

# Derivation and Validation of a Clinical Rule to Detect Bacteremia Versus Contaminants in Positive Pediatric Blood Cultures: A Retrospective Cohort Study



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**Study objectives:** Fifty percent of positive blood cultures in the pediatric emergency department (ED) are contaminants. We derived and validated a clinical decision rule discriminating bacteremia from contaminants among children seen in the ED with a positive blood culture.

**Methods:** We used 2 cohorts of children with positive blood cultures from a Canadian pediatric ED in 2018 to 2022 (derivation) and 2023 to 2024 (validation). The primary outcome was bacteremia. Potential predictors of bacteremia were derived from a literature review and experts' consensus. We used Classification and Regression Tree models to derive a highly sensitive clinical decision rule. The validity was assessed by measuring the proportion of children with true bacteremia classified at high or moderate risk by the clinical decision rule (sensitivity) and the proportion of contaminants classified at low risk (specificity). The clinical utility was measured by comparing the clinical decision rule to the treating physician's management.

**Results:** A total of 747 children, including 368 cases of bacteremia were included in the derivation (total 574; 285 bacteremia) and validation (total 173; 83 bacteremia) cohorts. The clinical decision rule classifies children into 3 categories (high, moderate, and low risk) based on 4 criteria. It demonstrated a sensitivity of 99% (95% confidence interval [CI] 94 to 100) and a specificity of 60% (95% CI 50 to 70) in the validation cohort. Using the clinical decision rule among the 43 children initially discharged in the validation cohort would decrease the number of hospitalizations from 34 to 21 without missing a true bacteremia.

**Conclusion:** We created a very sensitive clinical decision rule to identify bacteremia in children with positive blood culture. Adopting this clinical decision rule could significantly impact health system resources. [Ann Emerg Med. 2025;86:576-585.]

Please see page 577 for the Editor's Capsule Summary of this article.

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## INTRODUCTION

### Background

Fever is the single most common presenting symptom in children evaluated in the emergency department (ED), accounting for 20% to 40% of all pediatric ED visits.<sup>1,2</sup> Although most children with fever have a viral infection, some have a bacterial infection including bacteremia, a potentially life-threatening infection that requires urgent treatment to avoid sepsis and possible death. For febrile children with concerning signs of bacteremia, a blood culture is the diagnostic standard of care.<sup>3-7</sup> A common complication of obtaining blood cultures is contamination of the samples, leading to false positive results. Given the

low actual risk of true bacteremia (1% to 2% of blood cultures) and a contamination probability of 2% to 3% of blood cultures, studies revealed that 40% to 80% of all preliminary positive blood cultures conducted in pediatric EDs are in fact contaminants.<sup>8-12</sup> This rate has been reported to be higher among younger children.<sup>12</sup>

### Importance

A preliminary positive blood culture must be evaluated and acted on quickly to avoid morbidity and mortality. In most settings, ED staff are notified immediately when a blood culture collected in the ED becomes positive. Although the Gram stain is generally available immediately

**Editor's Capsule Summary***What is already known on this topic*

Approximately half of positive blood cultures grow contaminants rather than bacterial pathogens.

*What question this study addressed*

Can we identify children with a positive blood culture who are at low risk for bacteremia?

*What this study adds to our knowledge*

A 4-factor clinical decision rule had a sensitivity of 99% (1/83) and a specificity of 60% (54/90).

*How this is relevant to clinical practice*

After external validation, implementation of this clinical prediction rule might reduce hospitalization for children with contaminated blood cultures.

Diagnosis, Strengthening the Reporting of Observational Studies in Epidemiology, and REporting of studies Conducted using Observational Routinely-collected health Data guidelines.<sup>16-18</sup> We included 2 cohorts of children selected at a single tertiary-care pediatric university-affiliated hospital in Montréal, Canada selected at 2 time periods. In the derivation (retrospective) cohort, we included children evaluated in a previous study aiming to evaluate the Hospital for Sick Children algorithm among patients evaluated at our ED between January 2018 and December 2022.<sup>12</sup> Following the derivation of the clinical decision rule, we collected a validation cohort composed of children evaluated at the same ED between January 2023 and May 2024.

**Participants**

We included all children under 18 years of age who had a positive blood culture obtained in the ED. We excluded duplicates of positive blood cultures (ie, if a patient had 2 positive blood cultures during the same visit, only the first was included). In the validation cohort, we excluded children transferred from another facility who had received intravenous antibiotics prior to transfer to minimize the impact of antibiotics administered before blood culture sampling at our center.

**Outcomes**

The primary outcome, presence of true bacteremia versus contaminant, was defined in a 2-step process described previously.<sup>12</sup> In brief, the first step initially classified the blood culture as true positive, equivocal or contaminant based on the pathogen identified in the final culture.<sup>8</sup> For equivocal or presumed contaminant, we assessed the medical chart, considering factors such as a second positive culture in a sterile sample (eg, blood, cerebrospinal, or synovial fluid), the physician's final diagnosis (eg, contamination), or given treatment (eg, antibiotics for immunocompromised patients).

once the culture becomes positive, the identification of bacterial species often requires 24 to 48 hours.<sup>13,14</sup> This delay adds to the clinical uncertainty for health care providers regarding whether the positive result is true bacteremia or contamination. It can be especially challenging as many ED patients have already been discharged when these results are available. To our knowledge, the Hospital for Sick Children algorithm is the only published guideline for the management of children with positive blood culture.<sup>12</sup> It was developed from a consensus of experts to standardize practices and optimize resource utilization.<sup>15</sup> A retrospective study demonstrated that this algorithm was 100% sensitive to detect children with bacteremia but showed a specificity of 11% to 26%.<sup>12</sup> A subanalysis demonstrated that the application of the Hospital for Sick Children algorithm would likely have minimal impact on practice in this single site study.

