Cost Analysis of Emergency Department Criteria for Evaluation of Febrile Infants Ages 29 to 90 Days

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Objective To compare the medical costs associated with risk stratification criteria used to evaluate febrile infants 29-90 days of age.

Study design A cost analysis study was conducted evaluating the Boston, Rochester, Philadelphia, Step-by-Step, and PECARN criteria. The percentage of infants considered low risk and rates of missed infections were obtained from published literature. Emergency department costs were estimated from the Centers for Medicare and Medicaid Services. The Health Care Cost and Utilization Project databases were used to estimate the number of infants ages 29-90 days presenting with fever annually and costs for admissions related to missed infections. A probabilistic Markov model with a Dirichlet prior was used to estimate the transition probability distributions for each outcome, and a gamma distribution was used to model costs. A Markov simulation estimated the distribution of expected annual costs per infant and total annual costs.

Results For low-risk infants, the mean cost per infant for the criteria were Rochester: $1050 (IQR $1004-$1092), Philadelphia: $1416 (IQR, $1365-$1465), Boston: $1460 (IQR, $1411-$1506), Step-by-Step $942 (IQR, $899-$981), and PECARN $1004 (IQR, $956-$1050). An estimated 18 522 febrile 1- to 3-month-old infants present annually and estimated total mean costs for their care by criteria were: Rochester, $127.3 million (IQR, $126.1-$128.5); Philadelphia, $129.9 million (IQR, $128.7-$131.1); Boston, $128.7 million (IQR, $127.5-$129.9); Step-by-Step, $ 126.6 million (IQR, $125.4-$127.8); and PECARN, $125.8 million (IQR, $124.6-$127).

Conclusions The Rochester, Step-by-step, and PECARN criteria are the least costly when evaluating infants 29-90 days of age with a fever. *(J Pediatr 2021;231:94-101)*.

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The approach to evaluating a febrile young infant has been debated heavily in the literature.[1-23] Infants are stratified into low-risk and high-risk groups based on clinical and laboratory evaluation. Infants less than 28 days of age are considered to be relatively higher risk, with double the rates of bacteremia and meningitis as older infants,[24] and therefore receive blood, urine, and cerebrospinal fluid evaluation followed by admission for parenteral antibiotics.[25] There is more variation in the workup and treatment of infants from 29 to 90 days of age.[12,16,17,21,22]

Multiple risk stratification criteria have been derived for the management of low-risk febrile infants ages 29-90 days (**Table I**)[12,16,17,21,22] and have become known as the Boston criteria, Philadelphia criteria, Rochester criteria, Step-by-Step approach, and the PECARN clinical prediction rule. The major differences between the criteria are the use of different laboratory markers (eg, procalcitonin vs white blood cell count), necessity of lumbar puncture (LP), chest radiograph, and use of antibiotics for low-risk infants. A prior cost effectiveness study showed that the use of the Boston criteria was the most cost-effective strategy[5]; however this study was completed prior to the introduction of the *Haemophilus influenzae* type B and pneumococcal vaccines as well as the common use of laboratory sepsis biomarkers. Another analysis showed that multiple risk stratification criteria are accurate at identifying serious bacterial infections (SBI), but that costs need to be considered.[26] There has also been a notable shift in the types of SBI among infants with urinary tract infections (UTI) now accounting for up to 92% of SBI vs only 30%-55% previously.[27]

With the presence of multiple criteria, costs must be considered in the evaluation of febrile infants. The primary aim of this study was to compare the mean

ED	Emergency department
LP	Lumbar puncture
NEDS	National Emergency Department Sample
SBI	Serious bacterial infection
SEDS	State Emergency Department Sample
UTI	Urinary tract infection

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medical costs per infant using the 5 criteria for low-risk infants 29-90 days old. Given the lack of bacterial meningitis identified in this age group in recent studies[2,9,13,15,19] and the high negative predictive values of the Step-by-Step approach[2,21,23] and PECARN clinical prediction rule,[22] it was hypothesized that these criteria would be the least costly. As a secondary aim, we evaluated the total annual costs for evaluating febrile infants 29-90 days of age (both low and high risk), given that each criterion has different variables for risk stratification which affects total cost of care.

Methods

A decision tree was constructed for the evaluation of a febrile infant (**Figure 1**). Febrile infants ages 29-90 days evaluated in US emergency departments (EDs) proceeded through the decision tree until they reached a terminal end point. Terminal end points were determined to be a negative workup, meningitis, UTI, UTI with complications, bacteremia, or bacteremia with complications. Complications were defined as any progression of a missed illness. Bacteremia from a UTI was defined as a UTI with complications. If an infant had multiple infections, their course terminated with the most complicated and expensive end point that was applicable. The total number of infants ages 29-90 days presenting with fever each year was estimated by using the number of infants 1-2 months of age who received a blood culture as part of their ED evaluation using the 2014 National Emergency Department Sample (NEDS)[28] and the 2011 State Emergency Department Sample (SEDS).[29] Because NEDS only provides the number of children less than 1 year of age who had a blood culture drawn, SEDS state data were used to estimate the proportion of infants that fall between 29 and 90 days. SEDS data were used from Arizona, California, Iowa, Kentucky, Maryland, North Carolina, Nebraska, New Jersey, Nevada, New York, and Vermont.

