ISSN: 3152-8686

Vol3; Issue4, Nov. 2026

JOURNAL OF
TAZEEZ FOR PUBLIC HEALTH

AN OFFICIAL JOURNAL OF SAUDI HEALTH PROMOTION AND EDUCATION ASSOCIATION

Systematic review

Recognition of Serious Bacterial Infections (Sepsis, Meningitis, and Urinary Tract Infection) in Febrile Infants Presenting to the Emergency Department: A Systematic Review of Clinical Prediction Rules

Mazi Mohammed Alanazi[1], Bayan Abdullah Alsofyani[2], Layan Talal Alraddadi[3], Halimah Mohammed Mujayri[4], Haifa Mohammed Alhamad[5], Raghad Abdulmajeed Khalmorad[6], Shaimaa Osamah Salamah[7], Zainab Saleh Aljasim[8], Huda Saleh Alzubaidi[9], Rahaf Hani AlHazmi[10]

1. Saudi and Jordanian Board Emergency Medicine, Emergency Department, Head of Emergency Research Unit, First Health Cluster, Riyadh, Saudi Arabia. ORCID: 0009-0003-5836-8086.
2. Medical Intern, College of Medicine, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia. Email: bayan9603@gmail.com
3. Medical Intern, College of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia. Email: layan.t.800@gmail.com
4. Medical Intern, College of Medicine, Jazan University, Jazan, Saudi Arabia. Email: Hlooom22c@gmail.com
5. Medical Intern, College of Medicine, Dar Al-Uloom University, Riyadh, Saudi Arabia. Email: 2218601@du.edu.sa
6. Medical Intern, College of Medicine, Al-Rayan National College, Madinah, Saudi Arabia. Email: Raghad.murad19@gmail.com
7. Medical Intern, Kasr Al Ainy Faculty of Medicine, Cairo University, Cairo, Egypt. Email: Shaymaa435@gmail.com
8. Medical Intern, College of Medicine, Arabian Gulf University, Manama, Bahrain. Email: Zainabaljasim66@gmail.com
9. General Physician, Al Qunfudah College of Medicine, Umm Al-Qura University, Al Qunfudah, Saudi Arabia. Email: huda.alzubaidi25@gmail.com
10. Medical Intern, College of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia. Email: rahaf.alhaz@gmail.com

Published: 11 Nov, 2026

https://doi.org/10.65759/5wx65j72

Copyright © 2025 The Author(s). Published by Lizzy B. This is an open-access article distributed under the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited).

11/11/2026

ISSN: 3152-8686

Abstract

Background: Fever in infants aged 90 days or younger often leads to lumbar puncture, hospital admission and empirical antibiotics, although only a minority of these infants have a serious bacterial infection (SBI). Clinical prediction rules were developed to separate low-risk infants from those who need a full evaluation. Objective: To synthesize evidence on how well clinical prediction rules identify SBI and invasive bacterial infection (IBI) in febrile infants presenting to the emergency department. Methods: This systematic review followed the PRISMA 2020 statement. Two authors independently searched PubMed, Scopus, Web of Science and the Cochrane Library from inception to 31 May 2026. They screened records, extracted data and assessed risk of bias with QUADAS-2. Eligible studies derived or validated a prediction rule in febrile infants aged ≤90 days and reported accuracy against culture-confirmed SBI or IBI. Narrative synthesis was used because the studies were heterogeneous. Results: Ten studies met the inclusion criteria. Together they covered more than 17,000 infant evaluations, with partial overlap between cohorts. Rules combining urinalysis, absolute neutrophil count and procalcitonin gave the best balance of sensitivity and specificity: sensitivity was 92.0-97.7% and negative predictive value was above 99%. The updated PECARN rule kept 94.2% sensitivity in neonates and missed no case of meningitis. Used without procalcitonin, the American Academy of Pediatrics algorithm reached sensitivity of 88.9-100%, with specificity of 0-40.4%. Point-based rules and rules without procalcitonin showed lower specificity. Conclusion: Rules based on procalcitonin reliably identify febrile infants at low risk. External validation in neonates and in resource-limited settings is still limited.