**Goals of This Investigation**

We aimed to derive and validate a clinical decision rule to discriminate bacteremia from contaminants among children who had a positive blood culture performed in the ED. Our ultimate goal was to develop a clinical decision rule that would more effectively reduce unnecessary care for children with blood culture contaminants, thereby supporting physicians managing positive blood culture results in pediatric patients.

**METHODS****Study Design and Setting**

This study follows Transparent Reporting of a multivariable prediction model for Individual Prognosis or

**Independent Variables**

We identified 18 independent variables from a literature review and a consensus of local experts in pediatric emergency, microbiology, infectious diseases, and pediatrics. Risk factors potentially associated with a higher risk of true bacteremia included demographics (age [years] and sex), factors related to the patient (eg, immunosuppression, sickle cell disease, prosthetic device or central line, vaccinal status, chronic heart or kidney problem, and past history of bacteremia), factors related to the symptoms (eg, presence of fever at index visit, persistence of fever at follow-up, vital signs at triage of the index visit, musculoskeletal pain, chest pain, travel outside

North America in the past month, and at index visit), factors related to blood test at index visit (eg, absolute neutrophile count, C-reactive protein levels, and procalcitonin levels), and factors related to the preliminary results (eg, time to positivity from blood sampling until positivity alarm and Gram stain).

## Procedure

We identified patients using the institutional microbiological database. The chart review was performed using standardized methodology.<sup>19-22</sup> A case report form was created before data extraction and used to collect all pertinent information by trained members of the research team. These raters were medical students and physicians, all co-authors of the current study.

We applied 2 different strategies to handle missing data, depending on the variable in question. When no information was recorded, we interpreted this as a negative response for the following variables as one would expect this to be charted in case of positivity: (1) recent travel history, (2) history of chronic medical conditions, and (3) suspected endocarditis or osteoarticular infection. Raters were instructed to classify any child whose medical record mentioned a limp, refusal to use a limb, or musculoskeletal pain as a suspected case of osteoarticular infection. Conversely, for variables concerning vaccination status, presence of fever, and blood test results, a lack of documentation was treated as missing data. However, our previous study demonstrated very low proportion (<1%) of missing data for the required independent variables.<sup>12</sup> There were no missing data for all other variables.

We assessed inter-rater reliability by reviewing a random sample of 10% of charts in duplicate. However, the primary outcome, contamination versus true bacteremia, was evaluated in duplicate for all patients, with discrepancies resolved by consensus. At least one physician specialized in pediatric emergency medicine or pediatric infectious disease was involved for each case.

## Analysis

We initially measured the inter-rater agreement of the chart review using the Kappa statistic for categoric variables, and intraclass correlation coefficient for continuous variables in 10% of the charts for each cohort.<sup>23,24</sup> All variables with a Kappa score or intraclass correlation coefficient higher than 0.6 were considered reliable and adequate to be involved in further analysis.

We calculated the prevalence of each independent variable for the total sample and for each group. Then, we derived the clinical decision rule using Classification and

Regression Tree (CART) models to distinguish true bacteremia and contamination cases.<sup>25</sup> Our aim was to develop a highly sensitive clinical decision rule to correctly identify bacteremia while minimizing false positives. We used the “rpart” package in R for the analysis, which uses machine learning for the automation of the processes of learning from the data and creating predictive models. Continuous variables were examined, and transformations were considered to optimize model performance. There was no imputation performed for missing variables because we expected them to be very low.

The initial CART model was fitted using the derivation cohort. The model’s performance was evaluated using 10-fold cross-validation procedure, and an optimal complexity parameter was selected as it controls the size of the tree by pruning it to prevent overfitting. We tested different loss matrices to further optimize the model. The loss matrix was used to assign different costs to misclassifications. In our case, a false negative (identifying a bacteremia as a contaminant) was more costly than false positives (identifying a contaminant as a bacteremia). The ratio of false positive to false negative was 40 using the loss matrix (0, 1, 40, and 0).

We validated the rule in a new cohort of children by measuring the proportion of children with true bacteremia who were classified at high or moderate risk by the clinical decision rule (sensitivity) and the proportion of contaminants that were classified at low risk by the rule (specificity). The clinical utility was evaluated by comparing the clinical decision rule to the treating physician’s management in participants who were discharged home at the index visit. For this, we performed 2 analyses:

In children with true bacteremia, we compared the proportion of children who would have been categorized at high or moderate risk according to the clinical decision rule (sensitivity) to the proportion of children with bacteremia who received intravenous antibiotics and/or were hospitalized in real-life practice. In children with contamination, we compared the proportion of children classified at low risk according to the clinical decision rule (specificity) to the proportion of children with contamination who did not receive any intravenous antibiotics nor were hospitalized. We calculated the number needed to treat, defined as the number of children who would need to be managed using the clinical decision rule to prevent one hospitalization. We also calculated the number needed to harm, defined as the number of children in whom the clinical decision rule would prevent a hospitalization despite the presence of bacteremia. Finally, we compared the clinical decision rule and the Hospital for Sick Children algorithm for their clinical utility. For all these analyses, we reported the differences and the 95% confidence interval (CI).