To determine the probabilities for each of the nodes on the decision tree for each criteria, a literature search was conducted using combinations of search terms "febrile infant," "lumbar puncture," "Boston criteria," "Philadelphia criteria," "Rochester criteria," "Step-by-Step," and "PECARN." A total of 17 articles were found assessing the criteria. Articles were excluded if they focused only on infants less than 28 days or if they did not describe the types of SBIs identified. Thirteen articles remained after exclusions (**Table II**). Data from the articles were pooled to create transition probabilities for each terminal node.

Costs were calculated for the evaluation of febrile infants 29-90 days using each of the 5 criteria. Costs were included from initial evaluations, admissions owing to missed infections, and immediate published complications. They were considered from the payer's perspective. Bundles were created following the evaluation and treatment recommended by the criteria in the original publication (**Table III**; available at www.jpeds.com). The ED costs for each bundle were estimated from the Centers for Medicare and Medicaid Services fee schedule using the national facility price.[30,31] Bundles that did not include an LP had costs for an ED visit charged at 99283, whereas criteria including an LP were bundled with an ED visit charged at 99284. This was determined based on a sample of charges from NEDS including the laboratory measures listed in the bundles. Costs for returning to the ED and admission to the hospital for a SBI were estimated using the 2009 Kid's Inpatient Database[32] for each diagnosis. All costs were converted to 2018 dollars using the Personal Consumption Expenditures[33] obtained from the Federal Reserve of Economic Analysis.

To account for the variations in public and private insurance, costs were adjusted. The Medicare Payment Advisory Committee released a report to congress in 2017 stating that Medicare payments were on average 0.78 of commercial insurance.[34] Medicare payments were used for this study as with the Patient Protection and Affordable Care Act Medicaid payments were raised to Medicare levels in all states with federal funds.[35] Using this information and data from the 2016 Survey of Children's Health showing 56.4% of children are estimated to have private insurance, costs were adjusted accordingly.[36] Discount rate used was 0% as illness is short and most infants recover without complications.[37]

The cost for the high-risk terminal node was estimated by taking the rates of SBI in infants 29-90 days of age[27] and multiplying by the number of infants falling down the high-risk pathway to determine the admission costs associated with SBI in this group. Because it is estimated that 13.5% of these infants will have an SBI, the costs for the additional 86.5% of high-risk infants were calculated by estimating the cost of an admission to the hospital for fever from the Centers for Medicare and Medicaid Services fee schedule.[38]

After all data were collected and put into the decision tree, a probabilistic Markov model with a Dirichlet prior was used to estimate the transition probability distributions for each outcome. The hierarchical Bayesian model effectively captures uncertainty in the event rates and costs, acting as a probabilistic sensitivity analysis. The prior event rate equaled the average across the 5 criteria, with some added prior probability (0.0001) for meningitis. Posterior distributions of transition probabilities for each criteria were obtained by factoring in the number of occurrences observed for each outcome for that criteria. More specifically, let $\alpha = (\alpha_1, \ldots, \alpha_K)$ represent the concentration hyperparameter for the prior distribution, where $1, \ldots, K$ is the number of outcomes and α_1 is the sum of outcome type 1 across all the studies. Let $\boldsymbol{c} = (c_1, \ldots, c_K)$ be the observed number of occurrences in each outcome for a given criteria. Then the posterior distribution for that criteria is Dirichlet with parameter vector $(c_1 + \alpha_1, \ldots, c_K + \alpha_K)$. A gamma distribution with mean equal to the variance was used to model costs and introduce variability. We ran 10 000 Markov simulations to estimate the distribution of expected annual costs per infant and total annual costs for all infants. To gauge

Table I. Criteria as described in their original publications[12,16,17,21,22]

Criteria	History	Laboratory tests	Disposition
Boston criteria	Well appearing by examination No evidence of infection on examination No vaccines in last 48 hours No antibiotics in last 24 hours	WBC <20 000 UA <10 WBCs/hpf CSF <10 WBCs/hpf	Give intramuscular ceftriaxone and discharge home with follow-up
Philadelphia criteria	Well appearing by examination No evidence of infection on examination	WBC <15 000 Band:neutrophil count <0.2 UA <10 WBCs/hpf CSF <8 WBCs/hpf CSF negative gram stain Chest radiograph negative	Discharge home with follow-up
Rochester criteria	Well appearing by examination Born at or after 37 weeks No prior antibiotic therapy No unexplained hyperbilirubinemia No chronic illness Not hospitalized longer than mother No evidence of infection on examination	WBC 5000-15 000 Absolute band count <1500 UA ≤10 WBCs/hpf	Discharge home with follow-up
Step-by-step approach	Well appearing by examination No evidence of infection on examination	UA <10 WBCs/hpf Procalcitonin <0.5 ng/mL CRP ≤20 mg/L ANC ≤10,000	Discharge home with follow-up
PECARN clinical Prediction rule	Well appearing No antibiotics in prior 48 hours Born at or after 36 weeks No existing medical conditions	UA <10 WBCs/hpf ANC ≤4090 Procalcitonin ≤1.7 ng/mL	Discharge home with follow-up

ANC, absolute neutrophil count; *CSF*, cerebrospinal fluid; *UA*, urinalysis; *WBC*, white blood cell.

