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SUPPLEMENTAL DATA

Presepsin as a diagnostic biomarker for sepsis across neonates, children, and adults: A meta-analysis

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Full article is available at the following link: Presepsin as a diagnostic biomarker for sepsis across neonates, children, and adults: A meta-analysis | Biomolecules and Biomedicine

Database search strategies

PubMed： ((presepsin[Title/Abstract]) OR (soluble CD14 subtype[Title/Abstract])) OR (P-SEP[Title/Abstract])) OR (sCD14-ST[Title/Abstract])) AND ((sepsis[Mesh] OR (sepsis[Title/Abstract]) OR (septic shock[Title/Abstract])) OR (septicemia[Title/Abstract]) AND ((sensitivity and specificity[Mesh]) OR (diagnostic[Mesh]) OR (ROC [Mesh]) OR ((Sensitivity[Title/Abstract]) OR (Specificity[Title/Abstract])) OR (diagnosis[Title/Abstract]) OR (Diagnostic Tests[Title/Abstract])) OR (ROC[Title/Abstract])) OR (diagnostic accuracy[Title/Abstract])) OR (AUC[Title/Abstract])

EMBASE:

1 'presepsin':ab,ti OR 'soluble CD14 subtype':ab,ti OR 'P-SEP':ab,ti OR 'sCD14-ST':ab,ti

#2 'sepsis':ab,ti OR 'septic shock':ab,ti OR 'septicemia':ab,ti

#3 'Sensitivity':ab,ti OR 'Specificity':ab,ti OR 'diagnosis':ab,ti OR 'diagnostic':ab,ti OR 'Diagnostic Tests':ab,ti OR 'diagnostic accuracy':ab,ti OR 'ROCc':ab,ti OR 'AUC':ab,ti

#4: # 1 AND #2 AND #3

Web Of Science

#1 TI= (presepsin OR sCD14-ST OR soluble CD14 subtype OR P-SEP)

#2 TI=(sepsis OR septic shock OR septicemia)

#3 TI=(Diagnostic OR Diagnostic Tests OR diagnosis OR sensitivity OR specificity OR ROC OR AUC OR diagnostic accuracy)

#4 ： #1 AND #2 AND #3

Cochrane

1 (presepsin OR sCD14-ST OR soluble CD14 subtype OR P-SEP)

#2 (sepsis OR septic shock OR septicemia)

#3 (Diagnostic OR Diagnostic Tests OR diagnosis OR sensitivity OR specificity OR ROC OR AUC OR diagnostic accuracy)

#4：# 1 AND #2 AND #3

(presepsin OR sCD14-ST OR soluble CD14 subtype OR P-SEP) AND (sepsis OR septic shock OR septicemia) AND (Diagnostic OR Diagnostic Tests OR diagnosis OR sensitivity OR specificity OR ROC OR AUC OR diagnostic accuracy)

Table S1. Univariable meta-regression results

Parameter	Category	Studies	Sensitivity	p_1	Specificity	p_2	LRTChi^2	p	I^2
Year	Post-2020	18	0.80 (0.73-0.86)	< 0.001	0.76 (0.66-0.87)	< 0.001	12.44	< 0.001	84
	Pre-2020	29	0.87 (0.83-0.91)		0.90 (0.85-0.94)				
Country	Non-Asia	25	0.85 (0.80-0.89)	< 0.001	0.89 (0.84-0.94)	0.12	2.78	0.25	28
	Asia	22	0.84 (0.79-0.89)		0.81 (0.72-0.89)				
Study design	Retrospective study	3	0.81 (0.67-0.96)	0.07	0.72 (0.41-1.00)	0.18	1.53	0.47	0
	Prospective study	44	0.85 (0.81-0.88)		0.86 (0.81-0.91)				
Data sources	Multi-center	5	0.80 (0.67-0.92)	< 0.01	0.91 (0.81-1.00)	0.76	1.46	0.48	0
	Single-center	42	0.85 (0.81-0.89)		0.85 (0.79-0.90)				

Clinical setting	ICU	37	0.84 (0.80-0.88)	< 0.001	0.87 (0.82-0.92)	0.43	1.88	0.39	0
	Non-ICU	10	0.85 (0.78-0.92)		0.78 (0.65-0.92)				
Specimen type	Whole blood	17	0.87 (0.82-0.92)	< 0.001	0.91 (0.85-0.97)	0.24	5.12	0.08	61
	Plasma	30	0.83 (0.79-0.88)		0.82 (0.75-0.89)				
Analytical method	CLEIA	35	0.84 (0.81-0.88)	< 0.001	0.83 (0.77-0.90)	< 0.01	1.9	0.39	0
	ELISA	12	0.84 (0.77-0.91)		0.90 (0.84-0.97)				
Sample size	≥ 100	20	0.82 (0.77-0.87)	< 0.001	0.86 (0.79-0.93)	0.01	1.61	0.45	0
	< 100	27	0.86 (0.82-0.91)		0.85 (0.79-0.92)				

Abbreviations: ICU, intensive care unit; CLEIA, chemiluminescent enzyme immunoassay; ELISA, enzyme-linked immunosorbent assay; LRTChi², likelihood ratio test chi-square; I², I-squared statistic.

