

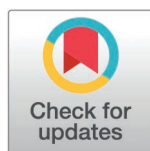
RESEARCH ARTICLE

Predictive value of SOFA, PCT, Lactate, qSOFA and their combinations for mortality in patients with sepsis: A systematic review and meta-analysis

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Abstract

Background

Sepsis is a leading cause of death, necessitating early prediction of mortality risk.

Objective

To systematically review the predictive efficacy of the Sequential Organ Failure Assessment (SOFA), procalcitonin (PCT), lactate, quick Sequential Organ Failure Assessment (qSOFA), and lactate-adjusted qSOFA (LqSOFA) for the risk of death in patients with sepsis.

Methods

According to PRISMA-DTA guidelines, PubMed, Embase, the Cochrane Library, and CNKI were searched (up to March 2025), and 29 studies were included (n=41,469). A bivariate random-effects model was used to pool the sensitivity, specificity, diagnostic odds ratio, and area under the receiver operating characteristic curve (AUROC). The Δ AUROC was compared using a random-effects model based on a paired-data design. Heterogeneity was evaluated by I^2 (>50%) and Cochrane's Q test.

Results

SOFA demonstrated superior predictive efficacy (AUROC=0.819, 95% CI: 0.783–0.850; sensitivity=0.77, 95% CI: 0.71–0.82; specificity=0.73, 95% CI: 0.67–0.79), significantly outperforming PCT (Δ AUROC=0.10, 95% CI: 0.04–0.16), lactate (Δ AUROC=0.07, 95% CI: 0.03–0.11), and qSOFA (Δ AUROC=0.08, 95% CI: 0.05–0.11). LqSOFA (AUROC=0.823, 95% CI: 0.787–0.854) demonstrated efficacy comparable to SOFA (Δ AUROC=0.02, 95% CI: –0.02–0.06) and significantly superior to qSOFA (Δ AUROC=0.06, 95% CI: 0.04–0.08), with a sensitivity of 0.46 (0.24–0.69).

OPEN ACCESS

Citation: Lu J, Dong Z, Ye L, Gao Y, Zheng Z (2025) Predictive value of SOFA, PCT, Lactate, qSOFA and their combinations for mortality in patients with sepsis: A systematic review and meta-analysis. PLoS One 20(9): e0332525. <https://doi.org/10.1371/journal.pone.0332525>

Editor: Inge Roggen, Universitair Kinderziekenhuis Koningin Fabiola: Hopital Universitaire des Enfants Reine Fabiola, BELGIUM

Received: April 17, 2025

Accepted: September 1, 2025

Published: September 17, 2025

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: <https://doi.org/10.1371/journal.pone.0332525>

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Data availability statement: All analytical datasets supporting the conclusions of this article are publicly available. Specifically: All analytical datasets supporting the conclusions of this article are publicly available from the Figshare repository. They can be accessed directly via the following Digital Object Identifier (DOI): [10.6084/m9.figshare.29881934](https://doi.org/10.6084/m9.figshare.29881934). No access restrictions apply to these datasets.

Funding: This research was funded by the Science and Technology Program of Zhejiang Provincial Health Commission, grant number 2021KY1016.

Competing interests: The authors have declared that no competing interests exist.

and specificity of 0.88 (0.80–0.93). Subgroup analyses revealed sustained high performance in both emergency department (ED) settings (AUROC = 0.82, 95% CI: 0.79–0.85) and low- and middle-income countries (LMICs) (AUROC = 0.81, 95% CI: 0.77–0.84).

Conclusion

SOFA remains the optimal predictor of sepsis mortality risk. qSOFA demonstrates suboptimal overall predictive ability, whereas LqSOFA achieves comparable accuracy to SOFA by combining the advantages of lactate and qSOFA. Its high specificity may be valuable for rapid risk exclusion in resource-limited settings (ED/LMICs). Future studies should validate LqSOFA across diverse clinical settings and underrepresented LMIC regions and should integrate dynamic lactate clearance metrics.

1. Introduction

Sepsis, an organ dysfunction syndrome caused by a dysregulated host immune response triggered by infection, is one of the leading causes of death among critically ill patients worldwide, accounting for more than 11 million deaths annually [1,2]. Early and accurate prediction of the mortality risk in patients with sepsis is crucial for optimizing clinical decision-making and resource allocation. Since its proposal in 1996, the Sequential Organ Failure Assessment (SOFA) score has been the gold standard for assessing organ dysfunction and prognosis in patients with sepsis [3,4]. However, its reliance on laboratory indicators (such as blood gas analysis, bilirubin, and creatinine) limits its application in low- and middle-income countries (LMICs) with limited resources [5]. To simplify assessment, the quick Sequential Organ Failure Assessment (qSOFA), proposed in the Sepsis-3 consensus in 2016, predicts excess mortality risk through three clinical indicators: systolic blood pressure ≤ 100 mmHg, respiratory rate ≥ 22 breaths per minute, and altered mental status [1]. Although qSOFA is convenient for use in non-intensive care unit (non-ICU) settings, its sensitivity (32%–65%) and specificity (67%–94%) vary significantly across populations, with inconsistent performance especially in LMICs, where the burden of sepsis is relatively high [6–8].

In recent years, the introduction of biomarkers such as procalcitonin (PCT) and lactate has provided new perspectives for prognostic assessment. Studies have shown that PCT levels are closely related to infection severity and mortality rates [9,10]. As a key indicator of tissue hypoperfusion, an elevated lactate level can independently predict the risk of death [11]. On this basis, researchers have attempted to optimize the predictive efficacy by integrating biomarkers with qSOFA. Shetty et al. [12] confirmed in an emergency department (ED) cohort that $LqSOFA \geq 2$ (qSOFA + lactate ≥ 2 mmol/L) increased the sensitivity for predicting adverse outcomes by 17.9% compared with qSOFA alone. Yu et al. [13] and Xia et al. [14] increased the predictive sensitivity to 86.5% and 90.9%, respectively, by combining PCT with qSOFA. However, studies have significant heterogeneity in terms of

indicator combination methods, population characteristics, and outcome definitions, leading to contradictions among the results. Current guidelines give these newer indicators a low recommendation grade [1], and there is an urgent need for higher-quality evidence to support clinical practice.

This study aims to systematically evaluate the efficacy of the SOFA score, PCT, lactate level, qSOFA score, and their combined indicators (the lactate-adjusted quick Sequential Organ Failure Assessment (LqSOFA) in predicting mortality in patients with sepsis through meta-analysis. By integrating current evidence, this study provides a basis for more accurate selection of prognostic assessment tools in clinical practice and offers evidence-based medical guidance for future research directions.

2. Materials and methods

2.1. Search strategy

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Test Accuracy Studies (PRISMA-DTA) [15] and was registered on the INPLASY platform (Registration Number: INPLASY202530075). A systematic search was conducted in the PubMed, Embase, Cochrane Library, and China National Knowledge Infrastructure (CNKI) databases (from the database inception to March 2, 2025). A combination of Medical Subject Headings (such as MeSH terms) and free terms was used in addition to Boolean logical operators (e.g., AND, OR). The search covered the following dimensions: ① study population: sepsis, suspected sepsis, severe sepsis, and septic shock; ② predictive indicators: SOFA, qSOFA, PCT, and lactate; ③ outcome indicator: mortality. No language restrictions were applied to the search, and the search was supplemented by manually screening the references of the included studies. The detailed search strategies for each database are shown in [S1 Table](#).

2.2. Inclusion and exclusion criteria

The inclusion criteria were diagnostic cohort studies involving adult patients (defined as those aged ≥ 18 years) with confirmed or suspected sepsis diagnosed according to Sepsis-2.0 or Sepsis-3.0 and studies reporting the performance of SOFA, PCT, lactate, or LqSOFA for mortality prediction. Included studies needed to report the values of true positives, false positives, false negatives, and true negatives or provide the original data to calculate sensitivity, specificity, and the area under the receiver operating characteristic curve (AUROC) with a clear association between model performance (e.g., AUROC, sensitivity, specificity) and mortality outcome.

The exclusion criteria were as follows: non-diagnostic accuracy studies, methodology studies, reviews, conference abstracts, case reports, or expert consensus; studies that did not provide fourfold table data or from which sensitivity, specificity, and AUROC values could not be calculated; pediatric patients (age < 18 years); and duplicate publications (only the latest data were retained for multiple time-point reports of the same study population).

2.3. Literature screening and data extraction

A double-blind screening method was adopted, and researchers LJM and ZZX independently conducted the literature screening. First, obviously irrelevant studies were excluded based on titles and abstracts, followed by a secondary screening of the full texts. Eligibility was assessed according to the established inclusion/exclusion criteria. In cases of divergence, researcher GY intervened, and discussions were carried out to reach a consensus. EndNote X8 software was used for reference management. The screening results at each step, such as the total number of retrieved studies deduplicated and ultimately included, were recorded in detail, and a PRISMA flow chart was generated.

Standardized Microsoft Excel forms were used for data extraction. Extracted information included study characteristics (such as the first author, publication year, country, research design, sample size, sex, age, diagnostic criteria for sepsis), follow-up time, predictive indicators (including SOFA and qSOFA cut-off values, evaluation time points, PCT and lactate

cut-off values, and combination methods), and mortality rates. Performance indicators of the predictive model, such as the AUROC value, sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio, were also collected. Researchers LJM and ZZX independently extracted the data, and inconsistencies were marked and arbitrated by researcher GY. To ensure the accuracy of data extraction, a pre-extraction test was first conducted on a small sample set, and the process was analyzed and optimized.

2.4. Quality assessment

The QUADAS-2 tool [16] was adopted for evaluation. The scope of evaluation covered four key areas: patient selection (i.e., consecutive inclusion/exclusion criteria), index testing (i.e., the preset threshold/operational independence), reference standards (i.e., the accuracy of the gold standard), and processing and time (i.e., the detection interval/data integrity). Two researchers independently assessed the risk level of each area and classified into three types: low, high, and unclear. Applicability assessment focused primarily on the first three items, e.g., the degree of matching with the characteristics of the sepsis population, the applicability of the adopted indicators to the research scenario of sepsis, and the consistency between the research outcomes and the sepsis-related outcomes, to judge their fit with the sepsis population, indicators, and outcomes. Disagreements between researchers LJM and GY when determining the risk level or conducting the applicability assessment were resolved through arbitration by DZZ as the third-party. The evaluation results are presented using bar charts and summary tables.