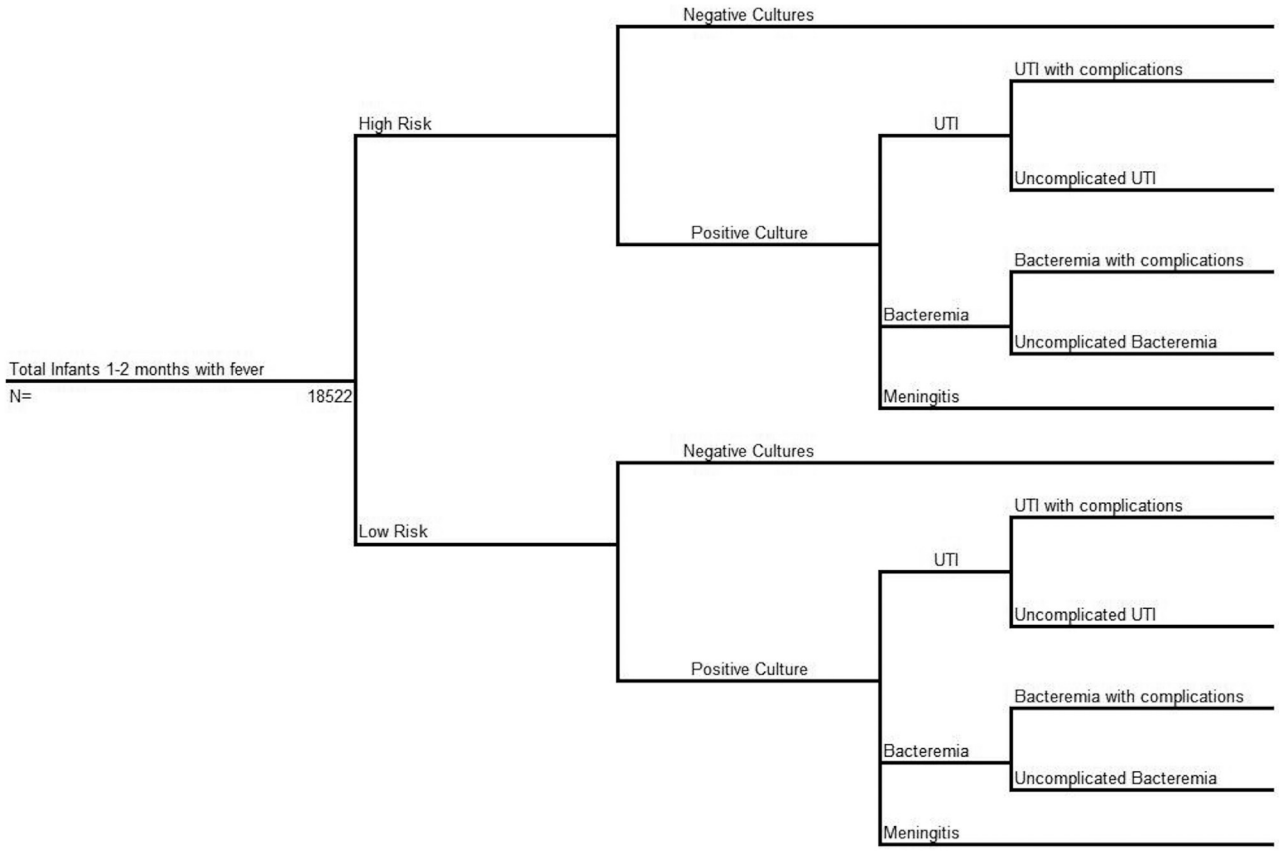

Figure 1. Decision tree for the evaluation of a febrile infant.

Table II. Articles used to create transition probabilities for each of the criteria

Studies	Year	Sample size	No. high risk	No. low risk	NPV	No. of low risk with SBI	Types of SBI in low-risk infants
Rochester criteria							
Dagan 1985[12]	1985	256	112 (44)	144 (56)	99.99%	0 (0.0)	None
Anbar 1986[20]	1986	126	56 (44)	70 (56)	95.70%	2 (2.8)	2 bacteremia
Dagan 1988[11]	1988	237	89 (37)	148 (63)	100.00%	0 (0.0)	None
Jaskiewicz 1994[7]	1994	1003	566 (56)	437 (44)	98.90%	5 (1.1)	2 bacteremia, 3 UTI
Garra 2005[10]	2005	259	186 (72)	73 (28)	97.30%	2 (2.7)	2 Bacteremia
Mintegi 2014[21]	2014	1123	665 (59)	458 (41)	98.90%	5 (1.1)	5 bacteremia
Gomez 2016[23]	2016	2185	1236 (57)	949 (43)	97.90%	20 (2.1)	16 bacteremia, 4 UTI
		5189					
Philadelphia criteria							
Baker 1993[17]	1993	747	460 (61.5)	287 (38.5)	99.70%	1 (0.3)	1 bacteremia
Brik 1997[15]	1997	492	196 (40)	296 (60)	97.00%	8 (3.0)	8 bacteremia
Garra 2005[10]	2005	181	147 (81)	34 (19)	97.10%	1 (2.9)	1 bacteremia
		1420					
Boston criteria							
Baskin 1992[16]	1992	503		503	94.60%	17 (3.5)	7 bacteremia, 1 bacteremia complicated by osteomyelitis, 8 UTI, 1 UTI with bacteremia
Kaplan 2000[6]	2000	2190	1044 (48)	1146 (52)	98.10%	23 (1.9)	6 bacteremia, 17 UTI
		2693					
Step-By-Step							
Mintegi 2014[21]	2014	1123	635 (57)	488 (43)	99.80%	1 (0.2)	1 bacteremia
Gomez 2016[23]	2016	2185	1194 (55)	991 (45)	98.90%	11 (1.1)	7 bacteremia, 4 UTI
Mintegi 2017[2]	2017	1416	740 (52)	676 (48)	99.999%	1 (0.001)	1 bacteremia
		4724					
PECARN							
Kupperman 2019[22]	2019	913	416 (46)	497 (54)	99.60%	3 (0.4)	1 bacteremia, 2 UTI
		913					