Table S2. Heterogeneity comparison among different diagnostic criteria

Comparison	Diagnostic criteria	Studies	Sensitivity	p_1	Specificity	p_2	LRTChi^2	p	I^2
1	Positive blood culture	19	0.85 (0.79-0.91)	< 0.01	0.94 (0.89-0.98)	0.38	4.03	0.13	50
	Sepsis-2	6	0.88 (0.78-0.97)		0.79 (0.62-0.95)				
2	Positive blood culture	19	0.85 (0.79-0.91)	< 0.001	0.94 (0.89-0.98)	0.51	14.6	< 0.001	86
	Sepsis-3	16	0.81 (0.74-0.87)		0.73 (0.61-0.85)				
3	Positive blood culture	19	0.85 (0.79-0.91)	0.01	0.94 (0.89-0.98)	0.92	1.52	0.47	0
	Clinical judgement	6	0.91 (0.83-0.99)		0.88 (0.79-0.97)				
4	Sepsis-2	6	0.88 (0.78-0.97)	< 0.01	0.79 (0.62-0.95)	0.41	3.17	0.21	37
	Sepsis-3	16	0.81 (0.74-0.87)		0.73 (0.61-0.85)				
5	Sepsis-2	6	0.88 (0.78-0.97)	0.09	0.79 (0.62-0.95)	< 0.001	1.96	0.37	0
	Clinical judgement	6	0.91 (0.83-0.99)		0.88 (0.79-0.97)				
6	Sepsis-3	16	0.81 (0.74-0.87)	< 0.001	0.73 (0.61-0.85)	< 0.01	7.19	0.03	72
	Clinical judgement	6	0.91 (0.83-0.99)		0.88 (0.79-0.97)				

Table S3. Heterogeneity comparison among different populations

Comparison	Population	Studies	Sensitivity	p_1	Specificity	p_2	LRTChi^2	p	I^2
1	Neonates	16	0.90 (0.86-0.95)	0.56	0.92 (0.87-0.96)	0.72	5.18	0.08	61
	Children	5	0.82 (0.69-0.95)		0.80 (0.67-0.93)				
2	Neonates	16	0.90 (0.86-0.95)	< 0.01	0.92 (0.87-0.96)	0.47	15.13	< 0.001	87
	Adults	26	0.81 (0.77-0.86)		0.81 (0.73-0.89)				
3	Adults	26	0.81 (0.77-0.86)	0.02	0.80 (0.71-0.90)	0.52	0.03	0.99	0
	Children	5	0.82 (0.69-0.95)		0.80 (0.67-0.93)				