2.5. Statistical analysis

All analyses were performed using Stata 18.0 software, with a P value < 0.05 defined as statistically significant. The 2×2 contingency tables (true positives, false negatives, false positives, and true negatives) of each research report were extracted along with the values of the AUROC and the 95% CI. Sensitivity and specificity were pooled using a bivariate random-effects model [17]. Pooled positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio values were calculated. A summary receiver operating characteristic curve was fitted to evaluate the predictive efficacy of the SOFA score, PCT, lactate, qSOFA, and LqSOFA for sepsis mortality. If the predictive efficacy of multiple different indicators was evaluated in the same patient cohort (for example, the AUROCs of both SOFA score and PCT were reported simultaneously), then, based on a paired-data design, the Δ AUROC (SOFA score vs. other indicators) was pooled through the random-effects model. Heterogeneity was evaluated using the I^2 statistic (with a threshold of $> 50\%$) and Cochrane's Q test. When significant heterogeneity was present, a random-effects model was adopted. Forest plots were used to display the Δ AUROC and 95% CI, and the P values of the Z test were marked. Publication bias was tested using Deeks' funnel plot. Subgroup analyses were performed to explore sources of heterogeneity using the following categorical variables: (1) clinical setting (ICU vs. ED); (2) economic region (HICs/LMICs per World Bank 2024 classifications); (3) sepsis definition (Sepsis-3.0 vs. Sepsis-2.0); (4) methodology (prospective/retrospective design; sample size ≥ 300 / < 300 ; publication year ≥ 2020 / < 2020); (5) outcome type (28/30-day mortality vs. in-hospital/other short-term mortality); and (6) geographic region (Asian/non-Asian studies). Subgroup analysis and meta-regression were combined to explore the sources of heterogeneity, and Fagan's nomogram was applied to assist in clinical decision-making.

3. Results

3.1. Research screening process

A total of 4,504 studies were initially retrieved. After duplicates were removed, 3,868 studies remained. Through the screening of titles and abstracts, 3,724 irrelevant studies were excluded, leaving 144 for the full-text evaluation stage. Subsequently, 115 studies were excluded that did not meet the inclusion criteria (e.g., missing data, non-target population, inconsistent design). Finally, 29 studies were included. The flow chart is shown in Fig 1.

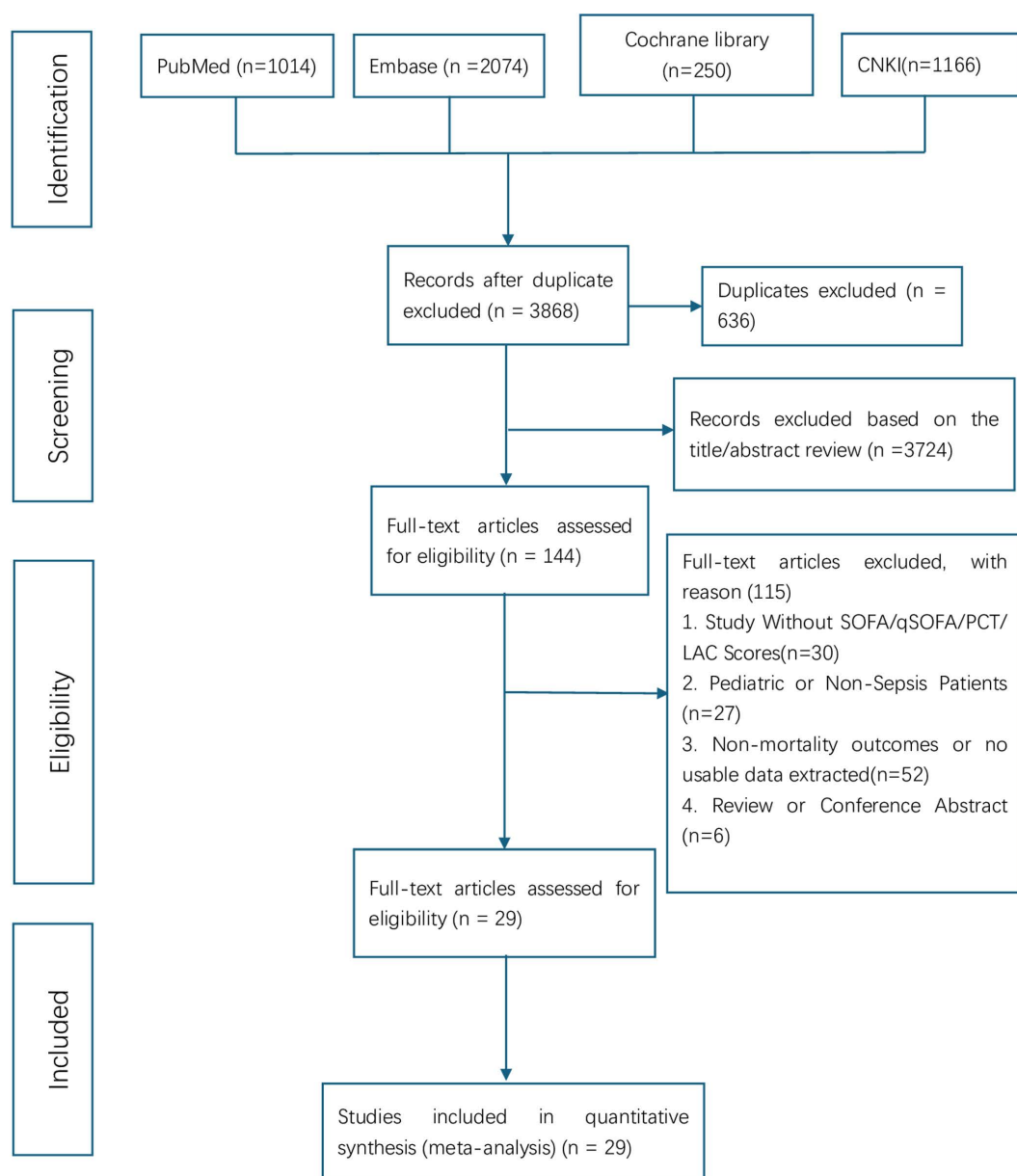


Fig 1. The PRISMA flow chart of literature screening and selection process.

<https://doi.org/10.1371/journal.pone.0332525.g001>

3.2. Characteristics of the included studies

A total of 29 studies with publication years ranging from 2010 to 2025 were included in this meta-analysis. Ten prospective cohort studies [4,18–26] and 19 retrospective cohort studies [12–14,27–42] were included. The geographical coverage was extensive and involved multiple countries and regions, such as China (n=12), India (n=3), Thailand (n=3), South Korea (n=2), Turkey (n=2), Spain (n=2), Indonesia (n=2), the United States (n=1), Australia (n=1), Portugal (n=1), Vietnam (n=1), and the Netherlands (n=1). The total sample size was 41,469 cases with 6,293 reported deaths. The research scenarios covered the ICU (n=14) and ED (n=14), with one study not specifying the exact clinical setting.

Mortality rates included the 28/30-day mortality rate ($n=19$), in-hospital mortality rate ($n=7$), 7-day mortality rate ($n=1$), ED mortality rate ($n=1$), and mortality rate within 72 hours ($n=1$). The diagnostic criteria for sepsis in the included studies were Sepsis-2.0 ($n=6$ studies) and Sepsis-3.0 ($n=23$ studies). With regard to the economic context, 22 studies (75.9%) originated from LMICs, while 7 studies (24.1%) were from HICs. Detection indicators included lactate, PCT, SOFA, qSOFA, and LqSOFA. The distribution of studies evaluating each indicator and their pairwise overlaps (e.g., cohorts enabling direct AUROC comparisons) are quantified in S1 Fig. Different cutoff values were set for each indicator, and the evaluation time was concentrated on key periods, such as within 24 hours of admission, at ICU admission, and during ED assessment. To distinguish the content of the Derivation Cohort External and Validation Cohort reported in two independent studies, namely, Wright, S. W. (2022) [25] and Li, F. (2023) [33], the derivation cohort external of Wright, S. W. (2022) was defined as Wright, S. W. 2022a, and its validation cohort was defined as Wright, S. W. 2022b, and the derivation cohort external of Li, F. (2023) was defined as Li, F. 2023a, and its validation cohort was defined as Li, F. 2023b. The detailed characteristics of the included studies are shown in [Tables 1](#) and [2](#).

3.3. Quality assessment

A total of 29 studies were evaluated using QUADAS-2 [16]. In terms of patient selection, 27 studies were judged as “yes”, indicating a low risk of bias. Two studies were judged as “uncertain” due to the lack of description of the exclusion criteria and issues with the enrollment method. In the field of index detection, all studies were judged as “yes”, indicating a low risk of bias in this area. Similarly, in the field of reference standards, all studies were judged as “yes”, indicating a low risk of bias. In terms of process and time, 6 studies were judged as “uncertain” due to the lack of description of the detection and evaluation time, and 4 studies were judged as “uncertain” due to the omission of the patient evaluation process. Overall, the reference standard field fully met the criteria. Most patient selection and index detection methods are standardized, and the process and time are generally controllable. The overall bias of all studies was mostly low, and the applicability was high. The included studies were high quality and had a good correlation with clinical practice. For details, refer to [S2–4 Figs](#).

3.4. Diagnostic efficacy indicators

3.4.1. Diagnostic efficacy of PCT. PCT demonstrated moderate diagnostic value for sepsis mortality in 12 studies ($n=6776$) with a sensitivity of 0.76 (95% CI: 0.65–0.84) and specificity of 0.65 (95% CI: 0.53–0.75), with an AUROC of 0.764 (0.725–0.800) ([Table 3](#), [Fig 2](#)). Fagan’s nomogram indicated that the positive posterior probability increased to 35% (vs. 20% pretest), while the negative probability decreased to 8% ([Fig 3](#)). Significant heterogeneity was observed (both $p<0.01$), with sensitivity heterogeneity associated with the sepsis definition ($p<0.01$) and specificity heterogeneity associated with publication year ($p<0.05$). Subgroup analyses aligned with the overall results. No publication bias was detected ($p=0.11$). For details, see [S5–7 Figs](#) and [S2 Table](#).