NPV, negative predictive value.
Values are number or number (%), unless otherwise indicated.

statistical significance in expected cost differences, Bayesian 95% credible intervals were calculated using the 2.5% and 97.5% percentiles of differences between criteria from the posterior distributions.

All analyses were run using the R statistical software, version 4.0.2.[39] The R package 'MCMCpack'[40] was used to facilitate Bayesian modeling and R packages 'lattice'[41] and 'Hmisc' for plotting. The R markdown file and associated compiled html file containing code and documentation to reproduce all analyses presented in the paper are available as supplemental material (**Supplemental File**). A Consolidated Health Economic Evaluation Reporting Standards checklist was used when creating this article.[37]

Results

An estimated 18 522 febrile infants 29-90 days of age are evaluated in US EDs each year. Based on the literature reviewed, if the criteria are applied, 8135 infants in the Rochester criteria, 8048 infants in the Philadelphia criteria, 9368 infants in the Boston criteria, 8450 in the Step-by-Step approach, and 10 082 in the PECARN clinical prediction rule proceed down the low-risk pathway of the decision tree.

The prior literature on the criteria was pooled and weighted to determine the rates of missed infections and adverse events for low-risk infants. Posterior mean and IQR for the proportion of low-risk infants in each terminal node using each criteria from the Bayesian Markov model are given in **Table IV** (available at www.jpeds.com). Literature reviewing the Rochester criteria showed that low-risk infants had a 0.48% risk of being discharged home with a missed UTI and a 0.93% chance of having missed bacteremia. Low-risk infants using the Philadelphia criteria had a 0.49% risk of having a missed UTI and a 0.90% chance of having missed bacteremia. The risk of a missed UTI was 0.71% and the risk of missed bacteremia was 0.83% for infants meeting the low-risk requirements of the Boston criteria. Using the Step-by-Step criteria, low-risk infants had a 0.45% risk of having a missed UTI and 0.74% risk of having missed bacteremia. Low-risk infants evaluated with the PECARN clinical prediction rule had a 0.52% risk of having a missed UTI and a 0.79% risk of having missed bacteremia.

The only adverse events in low-risk infants from these missed infections described in the literature included an infant evaluated with the Boston criteria with a UTI developing bacteremia and 1 infant who was found to have *Staphylococcus aureus* bacteremia that developed into osteomyelitis.[16] These infants were treated appropriately without additional reported complications. No other complications including intensive care unit admissions or death were reported in the studies. The literature showed no cases of bacterial meningitis in low-risk, well-appearing infants and the probabilistic sensitivity provided an estimated IQR of 0%-0.01%.

Expected costs per infant for the low-risk arm of the decision tree were calculated for each criteria and are shown in