**Table 1.** Baseline demographics of the participants.

Variables	Derivation N=574		Validation N=173	
	Bacteremia 285 (49.7%)	Contaminants 289 (50.3%)	Bacteremia 83 (48.0%)	Contaminants 90 (52.0%)
Sex, men, n (%)	154 (54)	158 (55)	49 (59)	45 (50)
Median age in mo (1 <sup>st</sup> and 3 <sup>rd</sup> quartiles)	42 (7 and 108)	16 (2 and 55)	32 (11 and 98)	24 (3 and 71)
<b>Vaccination status, n (%)</b>				
Has received > 1 dose of vaccine	224 (79)	194 (67)	66 (80)	59 (66)
Has received ≤ 1 dose of vaccine	60 (21)	94 (33)	16 (19)	29 (32)
Unknown	1	1	1	2
<b>Risk factor, n (%)</b>				
Any internal device	11 (4)	61 (21)	19 (23)	9 (10)
Immunocompromised	53 (19)	28 (10)	10 (12)	7 (8)
History of bacteremia	28 (10)	6 (2)	9 (11)	4 (4)
Sickle cell disease	8 (3)	14 (5)	4 (5)	6 (7)
Heart malformation	15 (5)	3 (1)	8 (10)	3 (3)
Age<3 mo	49 (17)	79 (27)	10 (12)	26 (29)
<b>Fever at initial visit, n (%)</b>				
No	23 (8)	48 (17)	5 (6)	21 (23)
Yes	260 (91)	241 (83)	78 (94)	69 (77)
Missing information	2	0	0	0
Traveled out of North America or Europe in the last 2 mo, n (%)	24 (8)	5 (2)	9 (11)	3 (3)
Median absolute neutrophile count (10 <sup>9</sup> /L) (first and third quartiles)	6.8 (3.5 and 11.7)	4.6 (2.6 and 7.8)	6.5 (4.3 and 13.5)	4.5 (2.6 and 8.8)
Median CRP level (ng/mL)* (first and third quartiles)	54 (23 and 118)	14 (3 and 43)	99 (46 and 180)	9 (1 and 35)
<b>Disposition at index visit, n (%)</b>				
Discharged home	60 (21)	104 (36)	14 (17)	29 (32)
Follow-up at day center	21 (7)	33 (11)	14 (17)	11 (12)
Hospitalization	205 (72)	152 (53)	55 (66)	50 (56)
Suspicion of osteoarticular infection, n (%)	51 (18)	9 (3)	15 (18)	2 (2)
Suspicion of endocarditis at first visit, n (%)	5 (2)	1 (0.3)	4 (5)	1 (1)
Median time for Gram positivity in h (first and third quartiles)	14 (12 and 18.8)	19 (17 and 25.5)	14 (13 and 17)	20 (17 and 26)
<b>Gram stain<sup>†</sup></b>				
Gram positive cocci in clusters	90 (32)	197 (68)	28 (34)	53 (59)
Gram positive cocci in chains	69 (24)	34 (12)	20 (24)	13 (14)
Gram positive cocci in pairs	6 (2)	12 (4)	3 (4)	3 (3)
Gram negative bacilli	111 (39)	7 (2)	34 (41)	2 (2)
Gram positive bacilli	3 (1)	53 (18)	0	18 (20)
Others	6 (2)	2 (1)	0	2 (2)

\*Not measured in 237 patients.

†Total higher than 100% as some may be multiple.

### Sample Size

We expected that 500 participants included in the derivation cohort would provide more than 250 cases of bacteremia based on previous studies.<sup>8-10</sup> This allows the

analysis of up to 25 potential risk factors, using a rule of 10 patients with the outcome for each independent variable.<sup>26,27</sup> A sample size of 170 patients in the validation phase was expected to provide at least 80 cases of true

bacteremia and contaminants, which provides narrow confidence intervals for sensitivity (expected 100%; 95% CI 95 to 100) and specificity (worst case scenario 50%; 95% CI 39 to 51).

The institutional Research Ethics Boards of CHU Sainte-Justine evaluated the project (Project 2023-4918). Because of the retrospective design, a waiver of consent was granted for this project.

## RESULTS

A total of 487,222 children were evaluated in the ED during the derivation ( $n=375,428$ ) and validation ( $n=111,794$ ) phases in whom 38,541 blood cultures were performed (29,279 in the derivation and 9,262 in the validation cohort). Among them, 747 (1.9%) children fulfilled the inclusion or exclusion criteria, and all were included in the analysis in the derivation ( $n=574$ ) and validation ( $n=173$ ) cohorts. There were 368 (49.3%) children with a true bacteremia and 379 (50.7%) with contaminated samples. Baseline demographics of these patients are provided in [Table 1](#). In brief, the median age was 25 months, and 207 (27.7%) were discharged home at the index visit. Children discharged home at the index visit were younger (median age: 24 versus 26 months) and less frequently had an identified risk factor (37 versus 49%). The most common pathogenic bacteria were *Staphylococcus aureus* ( $n=93$ ; 25.3%), *Escherichia coli* ( $n=58$ ; 15.8%) and *Streptococcus pneumoniae* ( $n=33$ ; 9.0%). The most common contaminant was *Staphylococcus epidermidis* ( $n=95$ ; 25.1%).

We evaluated in duplicate 81 (11.5%) charts demonstrating good inter-rater reliability with Kappa scores or intraclass correlation coefficients higher than 0.60 for all variables ([Table E1](#), available at <http://www.annemergmed.com>). There were no missing data for all variables except vaccination status ( $n=5$ ), fever at triage ( $n=2$ ) and C-reactive protein level ( $n=237$ ; 32%). Because of the large proportion of missing data for C-reactive protein levels, it was not included as a potential predictor.

## Derivation

We identified 4 variables permitting to stratify the risk of bacteremia in children with positive blood culture ([Figure 1](#)). Using these 4 variables, we created a clinical decision rule to classify children with positive blood culture into 3 categories: high, moderate and low risk ([Figure 2](#)). Children at high risk of bacteremia were identified based on the initial Gram stain. In the absence of high-risk Gram stain criteria, children were classified at moderate risk if they had 1 of 3 “moderate” risks factors (culture positive in

less than 17 hours; internal devices; suspicion of osteoarticular infection). Children without any of the previous 4 criteria were classified at low risk. In the derivation set, 255 children were classified at high risk of whom 203 (79.6%; 95% CI 74.2 to 84.1) had bacteremia, 131 were in the moderate risk category with 81 (61.8; 95% CI 53.3 to 70.1) bacteremia, whereas only 1 (0.5%; 95% CI 0 to 3.4) of 188 children at low risk had bacteremia ([Table 2](#)). This patient was a 14-year-old boy transferred from another facility for a known *Staphylococcus aureus* bacteremia. He had already received antibiotics before transfer but a blood culture collected in our ED detected the same bacteria after 21 hours of culture.