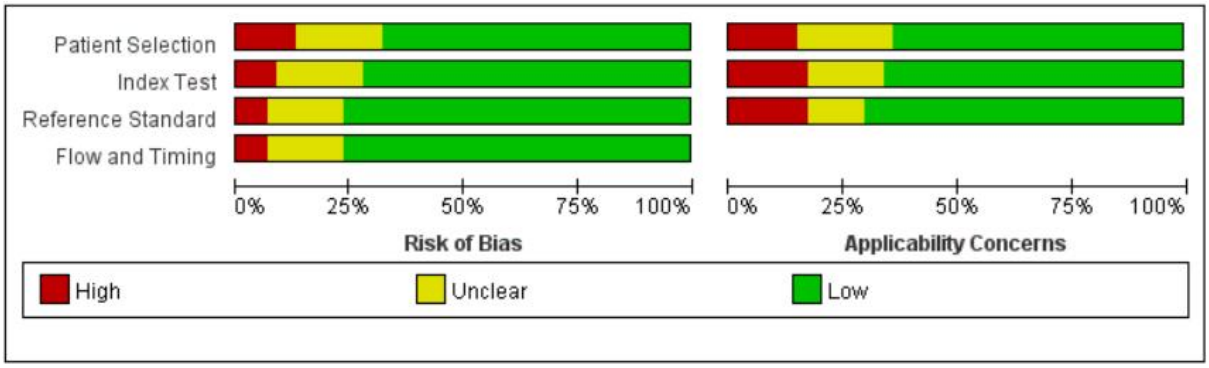

Figure S1. QUADAS-2 quality assessment of included studies. The figure summarizes the risk of bias and applicability concerns across the four quadas-2 domains: Patient selection, index test, reference standard, and flow and timing. Green indicates low risk/concern, yellow indicates unclear risk/concern, and red indicates high risk/concern. Seventeen studies showed unclear risk of bias in patient selection, index test, and flow and timing due to insufficient reporting. Six studies (12.8%) diagnosed sepsis solely on clinical judgment without a defined reference standard. Overall, most studies demonstrated low risk of bias and good applicability.

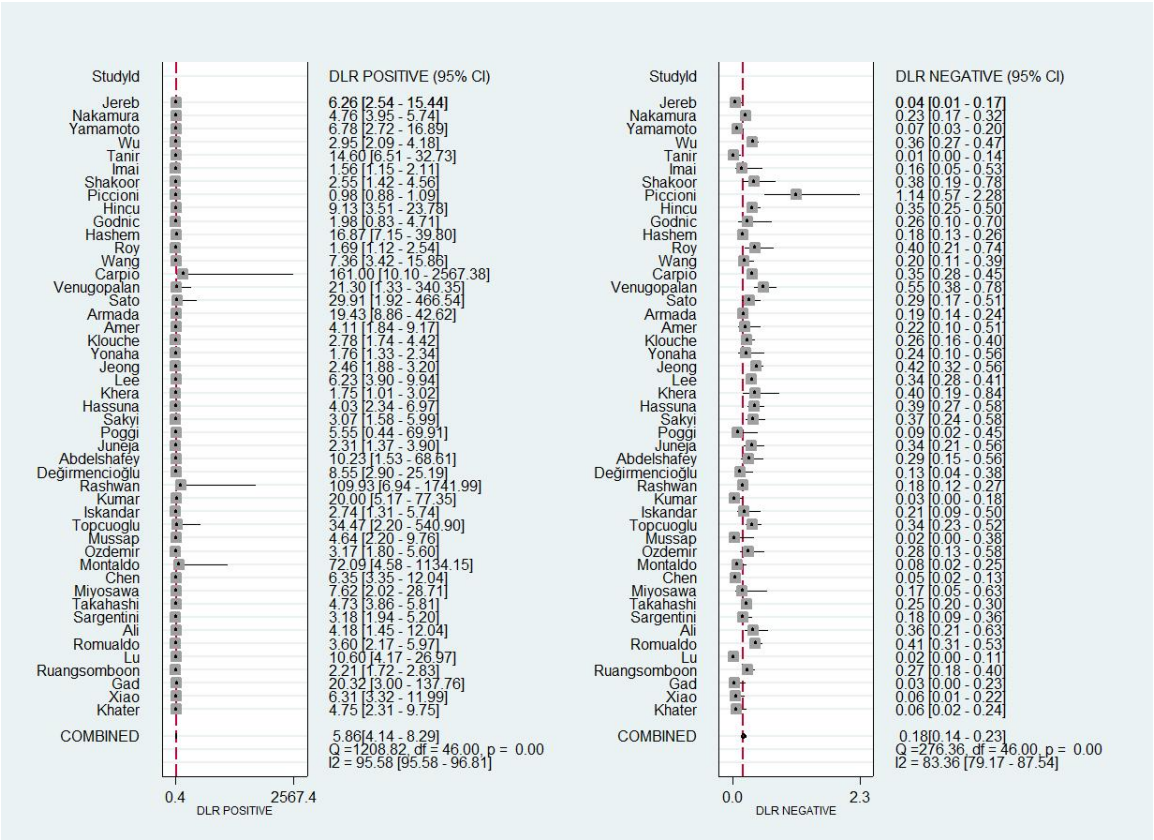

Figure S2. Pooled positive and negative likelihood ratios of included studies.

Forest plots show the individual study estimates and 95% CIs for the PLR and NLR. The diamond indicates the pooled effect size from 47 studies. The pooled PLR was 5.86 (95% CI: 4.14–8.29) and the pooled NLR was 0.18 (95% CI: 0.14–0.23). Substantial heterogeneity was observed across studies (PLR: $I^2 = 95.58\%$; NLR: $I^2 = 83.36\%$). Abbreviations: CI, confidence interval; NLR, negative likelihood ratio; PLR, positive likelihood ratio.