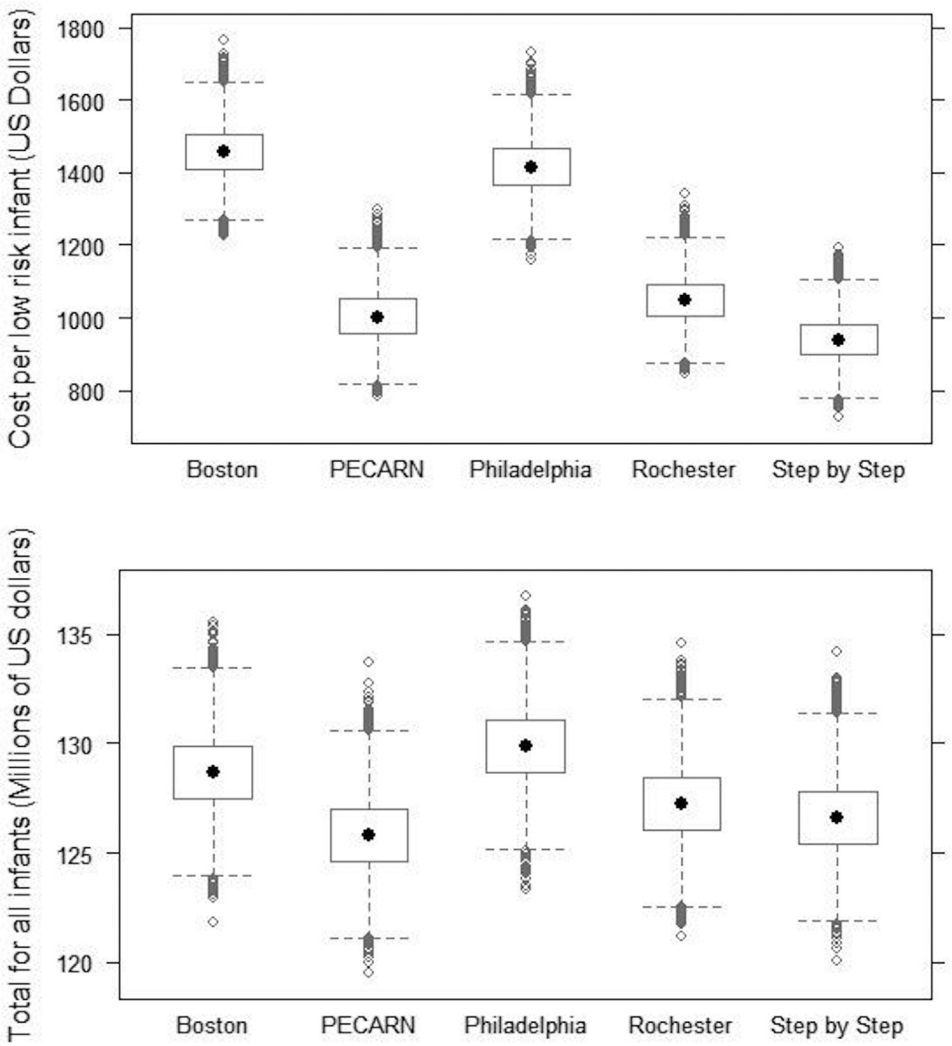

Figure 2. Box plots of the estimated mean 2018 cost (in US dollars) per low-risk infant, for infants ages 29-90 days evaluated by the 5 different criteria (*top*). Box plots of the estimated mean total 2018 costs (in millions of US dollars) for all febrile infants ages 29-90 days evaluated by the 5 different criteria (*bottom*).

the box plot in **Figure 2**. For low-risk infants, mean cost-per-infant was $1050 (IQR, $1004-$1092) for the Rochester criteria, $1416 (IQR $1365-$1465) for the Philadelphia criteria, $1460 (IQR $1411-$1506) for the Boston criteria, $942 (IQR $899-$981) for the Step-by-Step criteria, and $1004 (IQR $956-$ 1050) for the PECARN criteria.

Expected total annual costs per criteria for all infants ages 29-90 days with a fever is shown in **Figure 2**. If all infants are evaluated according to their stratification into high and low-risk arms, mean total costs would be $127.3 million (IQR, $126.1-$128.5) for the Rochester criteria, $129.9 million (IQR, $128.7-$131.1) for the Philadelphia criteria, $128.7 million (IQR, $127.5-$129.9) for the Boston criteria, $126.6 million (IQR, $125.4-$127.8) for the Step-by-step criteria, and $125.8 (IQR, $124.6-$127) for the PECARN criteria.

Bayesian 95% credible intervals comparing statistical significance between groups for both low-risk infants and total annual costs are shown in **Figure 3** (available at www.jpeds.com). Each criteria was directly compared with the other criteria for differences in costs of low-risk infants and total annual costs for all infants 29-90 days of age with a fever. There were no differences in costs for low-risk infants between the Rochester, Step-by-Step, and PECARN criteria. There were also no differences in costs for low-risk infants between the Boston and Philadelphia criteria. Costs for low-risk infants were significantly lower for the Rochester, Step-by-Step, and PECARN criteria when compared with the Boston and Philadelphia criteria. For total annual costs of all infants ages 29-90 days presenting to US EDs with a fever the Step-by-Step and PECARN guidelines were the least costly. The Philadelphia criteria were the costliest. There was no difference in costs between the Rochester, Step-by-Step, and PECARN criteria; however, when the Rochester criteria were compared with the Boston criteria, the 95% credible interval just hit 0.

Discussion

Our study demonstrated that the Step-by-Step, PECARN, and Rochester criteria are the lowest cost risk stratification criteria when considering mean costs per low-risk infant. This finding is likely because they do not include a LP, chest radiograph, or empiric antibiotics. The most costly outcome in our modeling was "missed infections." The costs of the evaluation of low-risk infants ranges from $307 to 735 depending on the criteria used while the cost of an admission for the infant who was discharged with *S aureus* bacteremia complicated by osteomyelitis exceeded $128 000. Admissions for missed infections are costly, but the existing literature suggested that these complication rates are low and similar across criteria; therefore, the less invasive criteria resulted in lower costs.

