; TN, true negative; TP, true positive.

Bedside performance and sensitivity analyses

At the prespecified high-sensitivity threshold, the full first-hour information set identified 127 of 139 infected encounters. It also flagged 23 of 35 non-infectious encounters, giving a sensitivity of 91.4% (95% CI, 85.5–95.0%) and a specificity of 34.3% (20.8–50.8%). This operating point would therefore support further infectious-disease assessment for most infected patients, but it would also prompt reassessment in approximately two thirds of patients whose final illness was non-infectious.

For Question 2, clinical and CBC information identified 103 of 110 sepsis encounters, with a sensitivity of 93.6% (87.4–96.9%) and specificity of 27.6% (14.7–45.7%). The full information set identified 104 of 110 sepsis encounters, with a sensitivity of 94.5% (88.6–97.5%) and specificity of 34.5% (19.9–52.7%). Because the two information sets used separately selected thresholds, these figures describe potential bedside trade-offs and do not show that one threshold strategy is superior.

Lactate was missing in 16.8% of encounters and PCT in 7.9%. Testing was least frequent in the non-infectious group: lactate was missing in 42.1% of non-infectious encounters, 23.4% of infections without sepsis and 6.6% of sepsis encounters; the corresponding proportions for PCT were 22.5%, 4.6% and 4.1% (Fig. 3). Among the 132 encounters in the 2025 sample with both biomarkers measured, the Question 1 AUROC increased from 0.772 to 0.851 (change, 0.079; 95% CI, 0.036–0.131). Among 115 infected encounters with both measured, the Question 2 AUROC changed from 0.822 to 0.829 (change, 0.007; 95% CI, − 0.058 to 0.072).

In the harder Question 1 comparison restricted to infection without sepsis versus non-infectious illness, AUROC was 0.677 with clinical and CBC information and 0.729 after adding lactate and PCT (change, 0.052; 95% CI, 0.000–0.119). Excluding chronic kidney failure or cirrhosis from Question 2 yielded similar AUROCs with and without lactate/PCT (0.748 and 0.746). Adding platelet count increased the Question 2 AUROC to 0.808, but this was not treated as independent evidence because platelet count contributes directly to SOFA. After the reference-standard audit, all 737 sepsis encounters had SOFA of at least 2, all 218 infection-without-sepsis encounters had SOFA below 2, and 239 of 240 non-infectious encounters had SOFA below 2; SOFA was unavailable for one non-infectious encounter.

Discussion

In this high-acuity emergency cohort, first-hour vital signs and CBC results discriminated final infection classification from non-infectious critical illness, and lactate plus PCT improved that discrimination. Among patients with infection, the same first-hour information showed moderate discrimination of 24-hour sepsis status, although lactate and PCT did not add to clinical and CBC data. The clinical logic is sequential—first clarify whether critical illness is likely infectious, then assess organ dysfunction—but the two questions were analysed separately rather than as a deployed bedside algorithm.

The first question addresses a common problem in the resuscitation room. Many infections are apparent from the history and examination, but typical symptoms may be absent in older, immunocompromised or severely ill patients. Conversely, shock, altered consciousness, hypothermia and inflammatory changes may arise from non-infectious disease. Pandey and colleagues showed that both underdiagnosis and overdiagnosis occurred during the first hour of care and that missed recognition delayed antimicrobials [4]. Hooper and colleagues likewise found clinically important disagreement between initial and final infection diagnoses among patients meeting Sepsis-3 criteria [5]. Our findings add a practical sequence to this evidence: vital signs and CBC provide a broadly available first assessment, while lactate and PCT can refine the probability of infection when they are obtained. This is consistent with prospective studies in which biomarkers added information to the clinician's initial infection judgement [6, 7].

The second question is different. PCT mainly informs the probability and burden of infection, whereas lactate reflects tissue stress and perfusion in many critical illnesses. Neither directly replaces assessment of organ dysfunction. In our cohort, clinical and CBC information achieved moderate separation of 24-hour sepsis status from infection without sepsis, but adding lactate and PCT did not

improve the observed AUROC. This differs from studies in which rapid host-response or biomarker assays improved sepsis classification in prospectively enrolled patients [8, 9]. The populations and targets are not the same: our analysis was restricted to patients ultimately judged to have infection and classified 24-hour status using the worst SOFA score in that period. The result is clinically coherent—information that helps establish infection need not add the same value once infection is already accepted and the remaining question is organ dysfunction.