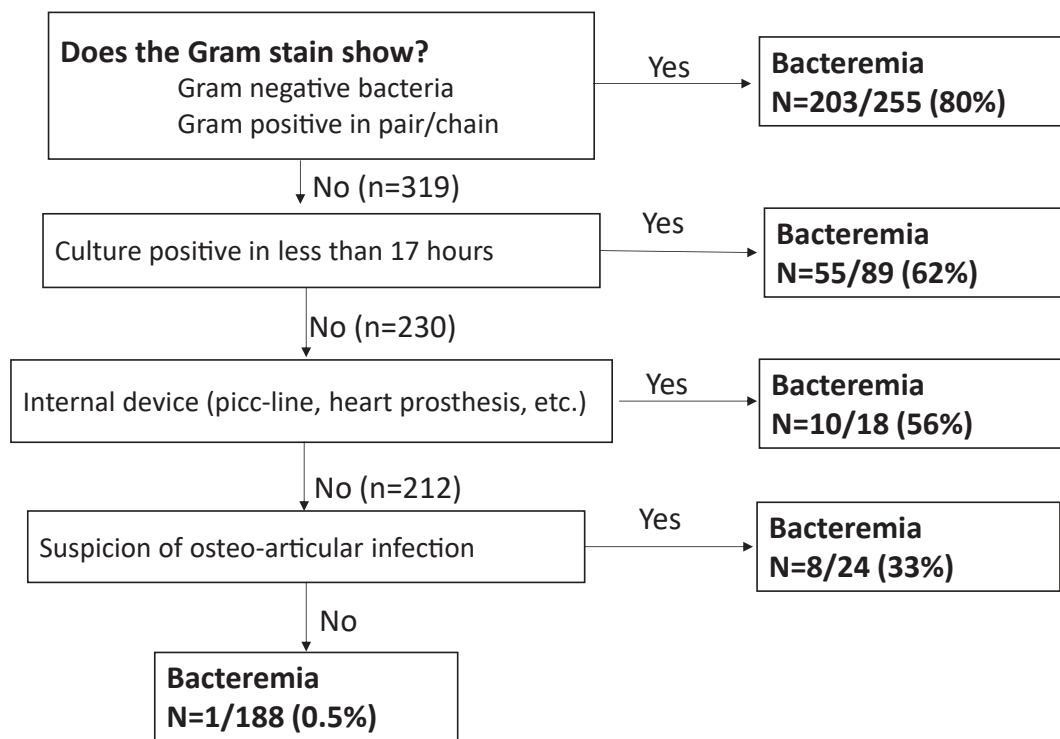
## Validation

The validation cohort included 173 children of whom 74 were classified at high risk, 44 at moderate risk and 55 at low risk ([Table 2](#)). There were 56 (76%; 95% CI 65 to 84) cases of bacteremia in the high-risk group, 26 (59%; 95% CI 44 to 72) cases in the moderate-risk group, and 1 (2%; 95% CI 0 to 10) in the low-risk group, leading to a sensitivity of 99% (94% to 100%) and a specificity of 60% (50 to 70). Only one patient was misclassified as having a contaminant while having a true bacteriemia. This patient was 3 months old and was already admitted for pulmonary empyema, for which the blood culture grew *Staphylococcus aureus*.

The clinical utility of the clinical decision rule was evaluated among the 43 children who were initially discharged from the ED in the derivation cohort ([Figure 3](#)). In this sample, using the rule would have led to 21 hospitalizations per day center follow-ups (instead of 33). It would also increase the number of patients discharged home without antibiotics from 10 to 22 for an absolute difference of 28% (95% CI 7 to 45). This finding translates to a number needed to treat of 4 (95% CI 3 to 15). Moreover, the reduction in hospitalizations did not increase the risk of missing true bacteremia cases, given a sensitivity of 100% (95% CI 78 to 100) and a corresponding number needed to harm of infinity (95% CI 12 to infinity). This was also better than for the Hospital for Sick Children algorithm who would have suggested hospitalization or day center follow-up in 30 patients while allowing discharge home without antibiotics in 13 children without missing a true bacteremia for a difference of 20.93% (95% CI 0.22 to 39.30) ([Figure E1](#), available at <http://www.annemergmed.com>).

## LIMITATIONS

Our study has some limitations. First, the derivation and validation phases were conducted in the same setting. To