3.4.2. Diagnostic efficacy of Lactate. Lactate demonstrated moderate diagnostic value for sepsis mortality in 14 studies ($n=14,485$) with a sensitivity of 0.68 (95% CI: 0.58–0.76) and specificity of 0.69 (95% CI: 0.62–0.75), and AUROC of 0.740 (0.700–0.777) ([Table 3](#), [Fig 2](#)). Fagan’s nomogram indicated a positive posterior probability of 36% (vs. 20% pretest) and a negative posterior probability of 10% ([Fig 3](#)). Significant heterogeneity was observed (both $p<0.01$), with specificity heterogeneity linked to study design and sepsis definition (both $p<0.01$). Subgroup analyses revealed that after 3 prospective studies were excluded, sensitivity increased to 0.82 (0.65–0.92) in small-sample studies (<300 patients). Other subgroup results were consistent with the overall findings. No publication bias was detected ($p=0.10$). For details, see [S5–7 Figs](#) and [S3 Table](#).

3.4.3. Diagnostic efficacy of qSOFA. The qSOFA score showed low diagnostic value for sepsis mortality in 14 studies ($n=30,137$) with a sensitivity of 0.52 (95% CI: 0.33–0.71), specificity of 0.77 (95% CI: 0.64–0.86), and AUROC of

Table 1. Characteristics of include studies.

ID	Author	Year	Country	Study design	Set- ting	Type of mortality	Sample (N)	Died (%)	Age	Detection index
1	Suárez-Santamaría, M.	2010	Spain	Prospective	ICU	28 – day mortality	253	55	65(range 19–94)	Lactate/PCT/ SOFA
2	Wang, J.	2016	China	Retrospective	ICU	In-hospital mortality	864	132	63.56 ± 15.80	SOFA/PCT
3	Shetty, A.	2017	Austra- lia, the Netherlands	Retrospective	ED	Mortality and/or ICU stay ≥72 h)	12555	572	The median age of patients across centers ranged from 47 to 72.4 years	SOFA/qSOFA/ LqSOFA
4	Zhao, R.	2017	China	Prospective	ICU	28 – day mortality	104	26	SIRS group: 58.8 ± 11.3; Sepsis group: 57.6 ± 12.9	PCT/SOFA
5	Liu, Z.	2019	USA	Retrospective	ICU	30-day mortality	1865	809	68 (IQR: 56–78.25)	Lactate/qSOFA/ SOFA/LqSOFA
6	Yu, H.	2019	China	Retrospective	ED	30-day mortality	1318	178	64 (IQR: 47–75)	qSOFA/ PqSOFA
7	Zhang, Y.	2019	China	Retrospective	ICU	28-day mortality	150	98	Control: 66.5 (25–89); Sepsis: 70 (24–91); Septic shock: 74.5 (24–89)	PCT/SOFA/ qSOFA
8	Sinto, R.	2020	Indonesia	Prospective	ED	28-day mortality	1213	421	51 (IQR: 38–60)	SOFA/Lactate/ qSOFA/LqSOFA
9	Xia, Y.	2020	China	Retrospective	ED	28-day mortality	821	173	Survival: 56.83 ± 17.79; Deceased: 59.92 ± 17.79	Lactate/ PCT/qSOFA/ PqSOFA/SOFA
10	Zhou, H.	2020	China	Retrospective	ED	28-day mortality	336	89	76 (IQR: 61–84)	Lactate/ SOFA/qSOFA/ LqSOFA/LSOFA
11	Liu, S.	2020	China	Retrospective	ED	In-hospital mortality	821	173	58.3 ± 17.09	LqSOFA/qSOFA
12	Daga, M. K.	2021	India	Prospective	ICU	7-day mortality	150	73	48.46 ± 15.28	SOFA/qSOFA/ Lactate/LqSOFA
13	Hao, C.	2021	China	Retrospective	ICU	28-day mortality	303	179	64.36 ± 15.62	Lactate/PCT/ SOFA
14	Kilinc Toker, A.	2021	Turkey	Retrospective	ED	ED mortality	499	115	72.5 ± 13.7	SOFA/qSOFA/ LqSOFA
15	Suttapanit, K.	2021	Thailand	Prospective	ED	28-day mortality	1139	118	Survival: 70 (69–71); Deceased: 70 (67–73)	LqSOFA/ qSOFA/SOFA
16	Guarino, M.	2022	Italy	Retrospective	ED	In-hospital mortality	556	218	79.9 ± 11.9	Lactate/qSOFA
17	Jaiswal, P.	2022	India	Retrospective	ICU	In-hospital mortality	280	121	59.38 ± 15.88	Lactate/SOFA
18	Sen, P.	2021	Turkey	Retrospective	ICU	28-day mortality	165	119	60.9 ± 17.9	PCT/SOFA
19	Silva, C. M.	2022	Portugal	Prospective	ICU	In-hospital mortality	1640	NR	NR	Lactate/SOFA
20	Wang, L.	2022	China	Prospective	ED	28-day mortality	175	41	66 (IQR: 53–77)	Lactate/PCT/ qSOFA/LqSOFA
21a	Wright, S. W.	2022	Thailand, Vietnam, Indonesia	Prospective	NR	28-day mortality	4980	816	57 (IQR: 41–71)	qSOFA/SOFA/ Lactate/ LqSOFA
21b							792	102	51 (IQR: 33–65)	qSOFA/SOFA/ Lactate/ LqSOFA

(Continued)

Table 1. (Continued)

ID	Author	Year	Country	Study design	Set-ting	Type of mortality	Sample (N)	Died (%)	Age	Detection index
22	Chi, H.	2023	China	Retrospective	ICU	28-day mortality	135	62	71.47 ± 15.36	SOFA/Lactate
23	Julián-Jiménez, A.	2023	Spain	Prospective	ED	30-day mortality	4439	459	67 ± 18	Lactate/qSOFA/LqSOFA
24a	Li, F.	2023	China	Retrospective	ICU	28-day mortality	340	102	56.00 (IQR: 44.25–68.00)	Lactate/PCT/SOFA/LSOFA
24b							75	37	61.00 (IQR: 44.00–71.00)	PSOFA/Lactate/PCT/SOFA
25	Noparatkailas, N.	2023	Thailand	Retrospective	ED	28-day mortality	448	99	71 (IQR: 59–87)	Lactate/qSOFA/LqSOFA
26	Shinde, V. V.	2023	India	Prospective	ICU	In-hospital mortality	80	30	58 ± 12	PCT/SOFA
27	Li, L.	2024	China	Retrospective	ICU	28-day mortality	200	67	NR	SOFA/PCT
28	Yoo, K. H.	2024	South Korea	Retrospective	ED	28-day mortality	3499	792	70 (IQR: 61–78)	Lactate/SOFA/qSOFA/PCT
29	Saqer M Althunayyan	2025	Saudi Arabia	Retrospective	ED	Mortality within 72h	1274	17	68.80 ± 17.9	qSOFA/LqSofa

Abbreviations: ICU, Intensive Care Unit; PCT, Procalcitonin; SOFA, Sequential Organ Failure Assessment; ED, Emergency Department; qSOFA, Quick Sequential Organ Failure Assessment; LqSOFA, Lactate-adjusted Quick Sequential Organ Failure Assessment; PQSOFA, Procalcitonin-adjusted Quick Sequential Organ Failure Assessment; LSOFA, Lactate-adjusted Sequential Organ Failure Assessment; NR, Not Recorded;

<https://doi.org/10.1371/journal.pone.0332525.t001>

0.721 (0.680–0.759) (Table 3, Fig 2). Fagan’s analysis indicated a positive posterior probability of 36% (vs. 20% pretest) and a negative probability of 13% (Fig 3). Significant heterogeneity was observed (both $p < 0.01$; $I^2 > 99\%$), although meta-regression revealed no significant moderators. Subgroup analyses showed notable variations in sensitivity across study designs and outcome subgroups. No publication bias was detected ($p = 0.71$). For details, see S5–7 Figs and S4 Table.

3.4.4. Diagnostic efficacy of LqSOFA. LqSOFA demonstrated superior diagnostic value for sepsis mortality in 9 studies ($n = 22,078$), with a sensitivity of 0.46 (95% CI: 0.24–0.69), specificity of 0.88 (95% CI: 0.80–0.93), and AUROC of 0.823 (0.787–0.854) (Table 3, Fig 2). Fagan’s analysis indicated a positive posterior probability of 49% (vs. 20% pretest) and a negative probability of 13% (Fig 3). Significant heterogeneity was observed (both $p < 0.01$; $I^2 > 97\%$), with no significant moderators identified by meta-regression. No publication bias was detected ($p = 0.71$). For details, see S5–7 Figures.

3.4.5. Subgroup analysis of LqSOFA diagnostic performance. For sepsis mortality prediction, LqSOFA showed consistently robust performance. Subgroup analyses by both sepsis definition and clinical setting were precluded due to homogeneity across all included studies: all studies ($N = 9$) exclusively used Sepsis-3 criteria and were conducted in ED settings. Similarly, in LMICs (7 studies), the pooled AUC reached 0.81 (95% CI: 0.77–0.84) with a sensitivity of 0.41 (95% CI: 0.17–0.70) and specificity of 0.88 (0.77–0.94). Subsequent analyses revealed improved 28/30-day mortality prediction (6 studies: AUC 0.85 [95% CI: 0.82–0.88], sensitivity 0.60 [0.50–0.69], specificity 0.86 [0.83–0.89]). Prospective studies ($n = 4$) showed higher sensitivity (0.64 [0.56–0.71] vs. 0.31 [0.09–0.68]) but comparable specificity (0.86 [0.81–0.90] vs. 0.90 [0.74–0.96]) compared to retrospective designs ($n = 5$). ICU, non-Asian, small-scale (< 300), and pre-2020 subgroups had insufficient data for pooled estimates. Detailed subgroup analysis findings are detailed in Table 4.

3.4.6. Diagnostic efficacy of SOFA. The SOFA score demonstrated high diagnostic value for sepsis mortality in 18 studies ($n = 23,802$), with a sensitivity of 0.77 (95% CI: 0.71–0.82), specificity of 0.73 (95% CI: 0.67–0.79), and AUROC of 0.819 (0.783–0.850) (Table 3, Fig 2). Fagan’s analysis indicated a positive posterior probability of 42% (vs. 20% pretest) and a negative probability of 7% (Fig 3). Significant heterogeneity was observed (both $p < 0.01$; $I^2 > 96\%$). Meta-regression identified multiple modifiers for sensitivity (publication year, economic level, setting, sample fraction, sepsis definition) and specificity

Table 2. Diagnostic and Detection Characteristics of Included Studies.