The high-sensitivity results clarify how these findings might be used. Question 1 detected 127 of 139 infections but would also have prompted further assessment in 23 of 35 patients with non-infectious illness. Question 2 captured most sepsis cases but showed low specificity. In a resuscitation room, this trade-off may be acceptable for a prompt to review the patient, repeat examination, search for a source and reassess organ function; it is not sufficient for an automatic antibiotic or escalation decision. Trials of electronic sepsis alerts have shown that clinical benefit depends on when a signal appears, whether clinicians act on it and what action follows [13, 14]. The present findings are therefore most relevant to structured assessment and reassessment within the first hour.

The study has several strengths: it examined both clinical questions in the same high-acuity setting, used complete-record physician review, kept repeated encounters separated between development and temporal assessment, and reported the absolute numbers of missed and additionally flagged patients. Its limitations define where the results apply. The cohort was single-centre, non-consecutive and selected through availability of residual CBC samples, and a complete source denominator was unavailable. Most infected encounters had sepsis; performance for the more difficult comparison of infection without sepsis versus non-infectious illness was lower and imprecise. Lactate and PCT were ordered at clinicians' discretion, so their apparent contribution includes the local decision to test. The clinical information set contained demographics and vital signs rather than symptoms, examination findings or clinicians' pretest probability. Reference review was retrospective and non-blinded, and the same laboratory results could have influenced treatment, discharge diagnosis and adjudication; the estimates therefore describe discrimination against the final local clinical classification and may include incorporation and review bias. Baseline SOFA was assumed to be zero, and the 24-hour endpoint did not distinguish sepsis present on arrival from sepsis reached later. Finally, the small 2025 sample was examined while the final analytical framing was developed. Confirmation requires a consecutive, prospectively specified cohort with blinded adjudication and uniform biomarker sampling.

A prospective study should now enrol consecutive resuscitation-room patients, obtain candidate biomarkers using a uniform protocol and record the exact times of sampling, result availability, infection suspicion, antimicrobial treatment and onset of organ dysfunction. The two questions should then be applied in sequence with prespecified thresholds, blinded outcome adjudication and measurement of clinical actions as well as diagnostic performance. Such a design would determine whether the two-stage framework shortens time to appropriate treatment while avoiding unnecessary testing and antimicrobial exposure.

Conclusions

In this selected resuscitation-room cohort, first-hour vital signs and CBC indices discriminated final infection classification from non-infectious critical illness, and lactate plus PCT improved that discrimination. Among infected patients, first-hour clinical and CBC information also discriminated 24-hour sepsis status, but lactate and PCT added no clear value. The results can inform structured early assessment and reassessment but do not establish a stand-alone treatment rule.

Abbreviations

AUPRC
area under the precision–recall curve
AUROC
area under the receiver operating characteristic curve
CBC
complete blood count
CI
confidence interval
IQR
interquartile range
NLR
neutrophil-to-lymphocyte ratio
NPV
negative predictive value
PCT
procalcitonin
PPV
positive predictive value
SOFA
Sequential Organ Failure Assessment.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. The Medical Ethics Committee of Sun Yat-sen Memorial Hospital, Sun Yat-sen University approved this retrospective study and waived the requirement for informed consent (approval no. SYSKY-2026-363-01).

Consent for publication

Not applicable.

Availability of data and materials

The patient-level datasets analysed during this study are not publicly available because they contain sensitive clinical information and unrestricted disclosure could compromise participant privacy. Ethics approval and the waiver of informed consent covered the retrospective research protocol and do not themselves authorise unrestricted public disclosure of patient-level hospital records. Any proposed release would require institutional data-release authorisation and ethics review of the sharing arrangements, including assessment of anonymisation and any additional consent requirements. Requests for controlled access may be directed to the corresponding author, Fengqing Song (songfq@mail.sysu.edu.cn), but access is subject to these approvals and cannot be guaranteed. Supplementary tables are provided in Additional file 1. Machine-readable aggregate source data underlying the reported tables and figures are provided in Additional file 2; these files do not contain patient-level records. Analysis code is available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' contributions