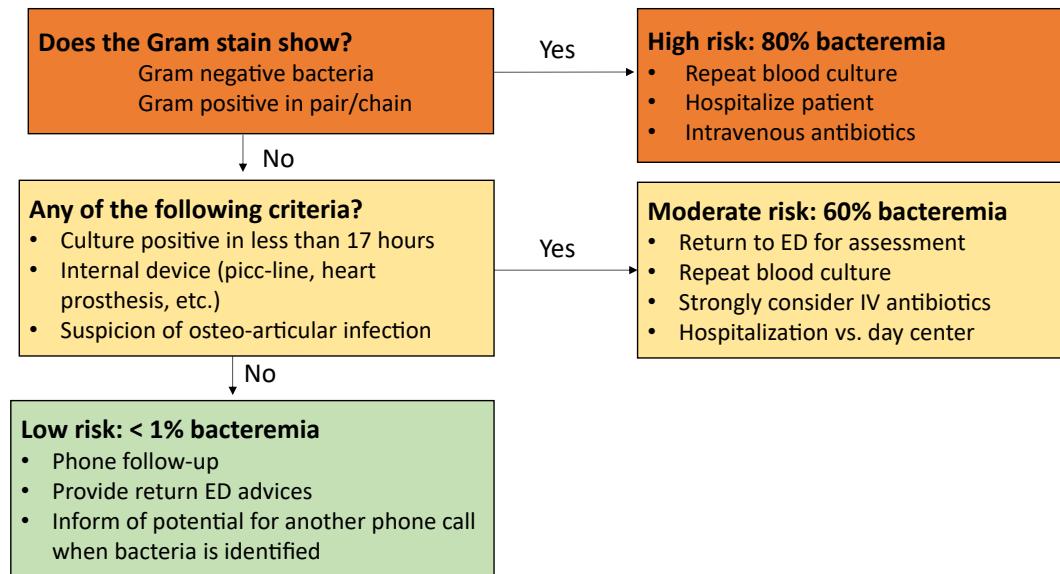


**Figure 1.** Cart model to stratify risk of bacteremia (derivation).

be widely accepted, external validation followed by impact analysis will be needed. The derivation of the cohort during the coronavirus disease 2019 (COVID-19) period may have affected the proportion of bacteremia as previous studies reported conflicting results regarding the risk of

bacteremia during COVID-19 period.<sup>28-30</sup> However, given the 7-year recruitment period, the impact of pandemic-related restrictions was limited to a relatively short timeframe. The use of a retrospective design does not allow the evaluation of the clinical acceptability of the rule. This

## The clinical decision rule for bacteremia



**Figure 2.** The clinical decision rule to stratify the risk of bacteremia in children with positive blood culture.

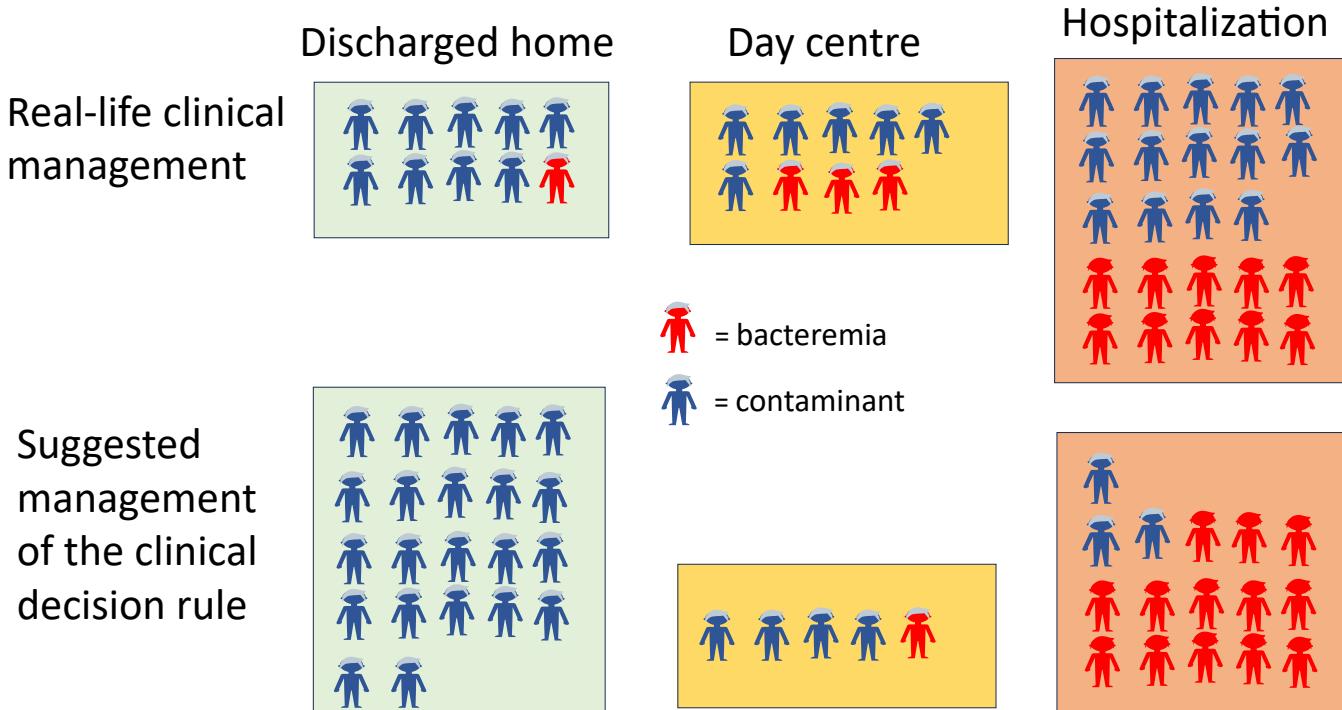
**Table 2.** Distribution of the children according to their risk of bacteremia.

Characteristics	High Risk	Moderate Risk	Low Risk	Sensitivity*	Specificity*
<b>Derivation (n)</b>	255	131	188		
Bacteremia, n (%)	203 (79.6%)	81 (61.8%)	1 (0.5%)	0.996 (0.98-1.00)	0.64 (0.59-0.70)
Contaminant n (%)	42 (17)	50 (38)	187 (99)		
<b>Validation (n)</b>	74	44	55		
Bacteremia n (%)	56 (76%)	26 (59%)	1 (2%)	0.99 (0.94-1.0)	0.60 (0.50-0.70)
Contaminant n (%)	18 (24)	18 (41)	54 (99)		
Patients discharged at index visit (n)	16	5	22		
Bacteremia (%)	13 (81%)	1 (20%)	0 (0%)	1.00 (0.79-1.00)	0.76 (0.58-0.88)
Contaminant n (%)	3 (19)	4 (80)	22 (100)		

\*Positivity was defined by all patients at high or moderate risk.