ID	Author	Year	Sepsis diagnosis	Detection index & cut-off value	Assessment/Detection Time
1	Suárez-Santamaría, M.	2010	Sepsis was defined as clinical infection evidence plus ≥ 2 SIRS criteria. (Sepsis-2)	Lactate: NR; PCT: NR; SOFA: NR	At admission
2	Wang, J.	2016	Diagnostic criteria refer to the "Diagnostic Criteria for Nosocomial Infection" issued by the Family Planning Commission in 2001 (Trial). (Sepsis-2)	SOFA: 6.37; PCT: 3.38 $\mu\text{g/L}$	Within 24 hours of ICU admission
3	Shetty, A.	2017	Adult patients with suspected or proven sepsis presenting to EDs, identified by SIRS screening. (Sepsis-3)	SOFA: ≥ 2 ; qSOFA: ≥ 2 ; LqSOFA: ≥ 2	Worst values during ED stay
4	Zhao, R.	2017	Adult patients with sepsis or systemic inflammatory response syndrome (SIRS). (Sepsis-2)	PCT: 7.68 $\mu\text{g/L}$; SOFA: 12.5	Within 24 hours of ICU admission
5	Liu, Z.	2019	Adult Patients who were diagnosed with 'sepsis', 'severe sepsis' and 'septic shock' on discharge (Sepsis-3)	Lactate: 3.225 mmol/L; qSOFA: ≥ 2 ; SOFA: NR; LqSOFA: NR	Within 24 hours of ICU admission
6	Yu, H.	2019	Adult patients presenting to ED/hospital with systemic infection symptoms. (Sepsis-3)	qSOFA: ≥ 2 ; PqSOFA: ≥ 2	Within 24 hours of admission
7	Zhang, Y.	2019	Adult patients diagnosed with sepsis or septic shock based on sepsis-3 criteria. (Sepsis-3)	PCT: 4.7; SOFA: 4; qSOFA: NR	At ICU admission
8	Sinto, R.	2020	Adult patients with suspected bacterial infection (on antibiotics and with cultures). (Sepsis-3)	SOFA: ≥ 2 ; Lactate: > 2 mmol/L; qSOFA: ≥ 2 ; LqSOFA: qSOFA ≥ 2 and Lactate > 2 mmol/L	Worst values 12 hours before enrolment
9	Xia, Y.	2020	Patients > 14 years old, treated at ED, and meeting Sepsis 2.0 criteria. (Sepsis-2)	Lactate: 2.35; PCT: 0.51; qSOFA: 2; PqSOFA: 2; SOFA: NR	Within 24 hours of admission
10	Zhou, H.	2020	new chest x-ray infiltrates, ≥ 2 symptoms (cough, fever, dyspnea, etc.), and CAP patients with SOFA score increase ≥ 2 according to sepsis 3.0.	Lactate: 2; SOFA: 4; qSOFA: 2; LqSOFA: 0.29 (probability threshold); LSOFA: 0.23 (probability threshold)	At admission
11	Liu, S.	2020	Per sepsis-3, patients enrolled had infection-induced SOFA score increase ≥ 2 . (Sepsis-3)	LqSOFA: NR; qSOFA: NR	At admission
12	Daga, M. K.	2021	Patients suspected of sepsis based on SEPSIS 3 guidelines (2016). (Sepsis-3)	SOFA: 8.5; Lactate: ≥ 2 mmol/L; qSOFA: NR; LqSOFA: NR	Within 24 hours of admission
13	Hao, C.	2021	Patients with septic shock hospitalized in the department of critical care medicine. (Sepsis-3)	Lactate: 3.55; PCT: 14.2; SOFA: 7.5;	Immediately after ICU admission
14	Kilinc Toker, A.	2021	For patients with sepsis, the diagnostic basis is not described in detail. (Sepsis-3)	SOFA: > 11 ; qSOFA: > 1 ; LqSOFA: > 3	During emergency assessment
15	Suttapanit, K.	2021	Patients 18 years and older who visited ED with suspected sepsis. (Sepsis-3)	LqSOFA: ≥ 3 ; qSOFA: ≥ 2 ; SOFA: ≥ 2	At admission
16	Guarino, M.	2022	patients identified by 'sepsis' and 'septic shock' in discharge letter. (Sepsis-3)	Lactate: ≥ 1.85 mmol/L; qSOFA: ≥ 2	At first ED assessment
17	Jaiswal, P.	2022	patients diagnosed with SIRS, Sepsis, Severe Sepsis, and septic shock. (Sepsis-2)	Lactate: > 3 ; SOFA: 9	At admission (Lactate); Within 24 hours of ICU admission (SOFA)
18	Sen, P.	2021	Sepsis identified per Sepsis-3 definition. (Sepsis-3)	PCT: 0.8ng/mL; SOFA: 7	Within 24 hours of ICU admission
19	Silva, C. M.	2022	Sepsis identified per Sepsis-2 definition. (Sepsis-2)	Lactate: NR; SOFA: NR	Within 12 hours of admission (Lactate); At admission (SOFA)
20	Wang, L.	2022	Sepsis identified per Sepsis-3 definition. (Sepsis-3)	Lactate: 1.855 mmol/L; PCT: 9.24 ng/mL; qSOFA: 1.5; LqSOFA: NR; PqSOFA: NR	Within 24 hours of admission (Lactate); At ED admission (qSOFA)
21a /b	Wright, S. W.	2022	Patients with ≥ 3 systemic manifestations (2012 Surviving Sepsis Campaign). (Sepsis-3)	qSOFA: NR; SOFA: NR; Lactate: NR; LqSOFA: NR	Calculated at enrolment (qSOFA/SOFA); Point-of-care measurement at enrolment (Lactate)

(Continued)

Table 2. (Continued)

ID	Author	Year	Sepsis diagnosis	Detection index & cut-off value	Assessment/Detection Time
22	Chi, H.	2023	Sepsis identified per Sepsis-3 definition. (Sepsis-3)	SOFA: 8.5; Lactate: 2.55	Immediately after transfer to ICU
23	Julián-Jiménez, A.	2023	Each patient diagnosed with suspected infection based on epidemiology. (Sepsis-3)	Lactate: ≥ 2 mmol/L; qSOFA: 2; LqSOFA: qSOFA ≥ 2 + Lactate ≥ 2	At ED presentation (Lactate); At admission (qSOFA)
24a/b	Li, F.	2023	Sepsis identified per Sepsis-3 definition. (Sepsis-3)	Lactate: 2.4; PCT: 8.03; SOFA: ≥ 6 ; Lac+SOFA: 2.4	Within 24 hours of ICU admission
25	Noparatkailas, N.	2023	Sepsis defined as suspected/confirmed infection with SIRS/qSOFA ≥ 2 . (Sepsis-3)	Lactate: ≥ 2 mmol/L; qSOFA: ≥ 2 ; LqSOFA: ≥ 2 mmol/L + Lactate: ≥ 2	Initial serum lactate at ED (Lactate); At admission (qSOFA)
26	Shinde, V. V.	2023	Sepsis identified per Sepsis-3 definition. (Sepsis-3)	PCT: 4.15; SOFA: 8	At admission
27	Li, L.	2024	Sepsis identified per Sepsis-3 definition. (Sepsis-3)	SOFA: NR; PCT: 4.05	At admission
28	Yoo, K. H.	2024	Patients with suspected/inconfirmed infection and refractory hypotension/hyperlactatemia. (Sepsis-3)	Lactate: 1.517; SOFA: 7.5; PCT: 4.517; qSOFA: NR	Time zero of sepsis (Lactate); At admission (qSOFA)
29	Saqer M Althunayyan	2025	Suspected sepsis: blood culture during ED visit and IV antibiotics administered. (Sepsis-3)	qSOFA: 2; LqSofa: 2	Calculated using initial ED triage data

Abbreviations: SIRS, Systemic Inflammatory Response Syndrome; NR, Not Recorded; SOFA, Sequential Organ Failure Assessment; ICU, Intensive Care Unit; ED, Emergency Department; qSOFA, Quick Sequential Organ Failure Assessment; LqSOFA, Lactate-adjusted Quick Sequential Organ Failure Assessment; PqSOFA, Procalcitonin-adjusted Quick Sequential Organ Failure Assessment; LSOFA, Lactate-adjusted Sequential Organ Failure Assessment.

<https://doi.org/10.1371/journal.pone.0332525.t002>

Table 3. Pooled Performance of PCT, Lactate, qSOFA, LqSOFA, and SOFA in Predicting Sepsis Patient Mortality.

	No of studies	SROC	Sensitivity	Specificity	PLR	NLR	DOR
PCT	12	0.764 [0.725, 0.800]	0.76 [0.65, 0.84]	0.65 [0.53, 0.75]	2.2 [1.6, 3.0]	0.37 [0.25, 0.56]	6 [3,11]
Lactate	14	0.740 [0.700, 0.777]	0.68 [0.58, 0.76]	0.69 [0.62, 0.75]	2.2 [1.9, 2.5]	0.46 [0.37, 0.58]	5 [4,6]
qSOFA	14	0.721 [0.680, 0.759]	0.52 [0.33, 0.71]	0.77 [0.64, 0.86]	2.2 [1.8, 2.8]	0.62 [0.46, 0.85]	4 [2,5]
LqSOFA	9	0.823 [0.787, 0.854]	0.46 [0.24, 0.69]	0.88 [0.80, 0.93]	3.8 [2.7, 5.3]	0.62 [0.42, 0.91]	6 [3,11]
SOFA	18	0.819 [0.783, 0.850]	0.77 [0.71, 0.82]	0.73 [0.67, 0.79]	2.9 [2.3, 3.5]	0.31 [0.25, 0.39]	9 [7,13]

Abbreviations: qSOFA, Quick Sequential Organ Failure Assessment; LqSOFA, Lactate-adjusted Quick Sequential Organ Failure Assessment; SOFA, Sequential Organ Failure Assessment; PLR, Positive Likelihood Ratio; NLR, Negative Likelihood Ratio; DOR, Diagnostic Odds Ratio; SROC, Summary Receiver Operating Characteristic.

<https://doi.org/10.1371/journal.pone.0332525.t003>

(publication year, economic level, sample fraction, sepsis definition) heterogeneity (all $p < 0.05$). Subgroup analyses revealed stable results across subgroups. Publication bias was detected ($p = 0.03$). For details, see [S5–7 Figs](#) and [S5 Table](#).