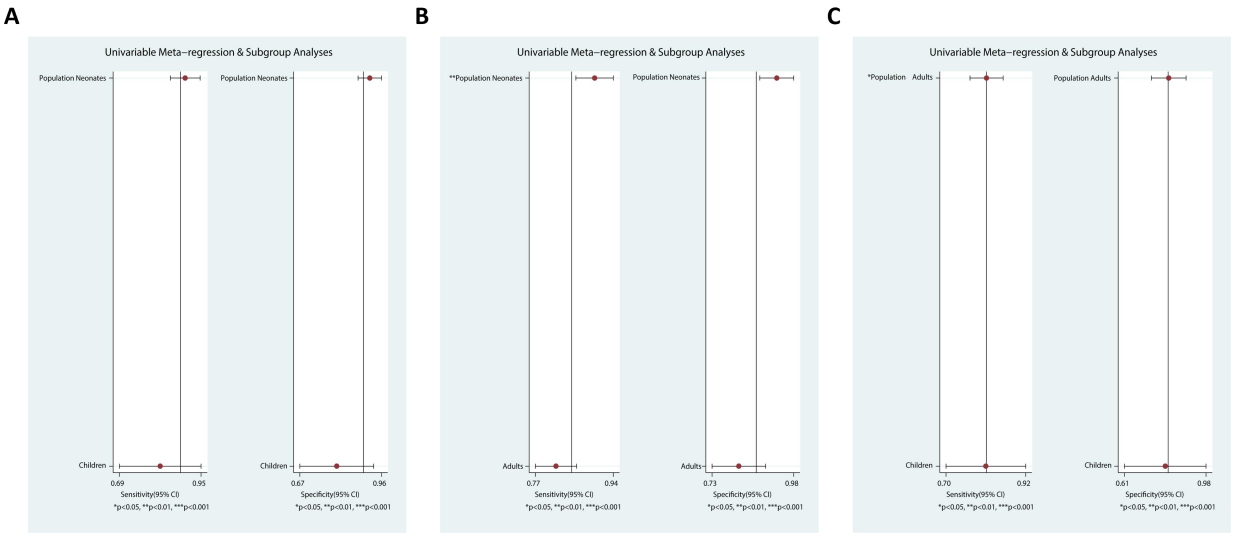

Figure S3. Subgroup analyses of heterogeneity by population. Forest plots of meta-regression results comparing (A) neonates and children; (B) neonates and adults; and (C) children and adults.