is especially important considering that our clinical decision rule had a sensitivity of 99% and some might expect that a clinical decision rule for predicting true bacteremia should be 100% sensitive. However, most guidelines in pediatric emergency medicine do not reach 100% sensitivity. For example, the PECARN head trauma rule has a sensitivity of 97% for identifying clinically important traumatic brain injury and the American Academy of Pediatrics guidelines have sensitivity of 95% to detect invasive bacterial infection among febrile infants.<sup>31,32</sup> Even though the 4 components of the rule are simple and demonstrate limited subjectivity

with Gram stain being technician dependent, it would be important to test usage of the rule in real-life setting and to see if clinicians can apply it correctly. The definition of what constitutes a bacteremia may be subjective in some situations. This is why it was evaluated in duplicate and demonstrated a high inter-rater reliability. There were many patients for whom C-reactive protein level was not measured and this could not be used in the derivation of the rule. It is possible that this information would have improved the criterion validity of the rule. Also, missing information regarding some predictors (eg, travel or

**Figure 3.** Clinical management of the 43 patients initially discharged at the moment of positive blood culture.

suspicion of endocarditis) was classified as negative and this may have lowered our capacity to find an association. Generalizing the clinical decision rule to a large age range also carries limitations and it should be validated in a larger sample to account for all age groups. Finally, we did not measure the impact of use of the clinical decision rule for admitted patients. This would need to be evaluated in future studies as positive blood cultures commonly lead to repeated blood tests.

## DISCUSSION

Using 2 retrospective cohorts from the same hospital, including a total of 368 bacteremia and 379 contaminated blood samples, we developed a very sensitive clinical decision rule to stratify the risk of true bacteremia versus contaminants in children with a positive blood culture. This rule classifies children into 3 risk categories, including high, moderate, and low, based on 4 criteria. The distribution of the patients and proportion of bacteremia in each category were similar in the derivation and the validation phases of the study. More importantly, only one of the 83 cases of bacteremia was classified at low risk, which leads to a sensitivity of 99% in the validation cohort. Furthermore, the clinical utility of the rule was demonstrated, as its application could have reduced the number of hospitalizations without increasing the number of missed cases.

Our study must be put in its context. To our knowledge, this is the first clinical decision rule to be developed using a rigorous methodology, rather than relying solely on expert opinion to discriminate bacteremia from contaminants in children with positive blood culture. A previous study evaluating the Hospital for Sick Children algorithm in this context reported a sensitivity of 100% and specificity of 11% when applied to all patients and 26% when applied to patients who were discharged at the index visit.<sup>12</sup> In comparison, our clinical decision rule had a sensitivity of 99.6% but a much better specificity at 65% for the same cohort in the derivation phase and in the validation cohort. There are variables included both in the Hospital for Sick Children algorithm and our clinical decision rule like the Gram stain findings, presence of a central line or suspicion of osteoarticular infection. However, presumed high-risk factors of the Hospital for Sick Children algorithm “age younger than 3 months old” and “sickle cell disease” were associated to lower risk of bacteremia and were not included in our clinical decision rule improving its specificity. Factors included in our rule are in agreement with previous studies evaluating independent variables potentially useful in differentiating

contamination from bacteremia. These included time to positivity and type of bacteria on the Gram stain.<sup>8,12,13,33-35</sup> We are unaware of a clinical decision rule for positive blood cultures in adults. In 2012, Elzi et al<sup>36</sup> reported that adults with coagulase-negative staphylococci blood infection with 3 systemic inflammatory response syndrome criteria or 2 criteria and a central line were at lower risk of contamination.

Considering the absence of a more robust option, this clinical decision rule should be used to guide clinicians managing children who had a positive blood culture in the ED. The use of the clinical decision rule would have numerous clinical impacts. In patients who were discharged at the initial ED visit one unnecessary hospitalization would be avoided for every 4 patients managed using the clinical decision rule. This reduces unnecessary testing and antibiotics in a subset of patients as false positive blood cultures lead to unnecessary testing, antibiotic overuse and hospitalization.<sup>9,37,38</sup> These have significant financial impacts on families (work absenteeism, transportation, etc) and on the health care system, as each ED visit has been estimated to cost more than 1,200 USD in the United States and Canada and each hospitalization cost between 5,000 and 13,000 USD.<sup>39-42</sup> Improving discrimination will also decrease pain and anxiety caused by repeated, unnecessary blood testing and intravenous insertion which is identified as the most traumatic medical procedure by hospitalized children.<sup>43,44</sup> Furthermore, antibiotic overuse has been identified as an important factor contributing to antibiotic resistance.<sup>45</sup> Equally important, the use of the rule can ensure identification of children with bacteremia leading to increased safety for this population and offer health care professionals an evidence-based diagnostic approach to evaluating cases of potential bacteremia.

The clinical utility of our findings should be interpreted in light of recent advancements in microbiology, allowing rapid identification of bacteria or yeasts directly from positive blood culture media, without awaiting a pure culture on agar media. Several protocols using matrix-assisted laser desorption or ionization time-of-flight (MALDI-TOF) mass spectrometry have been published.<sup>46,47</sup> This technology has been shown to decrease time to identification of bacteria, which can be performed immediately after Gram stain.<sup>46-49</sup> However, despite its promise, MALDI-TOF has shown variable accuracy in rapid bacterial identification, ranging from 33% to 95%.<sup>46,47</sup> Other recent advancements in diagnostics involve the use of multiplex polymerase chain reaction technology such as the BioFire Blood Culture Identification Panel.<sup>50</sup> This panel has demonstrated the ability to identify 88% to 91% of bacterial pathogens from

positive blood cultures.<sup>51,52</sup> However, similar to MALDI-TOF limitations, these molecular technologies are costly and not yet implemented in the majority of clinical laboratories. Therefore, for several years to come, we think that this clinical decision rule will still be useful in settings with no access to rapid identification methods or during shifts when this service is not offered (eg, night and weekends) or for all those cases where these technologies failed to provide a specific microorganism name and the ED clinician has to decide whether the patient has to come back for follow-up or not.