3.4.7. Comparison of the differences in AUROC among SOFA, PCT, LAC, qSOFA, and LqSOFA. Based on the meta-analysis of the AUROC differences for paired data, the AUROC of SOFA was 0.10 higher than procalcitonin ($n = 12$, 95% CI: 0.04–0.16; $I^2 = 84.7\%$), 0.07 higher than lactate ($n = 15$, 95% CI: 0.03–0.11; $I^2 = 88.7\%$), and 0.08 higher than qSOFA ($n = 11$, 95% CI: 0.05–0.11; $I^2 = 83.5\%$). In contrast, LqSOFA showed an AUROC increase of 0.06 versus qSOFA ($n = 14$, 95% CI: 0.04–0.08; $I^2 = 59.8\%$). However, there was no significant difference between SOFA and LqSOFA scores, with a difference of 0.02 ($n = 8$, 95% CI: -0.02 – 0.06 ; $I^2 = 89.2\%$) ([Fig 4](#)).

4. Discussion

Our study systematically assessed the predictive performance of PCT, lactate, qSOFA, LqSOFA, and SOFA for mortality risk in sepsis patients through a meta-analysis. The results demonstrated that the SOFA score (AUROC 0.819)

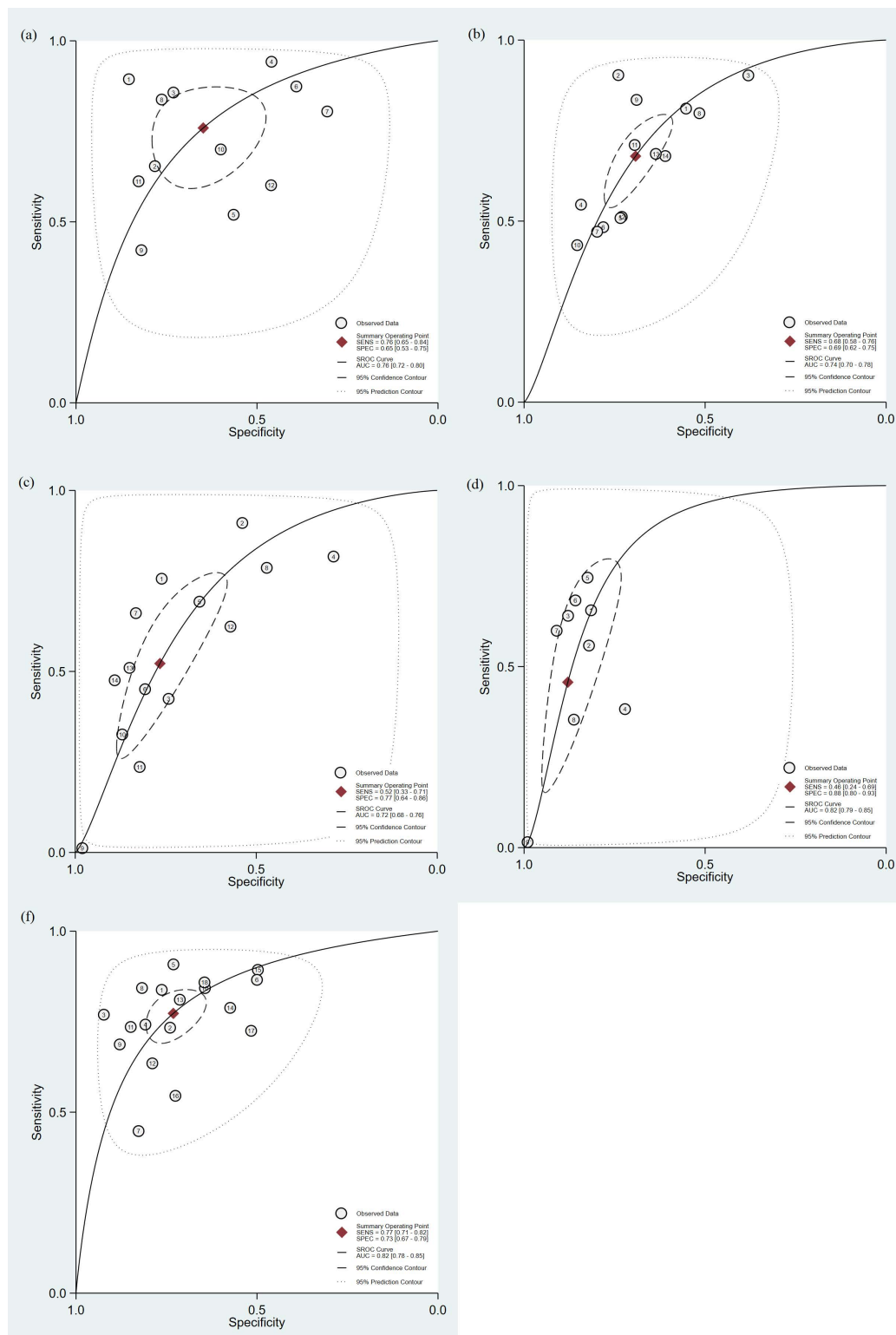


Fig 2. HSROC curve for predicting mortality in patients with sepsis. (a) PCT; (b) Lactate; (c) qSOFA; (d) Lqsofa; (f) Sofa.

<https://doi.org/10.1371/journal.pone.0332525.g002>

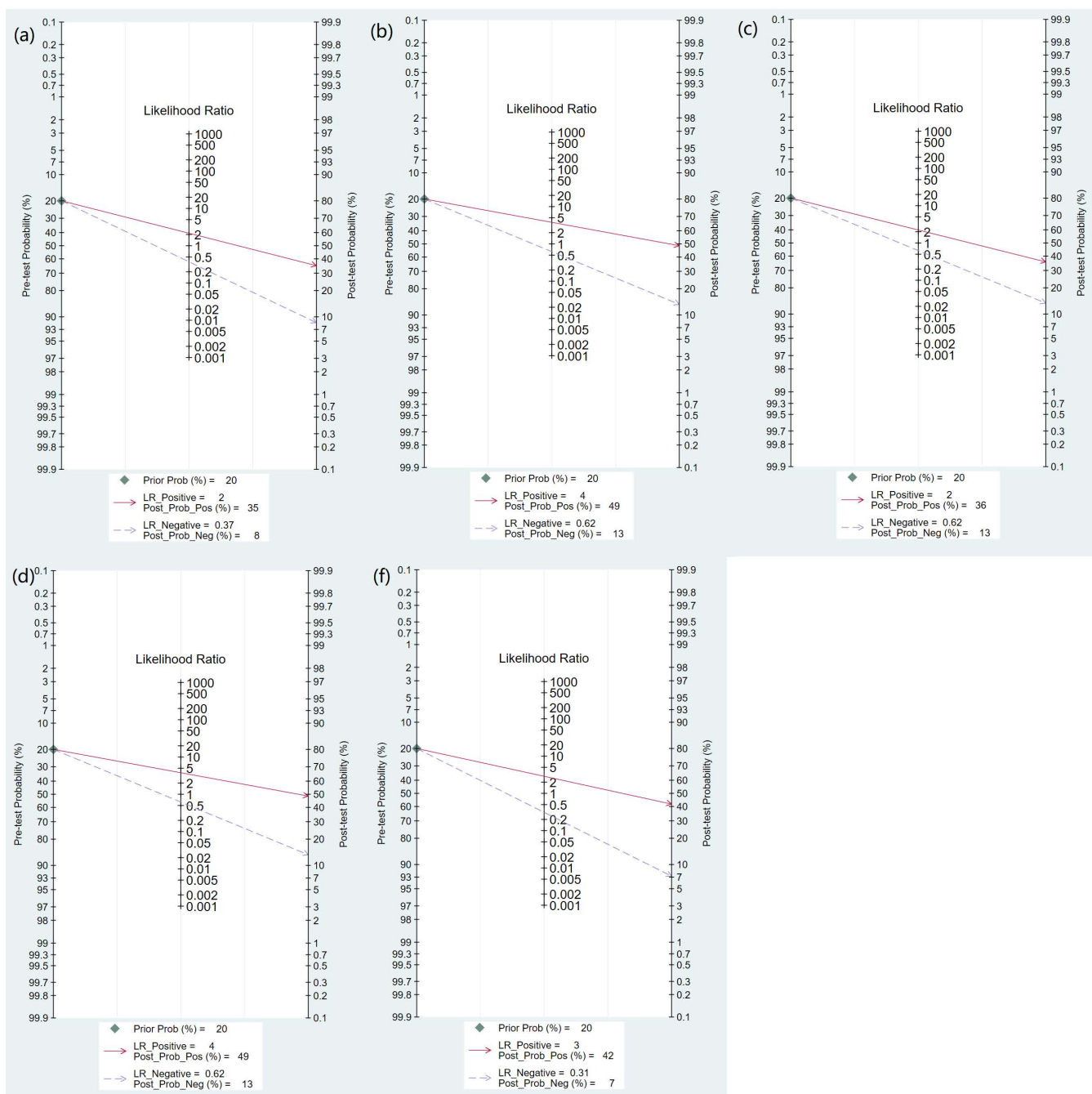


Fig 3. Fagan nomogram of pretest probability and negative posttest probability. (a) PCT; (b) Lactate; (c) qSOFA; (d) Lqsofa; (e) Sofa.

<https://doi.org/10.1371/journal.pone.0332525.g003>

significantly outperformed PCT (Δ AUROC 0.10), lactate (Δ AUROC 0.07), and qSOFA (Δ AUROC 0.08) in terms of predictive performance. Notably, LqSOFA exhibited comparable predictive power to SOFA (Δ AUROC=0.02; AUROC=0.823) and a clinically relevant improvement over qSOFA (Δ AUROC 0.06). Its high specificity (0.88) further demonstrated unique clinical value for rapidly ruling out patients with low mortality risk. Subgroup analyses further confirmed that LqSOFA

Table 4. Subgroup Analyses of Pooled Diagnostic Performance of LqSOFA in Predicting Sepsis Patient Mortality.