P.F.W., H.L., X.W. and F.S. conceived the study. P.F.W., H.L., X.W., T.Y. and F.S. developed the methodology. P.F.W., S.Y., X.W., H.L. and P.W. performed the investigation and curated the data. P.F.W. and S.Y. independently reviewed the clinical records and determined the study classifications, with disagreements adjudicated by F.S. P.F.W., H.L. and X.W. performed the statistical analysis and prepared the figures and tables. P.F.W., S.Y., H.L. and X.W. drafted the manuscript. L.L., T.Y. and F.S. supervised the study and provided resources. P.F.W. and F.S. coordinated the project. All authors reviewed and revised the manuscript, approved the final version and agreed to be accountable for the work.

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Not applicable.

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Figures

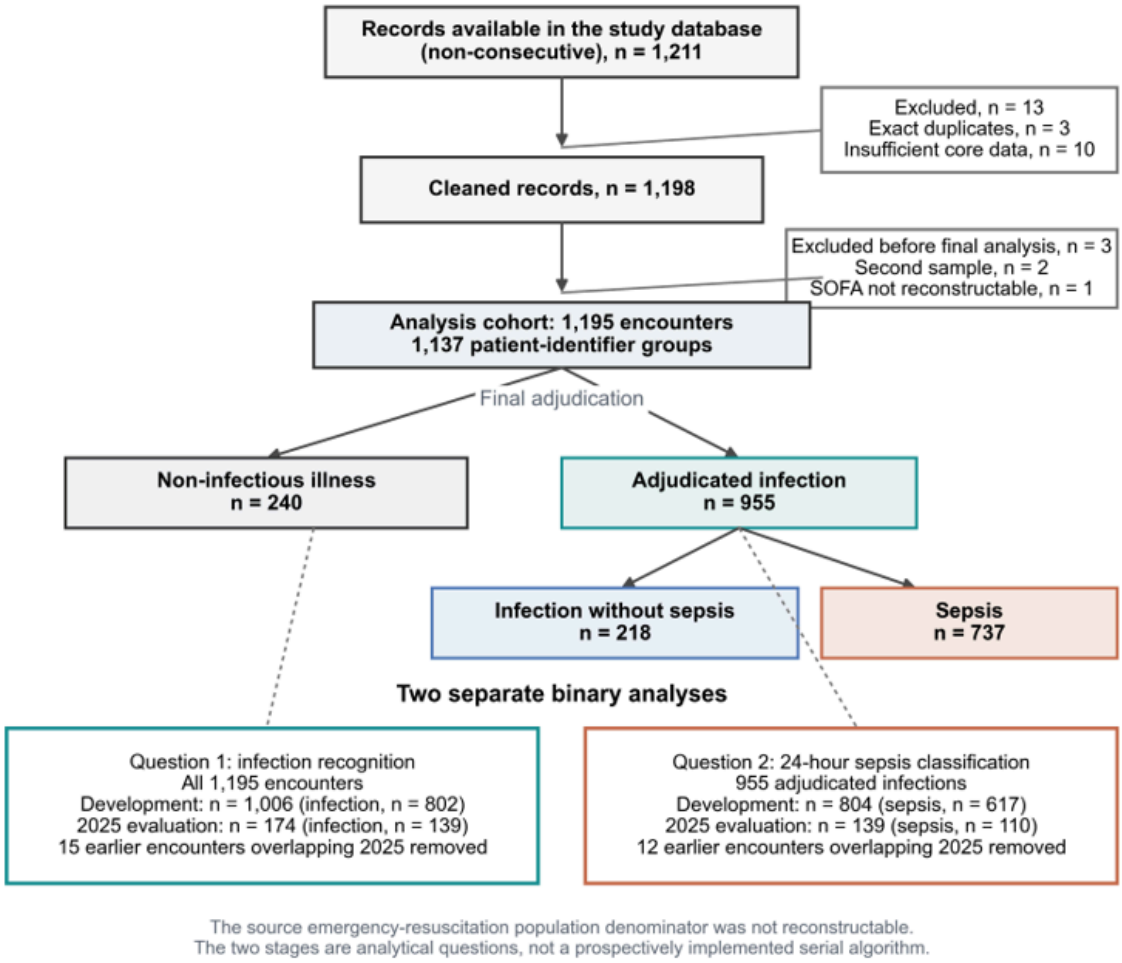


Figure 1

Cohort assembly and linked clinical questions. The study included 1,195 non-consecutive emergency-resuscitation-room encounters after one encounter with non-reconstructable SOFA was excluded during the final reference-standard audit. Question 1 examined infection, including sepsis, versus non-infectious