Keywords: Febrile infant; Serious bacterial infection; Invasive bacterial infection; Clinical prediction rule; Procalcitonin; Emergency department; Bacterial meningitis; Urinary tract infection

Introduction

Fever is one of the most frequent reasons infants aged 90 days or younger visit the emergency department (ED), and a minority of these infants have a serious bacterial infection (SBI). In a multicentre cohort of 4,778 febrile infants aged 60 days or younger, urinary tract infection (UTI) accounted for most bacterial infections, and Escherichia coli was the dominant pathogen (1). Bacteraemia and bacterial meningitis, grouped together as invasive bacterial infection (IBI), are less frequent and remain the main clinical concern in this age group. A meta-analysis reported a higher prevalence of bacteraemia and meningitis in febrile neonates than in infants in their second month of life (2).

The microbiology of bacteraemia in infants has changed over the past two decades. In a large integrated health-system cohort, E. coli replaced group B Streptococcus as the leading cause of bacteraemia in infants aged 1 week to 3 months. This change followed the widespread use of intrapartum antibiotic prophylaxis, and it altered the baseline risk on which older rules were built (3).

Early low-risk criteria, such as the Rochester criteria, combined clinical appearance, white blood cell count and urinalysis. In the Rochester appraisal, infants who met the low-risk criteria had a negative predictive value of 98.9% for SBI (4). A later literature review found that the Rochester, Philadelphia and Boston criteria achieved high negative predictive values, although evidence for their use in neonates was limited (5). In a large prospective cohort, the white blood cell count and the absolute neutrophil count each showed poor accuracy for IBI, which weakened rules that depended on these markers (6).

Newer approaches added procalcitonin and C-reactive protein and moved the primary outcome toward IBI. In 2021, the American Academy of Pediatrics (AAP) published a guideline for well-appearing febrile infants aged 8-60 days, with management stratified by age bands of 8-21, 22-28 and 29-60 days and guided by inflammatory markers (7). Several rules now coexist with different

11/11/2026

age ranges, biomarkers and outcome definitions, and clinicians lack a clear comparative evidence base (5,7). This systematic review therefore aimed to synthesize the diagnostic performance of clinical prediction rules for recognizing SBI, including sepsis with bacteraemia, meningitis and UTI, in febrile infants presenting to the ED.

Methods

Protocol and reporting

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. Two authors carried out every stage of the review independently. Disagreements were resolved by discussion until consensus was reached.

Eligibility criteria

Eligibility followed the PICOTS framework:

Population: febrile infants aged 90 days or younger (temperature ≥38.0 °C) evaluated in an ED; **Index test:** any clinical prediction rule, decision rule, score or guideline-based algorithm that combined clinical and/or laboratory variables; **Reference standards:** blood culture for bacteraemia, cerebrospinal fluid culture for bacterial meningitis and urine culture for UTI. SBI was defined as any of these three infections, and IBI as bacteraemia and/or bacterial meningitis; **Study designs:** prospective or retrospective cohorts, case-control studies and pooled cohort analyses that reported sensitivity, specificity or negative predictive value, or that gave enough data to calculate them.

Reviews, editorials and conference abstracts were excluded. Studies restricted to ill-appearing or premature infants, and studies of single biomarkers without a rule, were also excluded. Only full-text articles in English were considered.

Information sources and search strategy

PubMed/MEDLINE, Scopus, Web of Science Core Collection and the Cochrane Library were searched from inception to 31 May 2026. The PubMed strategy combined Medical Subject Headings with free-text terms:

("Infant"[MeSH] OR infant* OR neonat* OR newborn*) AND ("Fever"[MeSH] OR febrile OR fever) AND ("Bacterial Infections"[MeSH] OR "serious bacterial infection" OR "invasive bacterial infection" OR bacteremia OR bacteraemia OR meningitis OR "urinary tract infection" OR sepsis) AND ("Clinical Decision Rules"[MeSH] OR "prediction rule" OR "decision rule" OR "risk stratification" OR algorithm OR score OR criteria) AND ("Emergency Service, Hospital"[MeSH] OR "emergency department")

This string was adapted to the syntax of each database. The reference lists of included articles and relevant reviews were also searched by hand.