Subgroup Variables	Group Definition	No of studies	SROC	Sensitivity	Specificity	PLR	NLR	DOR
Setting	ICU	0	—	—	—	—	—	—
	ED	9	0.82[0.79, 0.85]	0.46 [0.24, 0.69]	0.88 [0.80, 0.93]	3.8 [2.7, 5.3]	0.62 [0.42, 0.91]	6 [3,11]
Income Group	HICs	2	—	—	—	—	—	—
	LMICs	7	0.81[0.77, 0.84]	0.41 [0.17, 0.70]	0.88 [0.77, 0.94]	3.4 [2.3, 5.2]	0.67 [0.44, 1.03]	5 [2,10]
Sepsis criteria	Sepsis-3	9	0.82[0.79, 0.85]	0.46 [0.24, 0.69]	0.88 [0.80, 0.93]	3.8 [2.7, 5.3]	0.62 [0.42, 0.91]	6 [3,11]
	Sepsis-2	0	—	—	—	—	—	—
Publish year	≥2020	8	0.82[0.79, 0.85]	0.43 [0.20, 0.69]	0.89 [0.79, 0.94]	3.8 [2.6, 5.6]	0.64 [0.43, 0.97]	6 [3,12]
	<2020	1	—	—	—	—	—	—
Region	Asia	7	0.81[0.77, 0.84]	0.41 [0.17, 0.70]	0.88 [0.77, 0.94]	3.4 [2.3, 5.2]	0.67 [0.44, 1.03]	5 [2,10]
	Non-Asia	2	—	—	—	—	—	—
Study design	Prospective	4	0.82[0.79, 0.86]	0.64 [0.56, 0.71]	0.86 [0.81, 0.90]	4.5 [3.4, 6.0]	0.42 [0.34, 0.52]	11 [7,16]
	Retrospective	5	0.78[0.74, 0.81]	0.31 [0.09, 0.68]	0.90 [0.74, 0.96]	3.0 [1.7, 5.1]	0.77 [0.53, 1.13]	4 [2,9]
Outcome	28/30-day mortality	6	0.85[0.82, 0.88]	0.60 [0.50, 0.69]	0.86 [0.83, 0.89]	4.4 [3.4, 5.6]	0.47 [0.36, 0.60]	9 [6,15]
	Other mortality	3	—	—	—	—	—	—
Sample size	≥300	8	0.82[0.78, 0.85]	0.43 [0.20, 0.69]	0.88 [0.79, 0.94]	3.7 [2.5, 5.3]	0.65 [0.43, 0.96]	6 [3,11]
	<300	1	—	—	—	—	—	—

Abbreviations: LqSOFA, Lactate-adjusted Quick Sequential Organ Failure Assessment; SROC, Summary Receiver Operating Characteristic; PLR, Positive Likelihood Ratio; NLR, Negative Likelihood Ratio; DOR, Diagnostic Odds Ratio; ICU, Intensive Care Unit; ED, Emergency Department; HICs, High-Income Countries; LMICs, Low- and Middle-Income Countries.

<https://doi.org/10.1371/journal.pone.0332525.t004>

demonstrated robust predictive ability across ED settings (AUROC 0.82) and LMICs (AUROC 0.81) and in predicting 28/30-day mortality (AUROC 0.85), providing an evidence-based rationale for streamlining clinical assessment workflows.

This meta-analysis confirmed that the SOFA score remains the gold standard for predicting sepsis mortality, supported by its comprehensive multisystem assessment and alignment with prior evidence. Qiu et al.'s systematic review further validated SOFA's optimal performance (sensitivity 0.89/specificity 0.69) for in-hospital mortality, particularly in 28/30-day screening within resource-limited settings [43]. Notably, qSOFA demonstrated significant predictive limitations in our cohort, with a sensitivity of only 0.52 (95% CI: 0.33–0.71) and a specificity of 0.77 (95% CI: 0.64–0.86), indicating insufficient standalone clinical utility. This finding aligns closely with the Sepsis-3 guidelines, which caution that qSOFA, when used as an isolated screening tool, has sensitivity deficiencies and should be combined with other biomarkers to optimize predictive performance [1]. Further analysis revealed that LqSOFA achieves comparable predictive performance to SOFA (AUROC=0.823, ΔAUROC=0.02) by synergistically integrating the advantages of lactate as a tissue perfusion marker with the value of qSOFA as an organ dysfunction screening tool. These findings align with Moncada-Gutierrez et al.'s meta-analysis (AUROC=0.807, n=23,551) [44]. Critically, in our study, the high specificity of LqSOFA (0.88, 95% CI: 0.80–0.93) provided an exceptionally low-risk patient exclusion capability, with negative predictive values consistently exceeding 90%.

Our subgroup analysis revealed the clinical utility of LqSOFA across diverse medical contexts. Among the 9 studies conducted in ED settings, LqSOFA demonstrated robust predictive performance (AUROC 0.82, 95% CI: 0.79–0.85; specificity 0.88, 95% CI: 0.80–0.93). Its high specificity significantly optimized triage decisions, yielding negative predictive

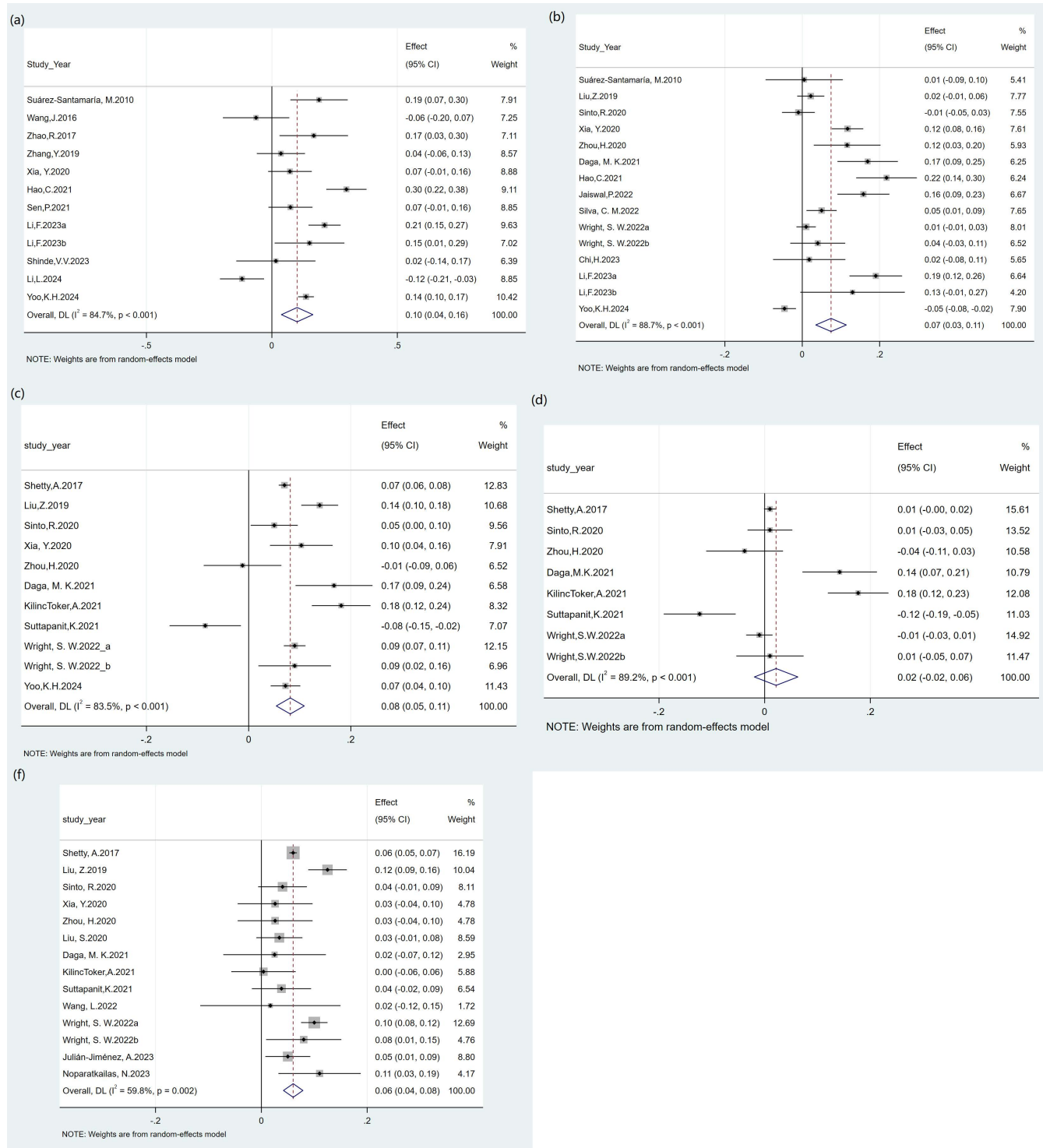


Fig 4. Forest Plot of Pooled AUROC Differences. (a) Sofa vs PCT; (b) Sofa vs Lactate; (c) Sofa vs qSOFA; (d) Sofa vs Lqsofa; (f) Lqsofa vs qsofa.

<https://doi.org/10.1371/journal.pone.0332525.g004>

values >90%. This conclusion is supported by multiple prospective studies: Kilinc Toker et al. reported a 47.8% reduction in ICU assessment demand through LqSOFA implementation [32], whereas Sinto et al. validated its ability to decrease ICU misdirected transfer rates by 39% in resource-limited settings, demonstrating performance parity with SOFA [21]. By enabling precise exclusion of low-risk patients, LqSOFA provides an efficient solution for emergency department triage. Across 7 studies in LMICs, LqSOFA maintained robust predictive ability (AUROC 0.81). Its core advantage lies in minimizing laboratory dependency: qSOFA components require only a sphygmomanometer and timer for bedside assessment, whereas lactate measurements can be rapidly obtained via portable devices or point-of-care arterial blood gas analyzers with a median turnaround time of just 15 minutes. This represents a >50% efficiency gain compared with conventional lab testing (typically 30–60 minutes) [18,25]. These features further enable the practical implementation of dynamic bedside LqSOFA monitoring, offering operational solutions for primary care hospitals.

