

Critical Review Form Meta-analysis

PGY-1

[England JT, Del Vecchio MT, Aronoff SC. Use of serum procalcitonin in evaluation of febrile infants: a meta-analysis of 2317 patients. J Emerg Med. 2014 Dec;47\(6\):682-8.](#)

Objectives: “to determine: 1) if serum concentrations of PCT [procalcitonin] in healthy, febrile infants < 91 days of age could discriminate between those infants with SBIs [serious bacterial infections] and those without; and 2) if the measurement of serum concentrations of PCT was a superior discriminator to the currently used clinical prediction rules.” (p. 683)

Methods: In performing the systematic review and meta-analysis, Medline was searched for relevant articles in September 2012 and again in March 2013. Relevant articles were those that included subjects < 91 days of age with a temperature of 38°C or greater by history of exam and a quantitative procalcitonin level obtained as part of the initial evaluation; an *a priori* protocol to define SBIs had to be used and patients with risk factors for infection (e.g. prematurity, heart defects, or congenital abnormalities) had to be excluded. The bibliographies of relevant articles were searched for additional citations. Data were extracted from selected articles by one author and reviewed by two additional authors.

Out of 158 articles identified by the literature search, 17 met inclusion criteria. Four of these were excluded because SBIs were not a reported outcome, two included only patients at risk for infection, two dialed to report quantitative PCT data, one did not look only at patients < 91 days of age, and one was a review. This left 7 studies to be included in the analysis, comprising 2317 patients < 91 days of age. These studies used varying PCT cutoff values but used similar definitions for SBI.

Guide	Question	Comments
I	<i>Are the results valid?</i>	
1.	Did the review explicitly address a sensible question?	Yes. There has been a great deal of research looking at the clinical utility of PCT in diagnosing bacterial infections (https://emergencymedicine.wustl.edu/items/procalcitonin-and-antibiotics-for-lower-respiratory-tract-infections , https://academic.oup.com/labmed/article/41/3/173/2504938 , https://pulmccm.org/review-articles/procalcitonin-suspected-infection-review). <u>The outpatient evaluation of febrile infants</u> is typically invasive and time-consuming, requiring, in many cases, blood cultures, lumbar puncture, and empiric antibiotic therapy. Use of quantitative PCT testing in febrile neonates, either alone or in conjunction

		with existing clinical decision rules, seems like a potentially, could potentially reduce the need for such invasive testing and potentially allow many patients to be discharged home.
2.	Was the search for relevant studies detailed and exhaustive?	No. The literature search was limited to Medline and did not include the Cochrane database, EMBase, CINAHL, conference abstracts, or the grey literature. This puts this meta-analysis at high risk of publication bias .
3.	Were the primary studies of high methodological quality?	Uncertain. The authors provide no assessment of the risk of bias for the included studies. Specifically, QUADAS-2 or a similar tool was not used to evaluate the studies.
4.	Were the assessments of the included studies reproducible?	No assessment of the studies was included.
II.	<i>What are the results?</i>	
1.	What are the overall results of the study?	<ul style="list-style-type: none"> • For the ability of serum PCT to discriminate between patients with and without SBI, the authors report a pooled relative risk (RR) of 3.97 (95% CI 3.41 to 4.62). • The pooled test characteristics of PCT for the diagnosis of SBI are as follows[†]: <ul style="list-style-type: none"> ○ Sensitivity = 80% ○ Specificity = 57% ○ LR+ = 2.83 (95% CI 2.51 to 3.19) ○ LR- = 0.54 (95% CI 0.49 to 0.60) [†] Calculated using http://araw.mede.uic.edu/cgi-bin/testcalc.pl
2.	How precise are the results?	See above
3.	Were the results similar from study to study?	The authors report an I ² value of 2.61, suggesting there was essentially no heterogeneity between study results.
III.	<i>Will the results help me in caring for my patients?</i>	
1.	How can I best interpret the results to apply them to the care of my patients?	While there does appear to be an association between a positive PCT and the presence of a SBI, the positive and negative likelihood ratios suggest that the test, in isolation, would do little to change the probability of an SBI being present, whether positive or negative. It is possible that PCT may be useful when used in conjunction with other findings, and may be useful as part of a clinical decision rule.
2.	Were all patient important outcomes considered?	No. The authors only considered the association between a “positive” PCT and the diagnosis of a SBI. Given the question being asked, this is likely adequate (although providing test characteristics such as likelihood ratios

		would have been more clinically meaningful). They did not consider how PCT results affected management or disposition, or if changes in management led to changes in patient-centered outcomes .
3.	Are the benefits worth the costs and potential risks?	No. These results suggest that PCT alone does not have adequate LR+ or LR- to significantly affect the probability of a SBI, whether positive or negative.

Limitations:

1. The authors do not report who performed the literature search and if it was performed by more than one investigator.
2. The literature search was limited to Medline and did not include the Cochrane database, EMBase, CINAHL, conference abstracts, or the grey literature ([publication bias](#)).
3. Despite the reported use of the Prisma Checklist in reporting on this article, no assessment of the risk of bias was performed, such as via the use of [QUADAS-2](#).
4. The authors report relative risks for the association between a “positive” procalcitonin and a SBI, but do not provide clinically meaningful test characteristics such as likelihood ratios, sensitivity, or specificity.

Bottom Line:

This meta-analysis of PCT in the diagnosis of a serious bacterial infection in children < 91 days of age found a significant association between a positive PCT and the diagnosis of a SBI (RR 3.97; 95% CI 3.41 to 4.62). Unfortunately, the positive and negative likelihood ratios are poor enough that the test would not have a significant impact on the probability of disease. PCT should not be used in isolation to diagnose a SBI, but further research may demonstrate its utility in conjunction with other signs and symptoms.