Study selection

Records were exported to a reference manager and duplicates were removed. Both authors independently screened titles and abstracts against the eligibility criteria and then assessed the full texts of potentially relevant records. Reasons for exclusion at the full-text stage were documented.

Data collection

A standardized extraction form was piloted on two studies and then applied independently by both authors. The extracted items were:

first author, year and country; setting, design and enrolment period; age range and sample size;

11/11/2026

outcome definitions and the prevalence of SBI and IBI; rule components and thresholds; diagnostic accuracy measures with 95% confidence intervals (CI). When accuracy measures were not reported directly, they were calculated from the reported counts.

Risk of bias assessment

Both authors independently appraised methodological quality with the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool. The tool covers four domains: patient selection, index test, reference standard, and flow and timing.

Data synthesis

Age strata, outcome definitions, biomarker thresholds and study designs differed substantially across studies, so no meta-analysis was performed. Results were synthesized narratively and grouped by prediction rule. Sensitivity, specificity and negative predictive value were the principal measures.

Results

The included studies were published between 2016 and 2026. Five came from North America and four from Europe, and one pooled cohorts from six countries (8-17). Most analysed prospectively collected cohorts (8-10,12,14,17). Two were retrospective (13,16), one derivation study used a case-control design (11) and one was a single-centre secondary analysis (15). The upper age limit was 90 days in three studies, 60 days in five and 28 days in one, and one study focused on infants aged 61-90 days (8-17). Where reported, IBI prevalence ranged from 2.0% to 4.5% and SBI prevalence from 9.3% to 20.5% (8,10,12-14,16,17). Table 1 summarizes the characteristics of the included studies.

Step-by-Step approach

The Step-by-Step approach was validated prospectively in 2,185 infants from 11 European EDs. It achieved a sensitivity of 92.0% and a negative predictive value of 99.3% for IBI, and it missed seven infections. In the same cohort, the Rochester criteria reached a sensitivity of 81.6% and the Lab-score 59.8%. The sequential approach assessed appearance, age, urinalysis and procalcitonin first, and C-reactive protein and neutrophil count afterwards (8).

PECARN rules

The PECARN rule was derived from 1,821 infants in 26 United States EDs (10). It classified an infant as low risk when urinalysis was negative, the absolute neutrophil count was ≤4,090/µL and procalcitonin was ≤1.71 ng/mL. In the validation set, sensitivity was 97.7%, specificity 60.0%, negative predictive value 99.6% and negative likelihood ratio 0.04, and no case of meningitis was missed (10).

When the rule was applied externally in a Spanish registry of 1,247 infants, sensitivity was lower: 26 of 256 SBIs and 5 of 38 IBIs occurred in infants classified as low risk (12). The updated PECARN rule uses procalcitonin ≤0.5 ng/mL and neutrophil count ≤4,000/mm³. Among 1,537 infants aged 28 days or younger, it showed 94.2% sensitivity, 41.6% specificity and 99.4% negative predictive value, with no missed meningitis (17).

AAP and United Kingdom guidelines

Applied without C-reactive protein and procalcitonin, the AAP algorithm had sensitivities of 100%, 88.9% and 93.3% in infants aged 8-21, 22-28 and 29-60 days, respectively. The corresponding specificities were 0%, 40.4% and 32.1% (13). In the prospective FIDO cohort of 1,821 infants, the AAP guideline and the British Society for Antimicrobial Chemotherapy (BSAC) guideline each reached a sensitivity of 0.99, with specificities of 0.23 and 0.20, respectively. In the same cohort, the National

11/11/2026

Institute for Health and Care Excellence (NICE) NG143 guideline showed a sensitivity of 0.93 and a specificity of 0.27 (14).