However, our study revealed considerable variability in LqSOFA sensitivity (range: 0.31–0.64), which remains a central challenge for clinical implementation. While its high specificity effectively rules out low-risk patients, its suboptimal sensitivity limits early identification of high-risk patients. This phenomenon is attributable primarily to inherent limitations in the assessment framework, where significant heterogeneity exists in threshold selection for both qSOFA scores and lactate levels across current protocols. Certain studies define positivity using qSOFA ≥ 2 points combined with lactate ≥ 2 mmol/L [12,21,37], consequently excluding patients with occult shock (qSOFA = 1 point but elevated lactate) from the high-risk cohort. This cohort of patients without hypotension (SBP > 100 mmHg) that exhibited tissue hypoperfusion (lactate ≥ 2 mmol/L) constituted 21.3% (95% CI: 18.7–24.1) of the ED sepsis population. These patients demonstrated significantly elevated SOFA scores, indicating increased risks of organ dysfunction and shock progression [32]. Similarly, Hwang et al. reported that 26.6% of sepsis patients initially presented with occult shock (lactate ≥ 4 mmol/L with normotension), with 72.4% progressing to manifest shock within 72 hours. Despite meeting single-point lactate thresholds, these patients experienced progressive deterioration, resulting in mortality rates as high as 27.4% [45]. Notably, a key contributor to LqSOFA's suboptimal sensitivity may be its reliance on single-point lactate measurements, which fail to identify patients with progressively deteriorating conditions. Daga et al.'s prospective study demonstrated that dynamic lactate clearance rate, not isolated lactate levels, serves as a critical prognostic indicator, with delayed clearance (<10%/hour) significantly increasing the mortality risk (adjusted OR 4.2, 95% CI: 2.7–6.5) [18]. This underscores the potential for incorporating serial lactate measurements into prognostic models to increase sensitivity. Given the dual limitations of single-point lactate measurement and inconsistent threshold standards, future research should (1) validate the real-world survival benefits of dynamic lactate monitoring (e.g., serial measurements every 2–4 hours) through multicenter prospective studies and (2) establish evidence-based precision cutoffs, ultimately developing context-specific risk identification frameworks for sepsis across diverse healthcare environments.

5. Discussion of limitations

This study has several limitations that require future research attention: (1) its exclusive focus on ED/ICU settings (100%) lacks data from critical LMIC contexts such as general wards and prehospital environments; (2) the absence of pathogen stratification (viral, bacterial, fungal) potentially underestimates biomarker differences (e.g., lower PCT in viral sepsis), impacting LqSOFA performance; (3) reliance on single biomarker measurements overlooks the value of dynamic indicators (e.g., lactate clearance) for prognosis and optimizing monitoring sensitivity; (4) significant heterogeneity in LqSOFA definitions (variable lactate cutoffs ≥ 2 – ≥ 4 /L, inconsistent logic) combined with insufficient data prevents analysis of their impact, limiting generalizability; (5) limited LMIC validation scope (7 studies, primarily Asian) necessitates broader assessment in diverse regions (e.g., Sub-Saharan Africa, Latin America) to gauge robustness across contexts; and (6) potential biases may arise from the predominance of retrospective studies (19/30), with the risk of selection bias/incomplete data, while Deeks' funnel plot asymmetry for SOFA suggests possible publication bias that may influence the results.

6. Conclusion

The SOFA score remains the optimal predictor of sepsis mortality risk, whereas the qSOFA score demonstrates suboptimal overall predictive ability. LqSOFA achieves comparable accuracy to SOFA by synergistically combining the advantages of lactate and qSOFA with high specificity, which is particularly valuable for rapid risk exclusion in resource-limited settings (ED/LMICs). Future studies should validate LqSOFA across diverse clinical settings and underrepresented LMIC regions and explore the integration of dynamic lactate clearance metrics.

Supporting information

S1 Fig. Distribution of Predictor Combinations in Included Studies. (a) SOFA vs. PCT; (b) SOFA vs. Lactate; (c) SOFA vs. qSOFA; (d) SOFA vs. LqSOFA; (f) LqSOFA vs. qSOFA. Caption: Venn diagrams quantify study overlap between predictors: Blue circles represent studies reporting SOFA data (Panel a: $n = 8$), green circles represent comparator metrics (Panel a: PCT $n = 2$), intersection values indicate studies with complete paired data (confusion matrices + AUROC/95% CI; Panel a: $n = 10$), and yellow circles with arrows represent studies with only AUROC/95% CI pairs (Panel a: $n = 2$). Analytical approach: 1) Metrics for individual predictors use all studies in their colored circles (e.g., SOFA specificity: $8 + 10 = 18$ studies); 2) AUROC comparisons combine intersection and yellow-circle studies (e.g., SOFA vs. PCT: $10 + 2 = 12$ studies).

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S2 Fig. Risk of bias and applicability concerns graph of included studies.

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S3 Fig. Risk of bias and applicability concerns graph of included studies.

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S4 Fig. Risk of bias and applicability concerns graph of included studies.

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S5 Fig. Forest plot of pooled sensitivity and specificity. (a) PCT; (b) Lactate; (c) qSOFA; (d) Lqsofa; (f) Sofa.

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S6 Fig. Deek's funnel plot for publication bias. (a) PCT; (b) Lactate; (c) qSOFA; (d) Lqsofa; (f) Sofa.

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S7 Fig. The results of univariable meta – regression and subgroup analyses. (a) PCT; (b) Lactate; (c) qSOFA; (d) Lqsofa; (f) Sofa.

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S1 Table. Search Strategies.

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S2 Table. Subgroup Analyses of Pooled Diagnostic Performance of PCT in Predicting Sepsis Patient Mortality.

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S3 Table. Subgroup Analyses of Pooled Diagnostic Performance of Lactate in Predicting Sepsis Patient Mortality.

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S4 Table. Subgroup Analyses of Pooled Diagnostic Performance of qSOFA in Predicting Sepsis Patient Mortality.

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S5 Table. Subgroup Analyses of Pooled Diagnostic Performance of SOFA in Predicting Sepsis Patient Mortality.
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S1 File. PRISMA 2009 checklist.
(DOCX)

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Writing – review & editing: Jinmei Lu, Zaixing Zheng.

References

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801–10. <https://doi.org/10.1001/jama.2016.0287> PMID: 26903338
2. Kempker JA, Martin GS. A global accounting of sepsis. *Lancet*. 2020;395(10219):168–70. [https://doi.org/10.1016/S0140-6736\(19\)33065-X](https://doi.org/10.1016/S0140-6736(19)33065-X) PMID: 31954445
3. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med*. 1996;22(7):707–10. <https://doi.org/10.1007/BF01709751> PMID: 8844239
4. Shinde VV, Jha A, Natarajan MSS, Vijayakumari V, Govindaswamy G, Sivaasubramani S, et al. Serum procalcitonin vs SOFA score in predicting outcome in sepsis patients in medical intensive care unit. *Indian J Crit Care Med*. 2023;27(5):348–51. <https://doi.org/10.5005/jp-journals-10071-24462> PMID: 37214125
5. Lie KC, Lau C-Y, Van Vinh Chau N, West TE, Limmathurotsakul D, for Southeast Asia Infectious Disease Clinical Research Network. Utility of SOFA score, management and outcomes of sepsis in Southeast Asia: a multinational multicenter prospective observational study. *J Intensive Care*. 2018;6:9. <https://doi.org/10.1186/s40560-018-0279-7> PMID: 29468069
6. Serafim R, Gomes JA, Salluh J, Póvoa P. A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality: A Systematic Review and Meta-Analysis. *Chest*. 2018;153(3):646–55. <https://doi.org/10.1016/j.chest.2017.12.015> PMID: 29289687
7. Machado FR, Cavalcanti AB, Monteiro MB, Sousa JL, Bossa A, Bafi AT, et al. Predictive Accuracy of the Quick Sepsis-related Organ Failure Assessment Score in Brazil. A Prospective Multicenter Study. *Am J Respir Crit Care Med*. 2020;201(7):789–98. <https://doi.org/10.1164/rccm.201905-0917OC> PMID: 31910037
8. Rudd KE, Seymour CW, Aluisio AR, Augustin ME, Bagenda DS, Beane A, et al. Association of the Quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) Score With Excess Hospital Mortality in Adults With Suspected Infection in Low- and Middle-Income Countries. *JAMA*. 2018;319(21):2202–11. <https://doi.org/10.1001/jama.2018.6229> PMID: 29800114
9. Endo S, Aikawa N, Fujishima S, Sekine I, Kogawa K, Yamamoto Y, et al. Usefulness of procalcitonin serum level for the discrimination of severe sepsis from sepsis: a multicenter prospective study. *J Infect Chemother*. 2008;14(3):244–9. <https://doi.org/10.1007/s10156-008-0608-1> PMID: 18574663
10. Lee C-C, Chen S-Y, Tsai C-L, Wu S-C, Chiang W-C, Wang J-L, et al. Prognostic value of mortality in emergency department sepsis score, procalcitonin, and C-reactive protein in patients with sepsis at the emergency department. *Shock*. 2008;29(3):322–7. <https://doi.org/10.1097/shk.0b013e31815077ca> PMID: 17724429
11. Casserly B, Phillips GS, Schorr C, Dellinger RP, Townsend SR, Osborn TM, et al. Lactate measurements in sepsis-induced tissue hypoperfusion: results from the Surviving Sepsis Campaign database. *Crit Care Med*. 2015;43(3):567–73. <https://doi.org/10.1097/CCM.0000000000000742> PMID: 25479113
12. Shetty A, MacDonald SP, Williams JM, van Bockxmeer J, de Groot B, Esteve Cuevas LM, et al. Lactate ≥ 2 mmol/L plus qSOFA improves utility over qSOFA alone in emergency department patients presenting with suspected sepsis. *Emerg Med Australas*. 2017;29(6):626–34. <https://doi.org/10.1111/1742-6723.12894> PMID: 29178274
13. Yu H, Nie L, Liu A, Wu K, Hsein Y-C, Yen DW, et al. Combining procalcitonin with the qSOFA and sepsis mortality prediction. *Medicine (Baltimore)*. 2019;98(23):e15981. <https://doi.org/10.1097/MD.00000000000015981> PMID: 31169735