In conclusion, we developed a sensitive clinical decision rule to identify true bacteremia among children seen in the ED with a preliminary positive blood culture. The use of this clinical decision rule will decrease the number of unnecessary testing and antibiotics in a subset of patients while ensuring treatment for children at high risk of true bacteremia. Next steps should be to evaluate the validity of the rule and its clinical utility in multiple settings.

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**Author contributions:** JG initiated the study, drafted the study protocol, participated in the chart review, performed the statistical analysis, drafted the first version of the manuscript and completed the submission. CG, ADL, and BN collaborated to the design of the study, participated in the chart review, provided feedback for the initial analysis and critically reviewed and revised the manuscript. SRD collaborated in the study design, performed statistical analysis and critically reviewed the manuscript. OO and EV collaborated to the design of the study, provided feedback for the initial analysis and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. JG takes responsibility for the paper as a whole.

**Data sharing statement:** Complete datasets and data dictionary are available from January 2026 on request to Dr. Jocelyn Gravel at [Jocelyn.gravel.med@ssss.gouv.qc.ca](mailto:Jocelyn.gravel.med@ssss.gouv.qc.ca) to investigators who provide an IRB letter of approval and after an agreement has been signed by both parties.

All authors attest to meeting the four [ICMJE.org](https://www.icmje.org) authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the

work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## REFERENCES

1. McCaig LF, Nawar EW. National Hospital Ambulatory Medical Care Survey: 2004 emergency department summary. *Adv Data*. 2006;1-29.
2. Ramgopal S, Ronson PL, Marin JR. United States' Emergency Department Visits for Fever by Young Children 2007-2017. *West J Emerg Med*. 2020;21:146-151.
3. Pantell RH, Roberts KB, Adams WG, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. *Pediatrics*. 2021;148:e2021052228.
4. Gomez B, Mintegi S, Bressan S, et al. Validation of the "step-by-step" approach in the management of young febrile infants. *Pediatrics*. 2016;138:e20154381.
5. Burstein B, Lurette MP, Beck C, et al. Management of well-appearing febrile young infants aged </=90 days. *Paediatr Child Health*. 2024;29:50-66.
6. Section on Hematology/Oncology Committee on G, American Academy of P. Health supervision for children with sickle cell disease. *Pediatrics*. 2002;109:526-535.
7. Morgan JE. Fifteen minute consultation: fever in children being treated for cancer. *Arch Dis Child Educ Pract Ed*. 2019;104:124-128.
8. El-Naggar MA, Al-Mulaabed SW, Al-Muharri Z, et al. Blood culture contaminants in a paediatric population retrospective study from a tertiary hospital in Oman. *Sultan Qaboos Univ Med J*. 2017;17:e202-e208.
9. Segal GS, Chamberlain JM. Resource utilization and contaminated blood cultures in children at risk for occult bacteremia. *Arch Pediatr Adolesc Med*. 2000;154:469-473.
10. Alpern ER, Alessandrini EA, Bell LM, et al. Occult bacteremia from a pediatric emergency department: current prevalence, time to detection, and outcome. *Pediatrics*. 2000;106:505-511.
11. Sard B, Bailey MC, Vinci R. An analysis of pediatric blood cultures in the postpneumococcal conjugate vaccine era in a community hospital emergency department. *Pediatr Emerg Care*. 2006;22:295-300.
12. Gravel J, Grandjean-Blanchet C, Demeain-Loghin A, et al. Validation of the Hospital for Sick Children algorithm for discriminating bacteremia from contaminants in children with a preliminary positive blood culture. *Ann Emerg Med*. 2024;84:490-499.
13. Biondi EA, Mischler M, Jerardi KE, et al. Blood culture time to positivity in febrile infants with bacteremia. *JAMA Pediatr*. 2014;168:844-849. <https://doi.org/10.1001/jamapediatrics.2014.895>