Aronson score

The Aronson IBI score assigns points for age below 21 days, temperature measured in the emergency department, neutrophil count ≥5,185/µL and abnormal urinalysis, and it had an area under the curve of 0.83 (11). At derivation, a score of 2 or higher gave 98.8% sensitivity and 31.3% specificity (11). In the FIDO cohort, external validation gave a lower sensitivity of 0.90, with a specificity of 0.30 (14).

Rules without procalcitonin and rules for older infants

In a single-centre cohort of 1,987 infants, a rule using C-reactive protein ≤22.2 mg/L, temperature ≤39.0 °C and neutrophil count ≤4,500/mm³ kept sensitivity at 100% and raised specificity to 83.8% (15). For infants aged 61-90 days, a PECARN Registry rule based on urinalysis and a maximum temperature ≤38.9 °C reached 86% sensitivity, 58.9% specificity and 99.5% negative predictive value. A companion rule combining procalcitonin ≤0.24 ng/mL with neutrophil count identified every IBI among the infants who had these tests (16). Across four international cohorts, eight statistically derived models showed variable performance, and the authors recommended them as adjunctive tools (9).

Risk of bias

Patient-selection bias was high in the case-control derivation of the Aronson score, because the case-control design fixed the case mix (11). Partial verification affected several cohorts: cerebrospinal fluid was not obtained in every infant, and follow-up was used to classify infants who had no lumbar puncture (10,17). The retrospective designs relied on recorded data and inconsistent biomarker testing, which raised concern in the index-test and flow domains (13,16).