critical illness. Question 2 examined 24-hour sepsis status versus infection without sepsis among encounters with adjudicated infection. The questions were analysed separately; Question 2 did not use the predicted output from Question 1. Earlier encounters from patient groups represented in 2025 were excluded from development.

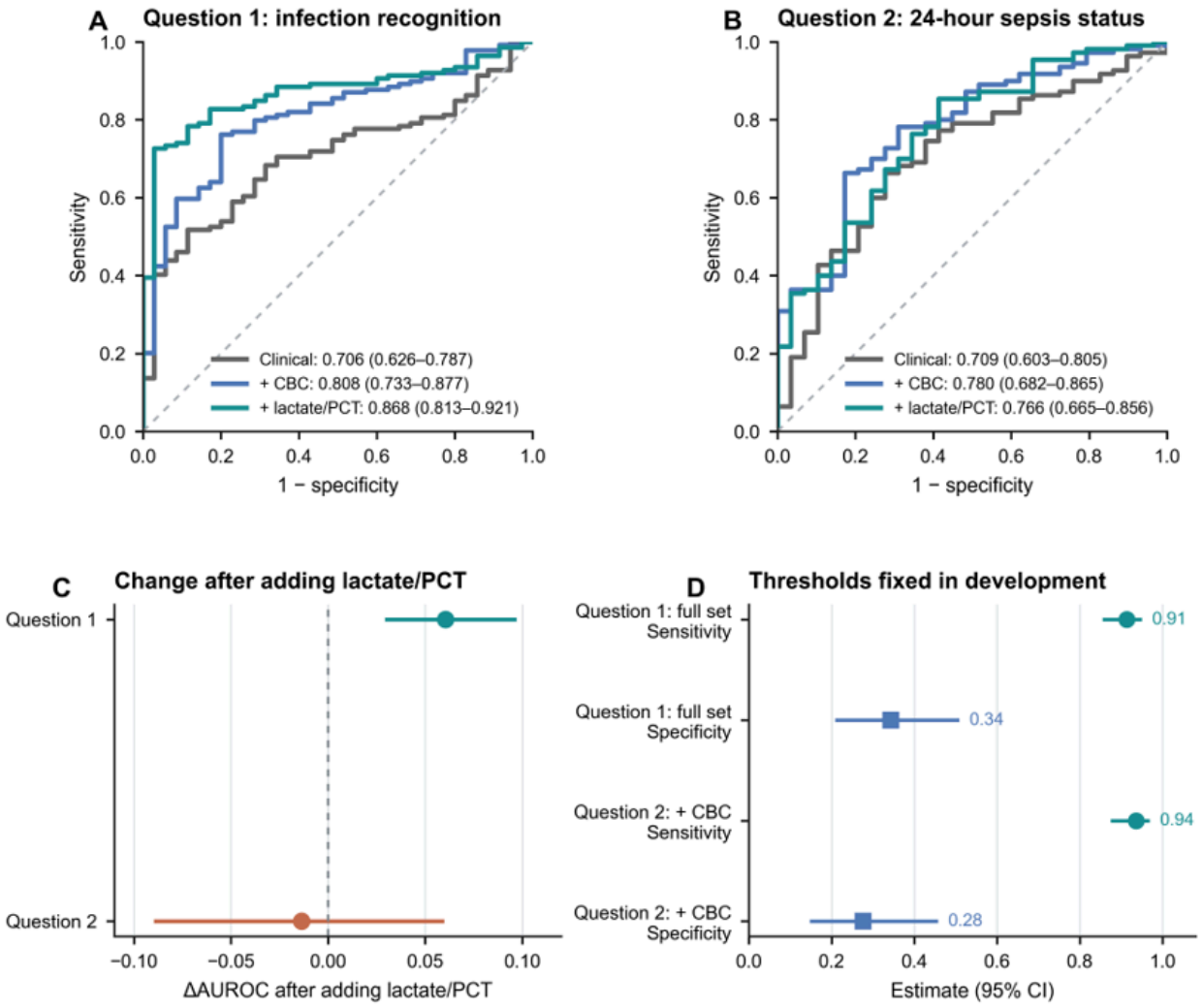


Figure 2

First-hour discrimination and high-sensitivity performance. Panels A and B show receiver-operating-characteristic curves for clinical information, clinical plus complete blood-count information and the addition of lactate and procalcitonin in the post hoc 2025 temporal sample. Panel C shows the paired AUROC change after adding lactate and procalcitonin. Panel D shows sensitivity and specificity at thresholds selected in development to target approximately 90% sensitivity: the full set for Question 1 and