14. Aronson PL, Wang ME, Nigrovic LE, et al. Time to pathogen detection for non-ill versus ill-appearing infants  $</=$ 60 days old with bacteremia and meningitis. *Hosp Pediatr*. Jul 2018;8:379-384.
15. Hospital NYG. Blood Culture Algorithm. North York General Hospital Emergency Department. Accessed December 4, 2023. <https://www.nyghemerg.com/post/blood-culture-algorithm>
16. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Epidemiology*. 2007;18:800-804.
17. Benchimol EI, Smeeth L, Guttman A, et al. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS Med*. 2015;12:e1001885.
18. Collins GS, Reitsma JB, Altman DG, et al. Transparent Reporting of a multivariable prediction model for Individual Prognosis or diagnosis (TRIPOD). *Ann Intern Med*. 2015;162:735-736.
19. Gilbert EH, Lowenstein SR, Koziol-McLain J, et al. Chart reviews in emergency medicine research: where are the methods? *Ann Emerg Med*. 1996;27:305-308.
20. Badcock D, Kelly AM, Kerr D, et al. The quality of medical record review studies in the international emergency medicine literature. *Ann Emerg Med*. 2005;45:444-447.
21. Worster A, Bledsoe RD, Cleve P, et al. Reassessing the methods of medical record review studies in emergency medicine research. *Ann Emerg Med*. 2005;45:448-451.
22. Kaji AH, Schriger D, Green S. Looking through the retrospectoscope: reducing bias in emergency medicine chart review studies. *Ann Emerg Med*. 2014;64:292-298.
23. Brennan RL, Prediger DJ. Coefficient Kappa: some uses, misuses, and alternatives. *Educ Psychol Meas*. 1981;41:687-699.
24. Bartko JJ. The intraclass correlation coefficient as a measure of reliability. *Psychol Rep*. 1966;19:3-11.
25. Faouzi J, Colliot O. Classic machine learning methods. In: Colliot O, ed. *Machine Learning for Brain Disorders*. Humana; 2023:25-75.
26. Stiell IG, Wells GA. Methodologic standards for the development of clinical decision rules in emergency medicine. *Ann Emerg Med*. 1999;33:437-447.
27. Concato J, Feinstein AR, Holford TR. The risk of determining risk with multivariable models. *Ann Intern Med*. 1993;118:201-210.
28. Mormeneo Bayo S, Palacián Ruiz MP, Moreno Hijazo M, et al. Bacteremia during COVID-19 pandemic in a tertiary hospital in Spain. *Enferm Infecc Microbiol Clin (Engl Ed)*. 2022;40:183-186.
29. Esquer Garrigos Z, Wingler MJB, Svoronos PA, et al. Increased rates of blood culture contamination during the coronavirus disease 2019 pandemic. *Infect Control Hosp Epidemiol*. 2022;43:1719-1721.
30. Driedger M, Daneman N, Brown K, et al. The impact of the COVID-19 pandemic on blood culture practices and bloodstream infections. *Microbiol Spectr*. 2023;11:e0263023.
31. Kuppermann N, Holmes JF, Dayan PS, et al. Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study. *Lancet*. 2009;374(9696):1160-1170.
32. Yankova LC, McDaniel CE, Kerns E, et al. Diagnostic performance of AAP-recommended inflammatory markers in febrile infants aged 60 days or younger. *Pediatrics*. 2025;155:e2024068856.
33. Joffe M, Avner JR. Follow-up of patients with occult bacteremia in pediatric emergency departments. *Pediatr Emerg Care*. 1992;8:258-261.
34. Kornberg AE, Jain N, Dannenhoffer R. Evaluation of false positive blood cultures: guidelines for early detection of contaminated cultures in febrile children. *Pediatr Emerg Care*. 1994;10:20-22.
35. Søgaard M, Nørgaard M, Schønheyder HC. First notification of positive blood cultures and the high accuracy of the gram stain report. *J Clin Microbiol*. 2007;45:1113-1117.
36. Elzi L, Babouee B, Vögeli N, et al. How to discriminate contamination from bloodstream infection due to coagulase-negative staphylococci: a prospective study with 654 patients. *Clin Microbiol Infect*. 2012;18:E355-E361.
37. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization. The true consequences of false-positive results. *JAMA*. 1991;265:365-369.
38. Gilligan PH. Blood culture contamination: a clinical and financial burden. *Infect Control Hosp Epidemiol*. 2013;34:22-23.
39. Alahmadi YM, Aldeyab MA, McElroy JC, et al. Clinical and economic impact of contaminated blood cultures within the hospital setting. *J Hosp Infect*. 2011;77:233-236.
40. Newgard CD, Smith M, Lin A, et al. The cost of emergency care for children across differing levels of emergency department pediatric readiness. *Health Aff Sch*. 2023;1:qxad015.
41. Gill PJ, Thavam T, Anwar MR, et al. Prevalence, cost, and variation in cost of pediatric hospitalizations in Ontario, Canada. *JAMA Netw Open*. 2022;5:e2147447.
42. Moore BJ, Freeman WJ, Jiang HJ. Costs of Pediatric Hospital Stays, 2016. Healthcare Cost and Utilization Project. Updated 2019. Accessed December 18, 2024. <https://hcup-us.ahrq.gov/reports/statbriefs/sb250-Pediatric-Stay-Costs-2016.jsp>
43. Cummings EA, Reid GJ, Finley AG, et al. Prevalence and source of pain in pediatric inpatients. *Pain*. 1996;68:25-31.
44. Kennedy RM, Luhmann J, Zempsky WT. Clinical implications of unmanaged needle-insertion pain and distress in children. *Pediatrics*. 2008;122(Suppl 3):S130-S133.
45. Aggarwal R, Mahajan P, Pandiya S, et al. Antibiotic resistance: a global crisis, problems and solutions. *Crit Rev Microbiol*. 2024;1:26.
46. Malcolmson C, Ng K, Hughes S, et al. Impact of matrix-assisted laser desorption and ionization time-of-flight and antimicrobial stewardship intervention on treatment of bloodstream infections in hospitalized children. *J Pediatric Infect Dis Soc*. 2017;6:178-186.
47. Cruz S, Abreu D, Gomes R, et al. An improved protocol for bacteria identification by MALDI-TOF MS directly from positive blood cultures. *Eur J Clin Microbiol Infect Dis*. 2024;43:605-610.
48. Chien JY, Lee TF, Du SH, et al. Applicability of an in-house saponin-based extraction method in bruker biotyper matrix-assisted laser desorption/ionization time-of-flight mass spectrometry system for identification of bacterial and fungal species in positively flagged blood cultures. *Front Microbiol*. 2016;7:1432.
49. Karadag D, Ergon MC. Investigation of different methods in rapid microbial identification directly from positive blood culture bottles by MALDI-TOF MS. *Microbiol Spectr*. 2024;12:e0063824.
50. Messacar K, Hurst AL, Child J, et al. Clinical impact and provider acceptability of real-time antimicrobial stewardship decision support for rapid diagnostics in children with positive blood culture results. *J Pediatric Infect Dis Soc*. 2017;6:267-274.
51. Andrei AI, Tălăpan D, Rafila A, et al. Influence of multiplex PCR in the management of antibiotic treatment in patients with bacteremia. *Antibiotics (Basel)*. 2023;12:1038.
52. Altun O, Almuhayawi M, Ullberg M, et al. Clinical evaluation of the FilmArray blood culture identification panel in identification of bacteria and yeasts from positive blood culture bottles. *J Clin Microbiol*. 2013;51:4130-4136.