11/11/2026

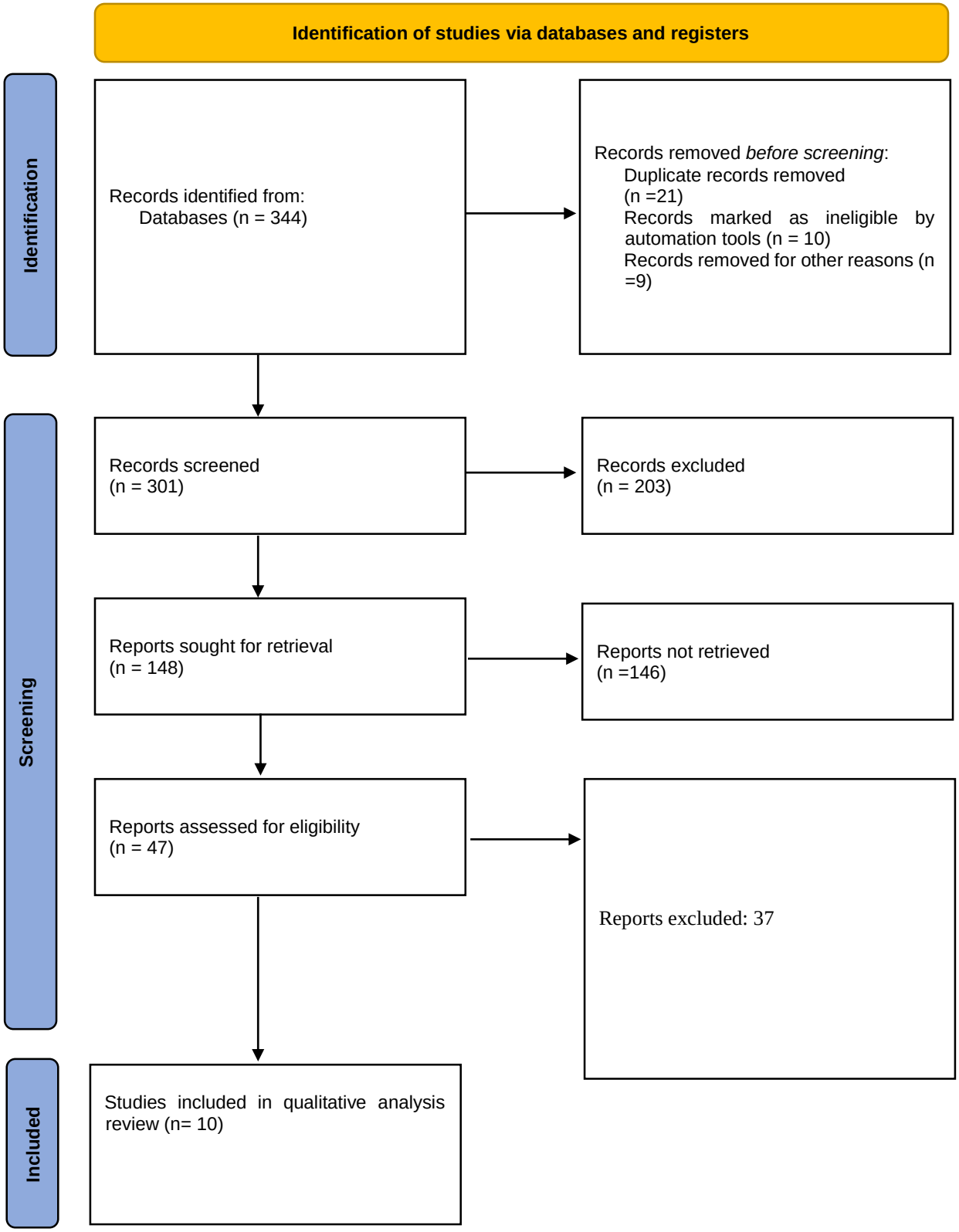


Figure 1: PRISMA flow chart

11/11/2026

Table 1. Characteristics of included studies

Study	Setting	Design	Age	Sample	Outcome prevalence	Rule(s) evaluated
Gomez 2016 (8)	11 European paediatric EDs	Prospective multicentre	≤90 d	2,185	IBI 87 (3.9%)	Step-by-Step, Rochester, Lab-score
de Vos-Kerkhof 2018 (9)	Spain, France, Netherlands	External validation, 4 cohorts	<3 mo (one cohort 3-12 mo)	4 cohorts	SBI	Eight clinical prediction models
Kuppermann 2019 (10)	26 US EDs (PECARN)	Prospective; derivation/validation	≤60 d	1,821	SBI 170 (9.3%)	PECARN rule
Aronson 2019 (11)	11 US EDs	Case-control	≤60 d	181 cases/362 controls	IBI	Aronson IBI score
Velasco 2021 (12)	Spanish tertiary ED	Secondary analysis of prospective registry	≤60 d	1,247	SBI 256 (20.5%); IBI 38 (3.1%)	PECARN rule
Nguyen 2023 (13)	Kaiser Permanente Northern California	Retrospective cohort	8-60 d	1,433	IBI 60 (4.2%)	AAP algorithm without CRP/PCT
Umana 2024 (14)	35 PERUKI sites, UK and Ireland	Prospective multicentre	≤90 d	1,821	IBI 67 (3.7%)	AAP, BSAC, NICE NG143, Aronson
Burstein 2025 (15)	Single paediatric ED, Montreal	Secondary analysis	≤60 d	1,987	IBI	AAP without PCT; derived CRP/ANC/temperature rule
Aronson 2025 (16)	17 PECARN Registry EDs	Retrospective cohort	61-90 d	4,952	IBI 100 (2.0%)	PECARN 61-90-day rules
Burstein 2026 (17)	Six countries	Pooled analysis of 4 prospective cohorts	≤28 d	1,537	IBI 69 (4.5%); meningitis 11 (0.7%)	Updated PECARN rule