In comparison with our study, a cost-effectiveness study in 1992 showed that a full laboratory evaluation (blood, urine, and cerebrospinal fluid), and if low risk, administration of ceftriaxone and discharge with close follow-up was the most economical approach. This practice most closely correlates with the Boston criteria.[5] This observation is likely due to the addition of routine pneumococcal and *H influenzae* type B vaccinations and increased sensitivity of urinalysis since this prior study was completed. The rates of adverse events and reduction in meningitis sequelae were also estimated in the 1992 study using a Delphi survey instead of reports in the literature. A missed case of meningitis produces one of the costliest admissions and has associated risks including long-term poor neurologic outcomes and death. In review of the contemporary literature, there were no cases of bacterial meningitis identified in the infants who stratified into the criteria's low-risk groups.[2,6,7,10-12,15-17,20-23,39,40] When calculating costs in our study, a complicated meningitis category was not considered for the low-risk treatment arm, but we did consider acute care costs for meningitis when estimating the cost of all admissions for febrile infants ages 29-90 days.

All criteria missed a small percentage of UTIs and bacteremia. With the exception of 1 study of the Boston criteria, no complications from these missed infections were identified in the literature.[2,6,7,10-12,15-17,20-23] In the study evaluating the Boston criteria, 1 infant had bacteremia and a UTI, and another infant developed osteomyelitis from inadequately treated staphylococcal bacteremia. Interestingly, this infant was well-appearing and stratified into the high-risk group by the Philadelphia criteria with a white blood cell count of 15 000. The literature from all criteria showed only 1 case of bacteremia associated with a UTI in the low-risk groups. This result is likely due to the increased sensitivity of urinalysis compared with earlier studies of febrile infants,[39,40] leading to fewer adverse events from untreated UTIs.

Differences in testing recommendations have additional considerations beyond missed infections. Past literature demonstrated that more than 47% of LPs are traumatic.[41] Newer literature shows that the cerebrospinal fluid white blood cell count can be adjusted in traumatic LPs,[42] but traumatic LPs may lead to more hospitalizations among otherwise low-risk infants owing to the difficulty of interpreting them.[43] In the studies validating the febrile infant criteria, there were no discussions about the exclusion of traumatic LPs or discussion of white blood cell correction, and these infants were stratified to the high-risk arm.

Efforts should be made to limit testing that causes harm, such as pain or radiation exposure, while providing limited benefit to the infant. The original Philadelphia criteria recommended a routine 2-view chest radiograph in addition to LP, in all febrile infants as part of the evaluation.[17] Multiple studies have shown that a chest radiograph contributes no additional information with a normal clinical examination in the absence of respiratory symptoms and is supported by the lack of pneumonia identified in infants deemed low risk.[44-47]

An important influence on institutional cost is the number of infants stratified to the low-risk treatment arm. Different parameters are used by each criteria to stratify infants. The Rochester criteria use additional historical parameters and the Step-by-Step and PECARN criteria use a stepwise laboratory approach. To account for these differences, the total costs for the criteria were calculated to include high-risk infants. These infants are known to have higher costs owing to hospital admission for intravenous antibiotics. When considering total annual costs for all infants' ages 29-90 days who present to EDs with fever, the Step-by-Step and PECARN criteria were the least costly. However, the Step-by-Step and PECARN criteria rely on procalcitonin, which may not be readily available in all settings.

Implementing criteria for evaluating febrile infants can result in substantial cost savings to institutions and insurers. In our analysis, the difference between the highest median total cost criteria (Philadelphia) and the lowest (PECARN) was $4.1 million. The 2 lowest total median cost criteria (Step-by-Step and PECARN) differed by $0.8 million. However, beyond selecting which criteria to follow, institutions should use quality improvement methods to optimize febrile infant guideline implementation. One study found that even though physicians easily identify the criteria they use, their ordering habits rarely follow the identified criteria.[48] Our search of the NEDS database when designing this study supported this finding; most of the infants had additional testing, including viral testing. Infants with identified viral infections may be at lower risk of SBI, but viral testing is not included in any of the criteria.[14] The literature demonstrates that clinical practice guidelines vary widely among institutions,[49] but institutions can successfully implement clinical practice guidelines for febrile infants allowing for significant cost reduction[13] and reduced time to antibiotic administration[50] without compromising care.

There are several recognized limitations of this study. This study generated estimates of bacterial infection rates based on the validation studies of the risk stratification criteria. Because each study had a small sample size, the data were pooled. These estimates may be limited by small sample sizes and a limited number of participating ED sites, and thus may

not be generalizable. Many of the studies conducted in the distant past included antibiotics given at the time of stratification into low- and high-risk groups, potentially mitigating the complications of missed infections. Several studies were conducted prior to standard pneumococcal and *H influenzae* vaccinations but included in our estimates because there were minimal contemporary data for these criteria. These earlier data may overestimate the current rates of bacteremia and meningitis for these criteria.

We considered infants ages 29-90 days; however, this age range was not validated for all 5 criteria and the studies did not stratify SBI by age; therefore, the SBI estimates may be inaccurate. Although many of these criteria are used for infant's ages 61-90 days, they are not all validated for this age range. We obtained our estimate for the total number of febrile infants' ages 29-90 days presenting to EDs by determining who had a blood culture obtained. This estimate is limited because it may include infants who presented for reasons other than fevers and does not include febrile infants evaluated in other settings. Overall costs may be inaccurate if the estimated total number of infants is inaccurate; however, it does not affect the calculated costs per infant because it would not change the ratios of infants at each terminal end point in the decision tree.