clinical plus CBC information for Question 2, the question-specific sets supported by the incremental analyses. AUROC, area under the receiver operating characteristic curve; CBC, complete blood count; PCT, procalcitonin.

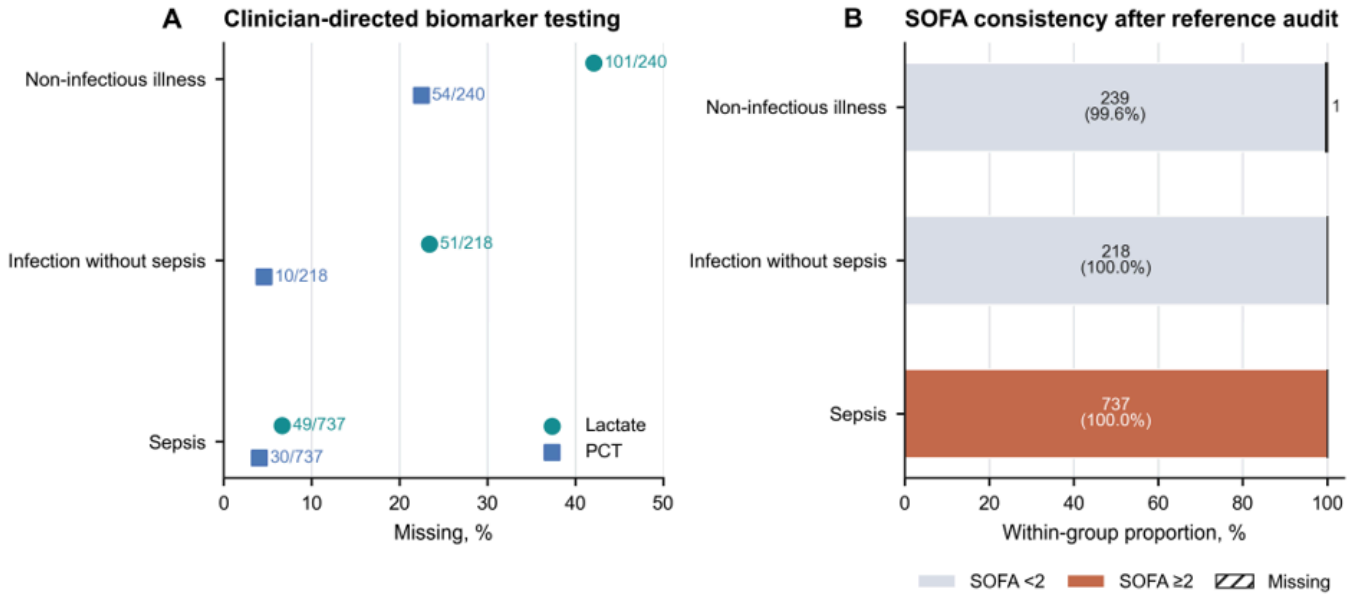


Figure 3

Selective biomarker measurement and reference-standard audit. Panel A shows missing lactate and procalcitonin measurements by final clinical group; labels are missing/total encounters. Panel B shows SOFA status within each group after the final reference-standard audit. All sepsis encounters had SOFA of at least 2; SOFA was unavailable for one non-infectious encounter. PCT, procalcitonin; SOFA, Sequential Organ Failure Assessment.

Supplementary Files

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

- 02Additionalfile1SupplementaryInformation.docx
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