Table 2. Diagnostic performance of clinical prediction rules

Rule	Study	Outcome	Sensitivity (%)	Specificity (%)	NPV (%)	Missed infections
Step-by-Step	Gomez (8)	IBI	92.0	NR	99.3	7 IBI
Rochester criteria	Gomez (8)	IBI	81.6	NR	98.3	NR
Lab-score	Gomez (8)	IBI	59.8	NR	98.1	NR
Eight CPMs	de Vos-Kerkhof (9)	SBI	Variable across cohorts	Variable	NR	NR
PECARN	Kuppermann (10)	SBI	97.7	60.0	99.6	1 bacteraemia, 2 UTI; no meningitis
Aronson score ≥2	Aronson (11)	IBI	98.8 (95.7-99.9)	31.3 (26.3-36.6)	NR	NR
PECARN	Velasco (12)	SBI / IBI	89.8 / 86.8*	NR	NR	26 SBI / 5 IBI
AAP (no CRP/PCT), 8-21 d	Nguyen (13)	IBI	100 (83.9-100)	0 (0-1.4)	NR	0
AAP (no CRP/PCT), 22-28 d	Nguyen (13)	IBI	88.9 (51.8-99.7)	40.4 (33.2-48.1)	NR	3 IBI across the 22-60-day groups
AAP (no CRP/PCT), 29-60 d	Nguyen (13)	IBI	93.3 (77.9-99.2)	32.1 (29.1-35.3)	NR	(included above)

11/11/2026

Rule	Study	Outcome	Sensitivity (%)	Specificity (%)	NPV (%)	Missed infections
AAP	Umana (14)	IBI	99 (92-100)	23 (21-25)	NR	1 IBI
BSAC	Umana (14)	IBI	99 (92-100)	20 (18-22)	NR	1 IBI
NICE NG143	Umana (14)	IBI	93 (83-98)	27 (25-30)	NR	NR
Aronson score	Umana (14)	IBI	90 (80-96)	30 (28-32)	NR	NR
Derived CRP/ANC/temperature rule	Burstein (15)	IBI	100 (88.6-100)	83.8 (82.1-85.4)	100 (99.7-100)	0
Urinalysis + temperature (61-90 d)	Aronson (16)	IBI	86	58.9	99.5 (99.2-99.7)	NR
Updated PECARN (≤28 d)	Burstein (17)	IBI	94.2	41.6	99.4	4 IBI; no meningitis

Discussion

This review found that prediction rules combining urinalysis, neutrophil count and procalcitonin gave the most consistent balance between sensitivity and specificity for recognizing bacterial infection in febrile infants. In large prospective cohorts, the PECARN and Step-by-Step approaches kept negative predictive values above 99% (8,10). Guideline algorithms used without procalcitonin preserved high sensitivity at the cost of low specificity, which limits how much invasive testing they avoid (13,14).

The earlier Boston and Philadelphia criteria were developed for infants older than 28 days and relied on white cell counts and clinical appearance (18,19). These protocols supported outpatient care for selected infants, although they were derived when group B Streptococcus predominated and before procalcitonin testing existed (18,19). In contemporary data, the Rochester criteria performed less well than the Step-by-Step approach, which is consistent with the weak accuracy of white cell indices for IBI (6,8).

In a European multicentre cohort, procalcitonin showed the highest diagnostic value for IBI among well-appearing young infants with fever without a source (20). A French multicentre study confirmed that procalcitonin outperformed C-reactive protein, white blood cell count and neutrophil count for IBI in febrile infants aged 7-91 days (21). These findings shaped the design of the Step-by-Step approach and the Lab-score, both of which place procalcitonin at the centre of risk assessment (22,23).

Neonates have historically been excluded from low-risk pathways because of their higher IBI prevalence (2,7). The updated PECARN rule classified 41.1% of infants aged 28 days or younger as low risk without missing meningitis, which supports shared decision-making about lumbar puncture in this group (17). Earlier external data showed lower performance in infants with a short duration of fever, which argues for caution with very early presentations (12).

Procalcitonin is not available in every ED, and this restriction shaped the evaluation of tools that do not use it in the United Kingdom and Ireland (14). In a single-centre cohort, a rule with relaxed C-reactive protein, temperature and neutrophil thresholds improved specificity without missing any IBI (15). This rule needs external validation in multicentre settings before it is adopted (15). For infants aged 61-90 days, rules based on urinalysis and temperature extend risk stratification beyond the AAP age range (7,16).