14. Xia Y, Zou L, Li D, Qin Q, Hu H, Zhou Y, et al. The ability of an improved qSOFA score to predict acute sepsis severity and prognosis among adult patients. *Medicine (Baltimore)*. 2020;99(5):e18942. <https://doi.org/10.1097/MD.00000000000018942> PMID: [32000414](#)
15. McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, and the PRISMA-DTA Group, et al. Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. *JAMA*. 2018;319(4):388–96. <https://doi.org/10.1001/jama.2017.19163> PMID: [29362800](#)
16. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011;155(8):529–36. <https://doi.org/10.7326/0003-4819-155-8-201110180-00009> PMID: [22007046](#)
17. Reitsma JB, Glas AS, Rutjes AWS, Scholten RJPM, Bossuyt PM, Zwinderman AH. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *J Clin Epidemiol*. 2005;58(10):982–90. <https://doi.org/10.1016/j.jclinepi.2005.02.022> PMID: [16168343](#)
18. Daga MK, Rohatgi I, Mishra R, Kumar N, Mawari G, Mishra TK, et al. Lactate enhanced-quick Sequential Organ Failure Assessment 2 (LqSOFA2): A new score for bedside prognostication of patients with sepsis. *Indian J Med Res*. 2021;154(4):607–14. https://doi.org/10.4103/ijmr.IJMR_319_20 PMID: [35435346](#)
19. Julián-Jiménez A, Rubio-Díaz R, González Del Castillo J, García-Lamberechts EJ, Huarte Sanz I, Navarro Bustos C, et al. Ability of qSOFA1-lactate to predict 30-day mortality in patients seen for infection in the Emergency Department. *Rev Esp Quimioter*. 2023;36(4):408–15. <https://doi.org/10.37201/req/008.2023> PMID: [37149901](#)
20. Silva CM, Baptista JP, Mergulhão P, Froes F, Gonçalves-Pereira J, Pereira JM, et al. Prognostic value of hyperlactatemia in infected patients admitted to intensive care units: a multicenter study. *Rev Bras Ter Intensiva*. 2022;34(1):154–62. <https://doi.org/10.5935/0103-507X.20220010-pt> PMID: [35766665](#)
21. Sinto R, Suwanto S, Lie KC, Harimurti K, Widodo D, Pohan HT. Prognostic accuracy of the quick Sequential Organ Failure Assessment (qSOFA)-lactate criteria for mortality in adults with suspected bacterial infection in the emergency department of a hospital with limited resources. *Emerg Med J*. 2020;37(6):363–9. <https://doi.org/10.1136/emmermed-2018-208361> PMID: [32317296](#)
22. Suárez-Santamaría M, Santolaria F, Pérez-Ramírez A, Alemán-Valls M-R, Martínez-Riera A, González-Reimers E, et al. Prognostic value of inflammatory markers (notably cytokines and procalcitonin), nutritional assessment, and organ function in patients with sepsis. *Eur Cytokine Netw*. 2010;21(1):19–26. <https://doi.org/10.1684/ecn.2009.0185> PMID: [20146986](#)
23. Suttapanit K, Wisan M, Sanguanwit P, Prachanukool T. Prognostic Accuracy of VqSOFA for Predicting 28-day Mortality in Patients with Suspected Sepsis in the Emergency Department. *Shock*. 2021;56(3):368–73. <https://doi.org/10.1097/SHK.0000000000001754> PMID: [33577246](#)
24. Combined suPAR and qSOFA for the prediction of 28-day mortality in sepsis patients. *SV*. 2021. <https://doi.org/10.22514/sv.2021.143>
25. Wright SW, Hantrakun V, Rudd KE, Lau C-Y, Lie KC, Chau NVV, et al. Enhanced bedside mortality prediction combining point-of-care lactate and the quick Sequential Organ Failure Assessment (qSOFA) score in patients hospitalised with suspected infection in southeast Asia: a cohort study. *Lancet Glob Health*. 2022;10(9):e1281–8. [https://doi.org/10.1016/S2214-109X\(22\)00277-7](https://doi.org/10.1016/S2214-109X(22)00277-7) PMID: [35961351](#)
26. Zhao R, Dong S. Clinical value of serum endocan and procalcitonin in early diagnosis and prognosis evaluation of sepsis. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2017;29(4):321–6. <https://doi.org/10.3760/cma.j.issn.2095-4352.2017.04.007> PMID: [28420465](#)
27. Althunayyan SM, Aledeny AA, Malabarey MA, Alshaqaaq AI, Haj-Ali EO, Alhomsy MW, et al. The utility of initial lactate for the quick sequential organ failure assessment (LqSOFA) for emergency septic patients. *Am J Emerg Med*. 2025;91:118–22. <https://doi.org/10.1016/j.ajem.2025.02.042> PMID: [40043552](#)
28. Chi H, Wang H, Li Q, Lian Z, Zhang C, Zhang S, et al. Prognostic value of serum sodium variability within 72 hours and lactic acid combined with severity score in patients with sepsis. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2023;35(5):458–62. <https://doi.org/10.3760/cma.j.cn121430-20221104-00966> PMID: [37308223](#)
29. Guarino M, Perna B, De Giorgi A, Gambuti E, Alfano F, Catanese EM, et al. A 2-year retrospective analysis of the prognostic value of MqSOFA compared to lactate, NEWS and qSOFA in patients with sepsis. *Infection*. 2022;50(4):941–8. <https://doi.org/10.1007/s15010-022-01768-0>
30. Hao C, Hu Q, Zhu L, Xu H, Zhang Y. Combined prognostic value of serum lactic acid, procalcitonin and severity score for short-term prognosis of septic shock patients. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2021;33(3):281–5. <https://doi.org/10.3760/cma.j.cn121430-20201113-00715> PMID: [33834968](#)
31. Jaiswal P, Agrawal S, Kumar S, Acharya S, Wanjari A, Bawankule S, et al. A two-year cross-sectional study on the impact of serial serum Lactate in comparison with APACHE IV and SOFA Scores in predicting outcomes in patients of sepsis at limited resources rural setup. *Journal of Emergency Medicine, Trauma and Acute Care*. 2022;2022(5). <https://doi.org/10.5339/jemtac.2022.29>
32. Kilinc Toker A, Kose S, Turken M. Comparison of SOFA Score, SIRS, qSOFA, and qSOFA + L Criteria in the Diagnosis and Prognosis of Sepsis. *Eurasian J Med*. 2021;53(1):40–7. <https://doi.org/10.5152/eurasianjmed.2021.20081> PMID: [33716529](#)
33. Li F, Ye Z, Zhu J, Gu S, Peng S, Fang Y, et al. Early Lactate/Albumin and Procalcitonin/Albumin Ratios as Predictors of 28-Day Mortality in ICU-Admitted Sepsis Patients: A Retrospective Cohort Study. *Med Sci Monit*. 2023;29:e940654. <https://doi.org/10.12659/MSM.940654> PMID: [37518978](#)
34. Li L, Yang L, Yuan Z, Wu Q, Lyu X. The Combination of Systemic Immune-Inflammation Index and Serum Procalcitonin has High Auxiliary Predictive Value for Short-Term Adverse Prognosis in Septic Shock Patients. *J Emerg Med*. 2024;67(4):e357–67. <https://doi.org/10.1016/j.jemermed.2024.05.005> PMID: [39183119](#)

35. Liu S, He C, He W, Jiang T. Lactate-enhanced-qSOFA (LqSOFA) score is superior to the other four rapid scoring tools in predicting in-hospital mortality rate of the sepsis patients. *Ann Transl Med.* 2020;8(16):1013. <https://doi.org/10.21037/atm-20-5410> PMID: [32953813](#)
36. Liu Z, Meng Z, Li Y, Zhao J, Wu S, Gou S, et al. Prognostic accuracy of the serum lactate level, the SOFA score and the qSOFA score for mortality among adults with Sepsis. *Scand J Trauma Resusc Emerg Med.* 2019;27(1):51. <https://doi.org/10.1186/s13049-019-0609-3> PMID: [31039813](#)
37. Noparatkailas N, Inchai J, Deesomchok A. Blood Lactate Level and the Predictor of Death in Non-shock Septic Patients. *Indian J Crit Care Med.* 2023;27(2):93–100. <https://doi.org/10.5005/jp-journals-10071-24404> PMID: [36865504](#)
38. Sen P, Demirdal T, Nemli SA, Sencan A. Diagnostic and prognostic value of new bioscore in critically ill septic patients. *Arch Physiol Biochem.* 2022;128(2):300–5. <https://doi.org/10.1080/13813455.2019.1677720> PMID: [31687850](#)
39. Wang J, Gao P, Guo S, Liu Y, Shao L, Kang H, et al. Analysis of death risk factors for nosocomial infection patients in an ICU: a retrospective review of 864 patients from 2009 to 2015. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue.* 2016;28(8):704–8. <https://doi.org/10.3760/cma.j.issn.2095-4352.2016.08.007> PMID: [27434560](#)
40. Yoo KH, Choi S-H, Suh GJ, Chung SP, Choi HS, Park YS, et al. The usefulness of lactate/albumin ratio, C-reactive protein/albumin ratio, procalcitonin/albumin ratio, SOFA, and qSOFA in predicting the prognosis of patients with sepsis who presented to EDs. *Am J Emerg Med.* 2024;78:1–7. <https://doi.org/10.1016/j.ajem.2023.12.028> PMID: [38176175](#)
41. Zhang Y, Khalid S, Jiang L. Diagnostic and predictive performance of biomarkers in patients with sepsis in an intensive care unit. *J Int Med Res.* 2019;47(1):44–58. <https://doi.org/10.1177/0300060518793791> PMID: [30477377](#)
42. Zhou H, Lan T, Guo S. Prognostic Prediction Value of qSOFA, SOFA, and Admission Lactate in Septic Patients with Community-Acquired Pneumonia in Emergency Department. *Emerg Med Int.* 2020;2020:7979353. <https://doi.org/10.1155/2020/7979353> PMID: [32322422](#)
43. Qiu X, Lei Y-P, Zhou R-X. SIRS, SOFA, qSOFA, and NEWS in the diagnosis of sepsis and prediction of adverse outcomes: a systematic review and meta-analysis. *Expert Rev Anti Infect Ther.* 2023;21(8):891–900. <https://doi.org/10.1080/14787210.2023.2237192> PMID: [37450490](#)
44. Moncada-Gutiérrez D, Vásquez-Tirado GA, Meregildo-Rodríguez ED, Quispe-Castañeda CV, Cuadra-Campos M, Abanto-Montalván PH, et al. Lactate-enhanced-qSOFA (LqSOFA) score as a predictor of in-hospital mortality in patients with sepsis: systematic review and meta-analysis. *Eur J Trauma Emerg Surg.* 2025;51(1):33. <https://doi.org/10.1007/s00068-024-02757-8> PMID: [39853387](#)
45. Hwang SY, Shin TG, Jo IJ, Jeon K, Suh GY, Lee TR, et al. Association between hemodynamic presentation and outcome in sepsis patients. *Shock.* 2014;42(3):205–10. <https://doi.org/10.1097/SHK.0000000000000205> PMID: [24978884](#)