Costs were estimated by creating criteria-specific bundles and may not represent a physician's true ordering behavior. This study did not include the rates or costs of contaminated specimens in the care of infants. This factor would likely only further increase the costs of the more aggressive approaches because obtaining more cultures would increase the chance of having a contaminated specimen. This study focused solely on healthcare costs and did not include costs to the family such as stress, missed time from work, or the impact of early hospitalization on the infant-parent dyad.

Finally, quality-adjusted life-years were not considered. Long-term complications from meningitis are known, but it is a rare infection and none of the studies reviewed found a case in infants stratified as low risk. The long-term complications from the most prevalent infections are unknown, such as hypertension or reduced renal function owing to neonatal pyelonephritis. Further, any differences in long-term outcomes owing to delays in treatment or administration of antibiotics in infancy are unreported. Although ideally quality-adjusted life-years would be considered, an evidence report from the Agency for Healthcare Research and Quality concluded that evidence was significantly lacking surrounding the costs and harms of febrile infant evaluations.[26] As more data become available to quantify long-term complications of febrile infant illnesses, this study can be expanded to include quality-adjusted life-years.

This analysis of acute care costs demonstrated that when evaluating infants at low risk of SBI, the less invasive criteria (Rochester, PECARN, and Step-by-Step) are the least costly. Long-term complications of missed infections are unknown and were not included in the analysis; however, the literature reviewed demonstrates low rates of missed infections and acute care complications when the criteria are followed. Based on the data from this study, clinicians can be reassured there are overall cost savings in the least aggressive approach, even if it means a small number of patients return for admission. Emerging methods for identifying bacterial infections will result in new management criteria for febrile infants and viral testing and rapid stool assays will likely be included in them. Going forward, cost comparisons must continue to be an important contributor to their appraisal. We must also consider access to these more specialized tests, as most pediatric patients are evaluated in general community EDs.[51] ■

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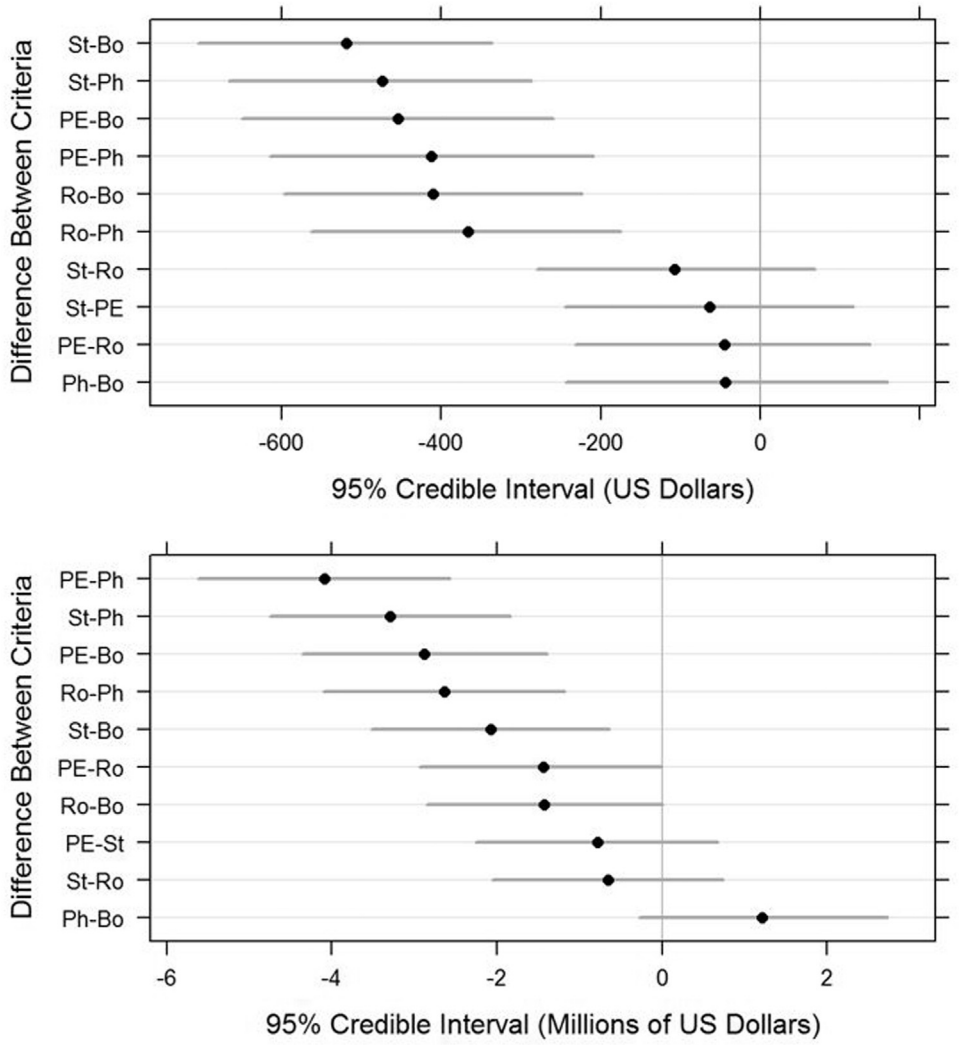