In a PECARN cohort, host RNA biosignatures separated infants with bacterial infection from those without, and they represent a possible future adjunct (24). Statistically derived models validated across European cohorts performed inconsistently,

11/11/2026

which supports their role as decision aids rather than replacements for clinical judgement (9).

This review has several limitations. Outcome definitions were heterogeneous, with some studies targeting SBI and others IBI (10,11). Partial verification by cerebrospinal fluid culture and overlapping cohorts in pooled analyses added further uncertainty (10,17). Most studies came from high-income tertiary centres, which limits generalizability to low-resource EDs (8-17).

Conclusion

Clinical prediction rules that combine urinalysis, absolute neutrophil count and procalcitonin, particularly the PECARN rule and the Step-by-Step approach, identify febrile infants at low risk of bacteraemia, meningitis and urinary tract infection with high sensitivity and negative predictive value. Guideline algorithms used without procalcitonin keep high sensitivity but have poor specificity, and newer rules without procalcitonin need multicentre validation. The updated PECARN rule extends safe risk stratification to neonates. Prospective validation in low-resource and non-tertiary emergency departments, together with implementation studies, will define the place of these rules in routine practice.

List of Abbreviations

AAP: American Academy of Pediatrics

ANC: Absolute neutrophil count

BSAC: British Society for Antimicrobial Chemotherapy

CI: Confidence interval

CPM: Clinical prediction model

CRP: C-reactive protein

CSF: Cerebrospinal fluid

ED: Emergency department

FIDO: Febrile Infants Diagnostic assessment and Outcome

IBI: Invasive bacterial infection

NICE: National Institute for Health and Care Excellence

NPV: Negative predictive value

NR: Not reported

PCT: Procalcitonin

PECARN: Pediatric Emergency Care Applied Research Network

PERUKI: Paediatric Emergency Research in the UK and Ireland

PICOTS: Population, Index test, Comparator, Outcome, Timing, Setting

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies-2

SBI: Serious bacterial infection

UTI: Urinary tract infection

References

11/11/2026

1. Powell EC, Mahajan PV, Roosevelt G, Hoyle JD Jr, Gattu R, Cruz AT, et al. Epidemiology of bacterial infections in febrile infants aged 60 days and younger. Ann Emerg Med. 2018;71(2):211-216.
2. Biondi EA, Lee B, Ralston SL, Winikor JM, Lynn JF, Dixon A, et al. Prevalence of bacteremia and bacterial meningitis in febrile neonates and infants in the second month of life: a systematic review and meta-analysis. JAMA Netw Open. 2019;2(3):e190874.
3. Greenhow TL, Hung YY, Herz AM. Changing epidemiology of bacteremia in infants aged 1 week to 3 months. Pediatrics. 2012;129(3):e590-e596.
4. Jaskiewicz JA, McCarthy CA, Richardson AC, White KC, Fisher DJ, Dagan R, et al. Febrile infants at low risk for serious bacterial infection—an appraisal of the Rochester criteria and implications for management. Pediatrics. 1994;94(3):390-396.
5. Huppler AR, Eickhoff JC, Wald ER. Performance of low-risk criteria in the evaluation of young infants with fever: review of the literature. Pediatrics. 2010;125(2):228-233.
6. Cruz AT, Mahajan P, Bonsu BK, Bennett JE, Levine DA, Alpern ER, et al. Accuracy of complete blood cell counts to identify febrile infants 60 days or younger with invasive bacterial infections. JAMA Pediatr. 2017;171(11):e172927.
7. Pantell RH, Roberts KB, Adams WG, Dreyer BP, Kuppermann N, O'Leary ST, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. Pediatrics. 2021;148(2):e2021052228.