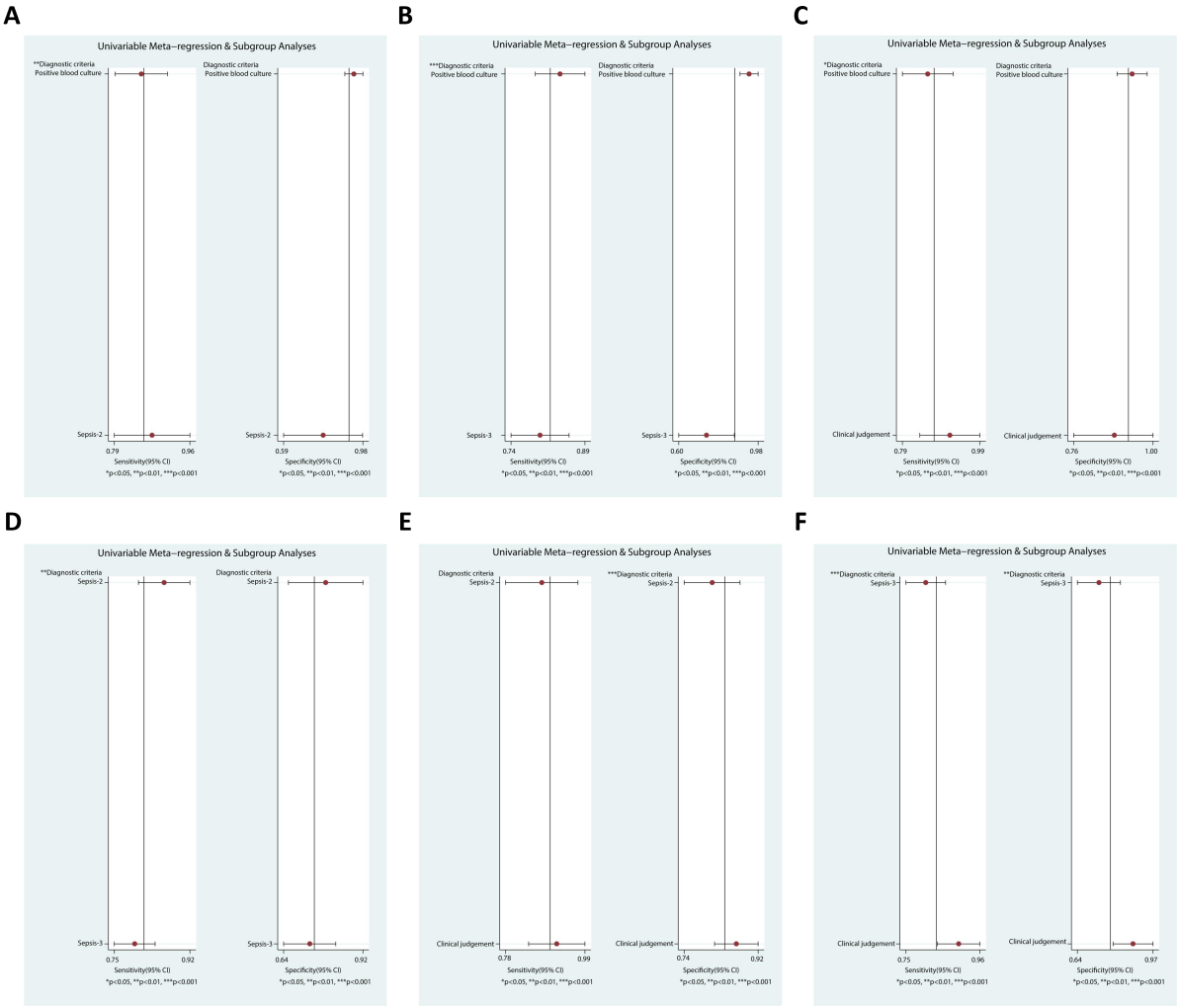

Figure S4. Analyses of heterogeneity sources in diagnostic criteria. (A) Positive blood culture and sepsis-2; (B) Positive blood culture and sepsis-3; (C) Positive blood culture and clinical judgement; (D) Sepsis-2 and sepsis-3; E: Sepsis-2 and clinical judgement; (F) Sepsis-3 and clinical judgement.

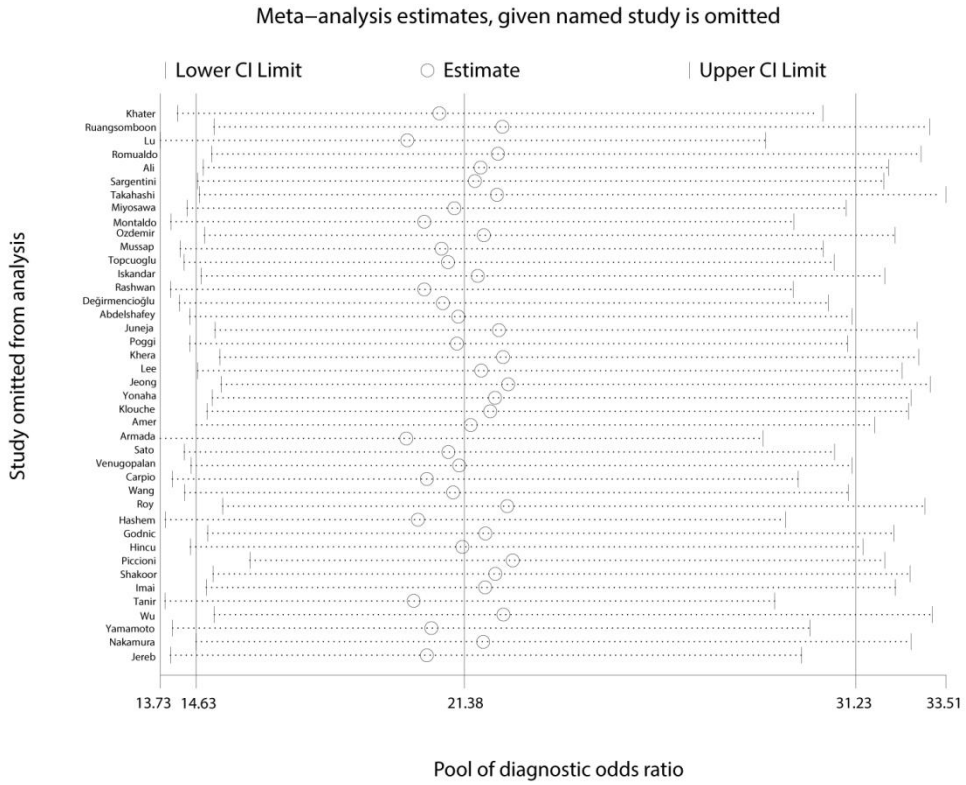

Figure S5. Sensitivity analysis of included studies (limited to studies with a clearly defined standard).