Figure 3. Dotplot indicating the median difference and 95% credible interval between criteria in expected 2018 cost (in US dollars) per low-risk infant, for infants ages 29-90 days evaluated by the 5 different criteria (*top*). Dotplot of the median difference and 95% credible interval between criteria in expected 2018 total costs (in millions of US dollars) for all febrile infants ages 29-90 days evaluated by the 5 different criteria. (*Bottom*) In both plots, the 95% credible interval is indicated by the horizontal blue line and differences were sorted from largest to smallest (in absolute value). A vertical line at zero indicates a null value of no difference. *Bo*, Boston; *PE*, PECARN; *Ph*, Philadelphia; *Ro*, Rochester; *St*, Step-by-Step.

Table III. Costs for the workup of each criteria and costs of admissions for missed infections

Name of items	Included charges	Year	CMS/KID cost ($)	2018 cost via personal consumption expenditures and weighted for payer source ($)
Boston Workup Bundle	Venipuncture, CBC with differential, blood culture, urine catheterization, urinalysis with microscopy, urine culture, LP, CSF cell count, CSF protein, CSF glucose, CSF culture, Ceftriaxone, Injection fee, ED visit level 4 physician charge, ED visit level 4 facility fee	2018	624.57	723.92
Philadelphia Workup Bundle	Venipuncture, CBC with differential, blood culture, urine catheterization, urinalysis with microscopy, urine culture, LP, CSF cell count, CSF protein, CSF glucose, CSF culture, chest radiograph technical fee, chest radiograph physician fee, ED visit level 4 physician charge, ED visit level 4 facility fee	2018	633.98	734.84
Rochester Workup Bundle	Venipuncture, CBC with differential, blood culture, urine catheterization, urinalysis with microscopy, urine culture, ED visit level 3 physician charge, ED visit level 3 facility fee	2018	307.10	355.88
Step by Step Workup Bundle	Venipuncture, CBC with differential, blood culture, urine catheterization, urinalysis with microscopy, urine culture, CRP, Procalcitonin, ED visit level 3 physician charge, ED visit level 3 facility fee	2018	346.57	401.70
PECARN Workup Bundle	Venipuncture, CBC with differential, blood culture, urine catheterization, urinalysis with microscopy, urine culture, CRP, Procalcitonin, ED visit level 3 physician charge, ED visit level 3 facility fee	2018	346.57	401.70
Admission for 24-48 hours		2018	7699.95	8655.36
Admission for meningitis		2009	98 369.00	112 435.77
Admission for osteomyelitis		2009	128 276.00	146 619.47
Admission for bacteremia		2009	48 958.00	55 958.99
Admission for UTI + bacteremia		2009	48 650.00	55 606.95
Admission for UTI		2009	29 677.00	33 920.81

CBC, complete blood count; *CMS*, Centers for Medicare and Medicaid Services; *CRP*, C-reactive protein; *CSF*, cerebrospinal fluid; *KID*, Kid's Inpatient Database.
Criteria workup costs calculated from CPT codes and associated CMS costs.[30,31] Costs were weighted for private insurers.[34-36] Admission costs obtained from the KID database[32] and converted to 2018 dollars.

Table IV. Mean and IQR for the proportion of low-risk infants along with each terminal node using each criteria

Criteria	Rochester	Philadelphia	Boston	Step-by step	PECARN
Low risk	0.4392	0.4345	0.5058	0.4562	0.5443
Negative culture	0.9858 (0.9850-0.9866)	0.9858 (0.9849-0.9868)	0.9841 (0.9832-0.9850)	0.9878 (0.9871-0.9886)	0.9865 (0.9856-0.9874)
Uncomplicated UTI	0.0048 (0.0042-0.0052)	0.0049 (0.0043-0.0054)	0.0071 (0.0065-0.0077)	0.0045 (0.0040-0.0049)	0.0052 (0.0046-0.0057)
Complicated UTI	0.0001 (0.0000-0.0001)	0.0001 (0.0000-0.0002)	0.0002 (0.0001-0.0003)	0.0001 (0.0000-0.0001)	0.0001 (0.0000-0.0002)
Uncomplicated bacteremia	0.0092 (0.0085-0.0098)	0.0090 (0.0082-0.0097)	0.0083 (0.0076-0.0089)	0.0074 (0.0067-0.0079)	0.0079 (0.0072-0.0086)
Complicated bacteremia	0.0001 (0.0000-0.0001)	0.0001 (0.0000-0.0002)	0.0002 (0.0001-0.0003)	0.0001 (0.0000-0.0001)	0.0001 (0.0000-0.0002)
Meningitis	0.0001 (0.0000-0.0001)	0.0001 (0.0000-0.0001)	0.0001 (0.0000-0.0001)	0.0000 (0.0000-0.0001)	0.0001 (0.0000-0.0001)

Results were obtained using a Bayesian Markov model with a Dirichlet prior distribution set to the weighted average of the estimates for each criteria pulled from the literature.[2,6,7,10-12,15-17,20-23]