8. Gomez B, Mintegi S, Bressan S, Da Dalt L, Gervaix A, Lacroix L; European Group for Validation of the Step-by-Step Approach. Validation of the "Step-by-Step" approach in the management of young febrile infants. Pediatrics. 2016;138(2):e20154381.
9. de Vos-Kerkhof E, Gomez B, Milcent K, Steyerberg EW, Nijman RG, Smit FJ, et al. Clinical prediction models for young febrile infants at the emergency department: an international validation study. Arch Dis Child. 2018;103(11):1033-1041.
10. Kuppermann N, Dayan PS, Levine DA, Vitale M, Tzimenatos L, Tunik MG, et al. A clinical prediction rule to identify febrile infants 60 days and younger at low risk for serious bacterial infections. JAMA Pediatr. 2019;173(4):342-351.
11. Aronson PL, Shabanova V, Shapiro ED, Wang ME, Nigrovic LE, Pruitt CM, et al. A prediction model to identify febrile infants ≤60 days at low risk of invasive bacterial infection. Pediatrics. 2019;144(1):e20183604.
12. Velasco R, Gomez B, Benito J, Mintegi S. Accuracy of PECARN rule for predicting serious bacterial infection in infants with fever without a source. Arch Dis Child. 2021;106(2):143-148.
13. Nguyen THP, Young BR, Ballard DW, Greenhow TL, Vinson DR, Mark DG, et al. Using AAP guidelines for managing febrile infants without C-reactive protein and procalcitonin. Pediatrics. 2023;151(1):e2022058495.
14. Umana E, Mills C, Norman-Bruce H, Mitchell H, McFetridge L, Lynn F, et al. Performance of clinical decision aids (CDA) for the care of young febrile infants: a multicentre prospective cohort study conducted in the UK and Ireland. EClinicalMedicine. 2024;78:102961.
15. Burstein B, Wolek C, et al. Optimizing management of febrile young infants without serum procalcitonin. Pediatrics. 2025;155(2):e2024068200.
16. Aronson PL, Mahajan P, Meeks HD, et al. Prediction rule to identify febrile infants 61-90 days at low risk for invasive bacterial infections. Pediatrics. 2025;156(3):e2025071666.

11/11/2026

17. Burstein B, Waterfield T, Umana E, Xie J, Kuppermann N. Prediction of bacteremia and bacterial meningitis among febrile infants aged 28 days or younger. JAMA. 2026;335(5):425-433.
18. Baskin MN, O'Rourke EJ, Fleisher GR. Outpatient treatment of febrile infants 28 to 89 days of age with intramuscular administration of ceftriaxone. J Pediatr. 1992;120(1):22-27.
19. Baker MD, Bell LM, Avner JR. Outpatient management without antibiotics of fever in selected infants. N Engl J Med. 1993;329(20):1437-1441.
20. Gomez B, Bressan S, Mintegi S, Da Dalt L, Blazquez D, Olaciregui I, et al. Diagnostic value of procalcitonin in well-appearing young febrile infants. Pediatrics. 2012;130(5):815-822.
21. Milcent K, Faesch S, Gras-Le Guen C, Dubos F, Poulalhon C, Badier I, et al. Use of procalcitonin assays to predict serious bacterial infection in young febrile infants. JAMA Pediatr. 2016;170(1):62-69.
22. Mintegi S, Bressan S, Gomez B, Da Dalt L, Blázquez D, Olaciregui I, et al. Accuracy of a sequential approach to identify young febrile infants at low risk for invasive bacterial infection. Emerg Med J. 2014;31(e1):e19-e24.
23. Galetto-Lacour A, Zamora SA, Andreola B, Bressan S, Lacroix L, Da Dalt L, et al. Validation of a laboratory risk index score for the identification of severe bacterial infection in children with fever without source. Arch Dis Child. 2010;95(12):968-973.
24. Mahajan P, Kuppermann N, Mejias A, Suarez N, Chaussabel D, Casper TC, et al. Association of RNA biosignatures with bacterial infections in febrile infants aged 60 days or younger. JAMA. 2016;316(8):846-857.

11/11/2026