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Derivation and Validation of Predictive Models for Early Pediatric Sepsis

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Why this matters

Leading Cause of Death

- *Sepsis kills kids worldwide*
- *75,000 children hospitalized with sepsis with 5-20% in-hospital mortality*

Delayed Diagnosis = Worse Outcomes

- *Delayed treatment increases mortality and organ dysfunction duration*

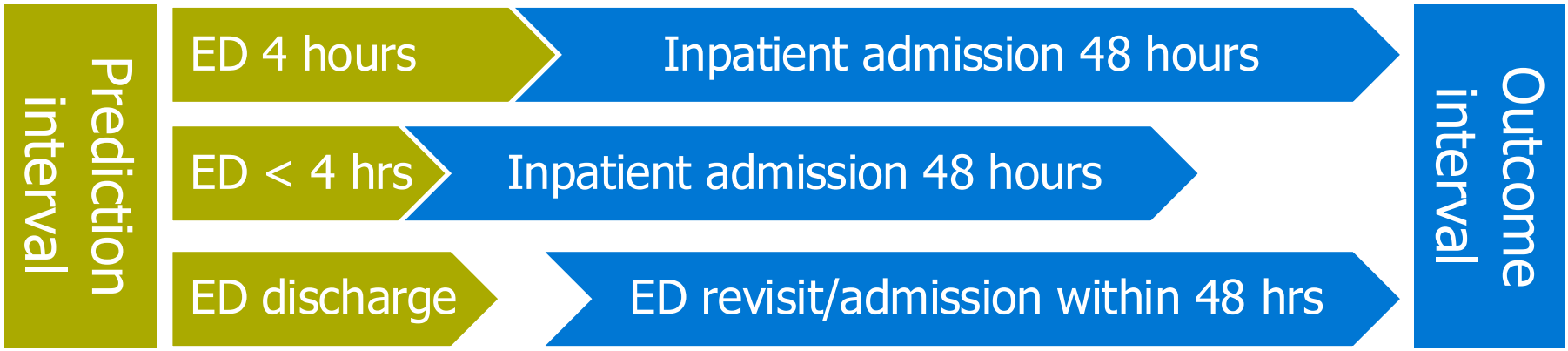
Gap in Existing Tools

- *No prior multicenter models predict sepsis before organ dysfunction in undifferentiated ED patients*

Study Objective and Design

Goal:

Derive and validate machine learning prediction model of pediatric sepsis that predicts organ dysfunction within 48 hours using ED EHR data from the first 4 hours of care



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Study Objective and Design

Setting: 5 PECARN health systems (5 quaternary & 3 affiliated EDs)

Source: Multi-site registry of EHR data

Population: ≥ 2 months to < 18 years of age

excluding 1) ED death or transfer; 2) trauma diagnosis; or 3) sepsis present during predictive features window

Timeframe:

Training: Jan 2016–Feb 2020

Validation: Jan 2021–Dec 2022

Features: Patient and physiologic characteristics within the first 4 hours of ED care

Outcome: Phoenix Sepsis and Septic Shock

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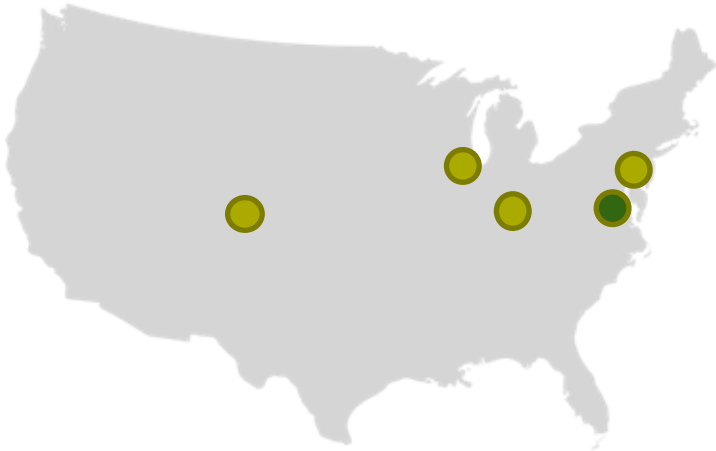
PED Screen and Beyond

Comprehensive ED and inpatient EHR data

- Demographics
- Clinical assessments
- Vital signs
- Medications
- Laboratory tests
- Imaging
- Lines/airways
- Notes
- ICD-10 dx & procedure codes



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- Lurie Chicago
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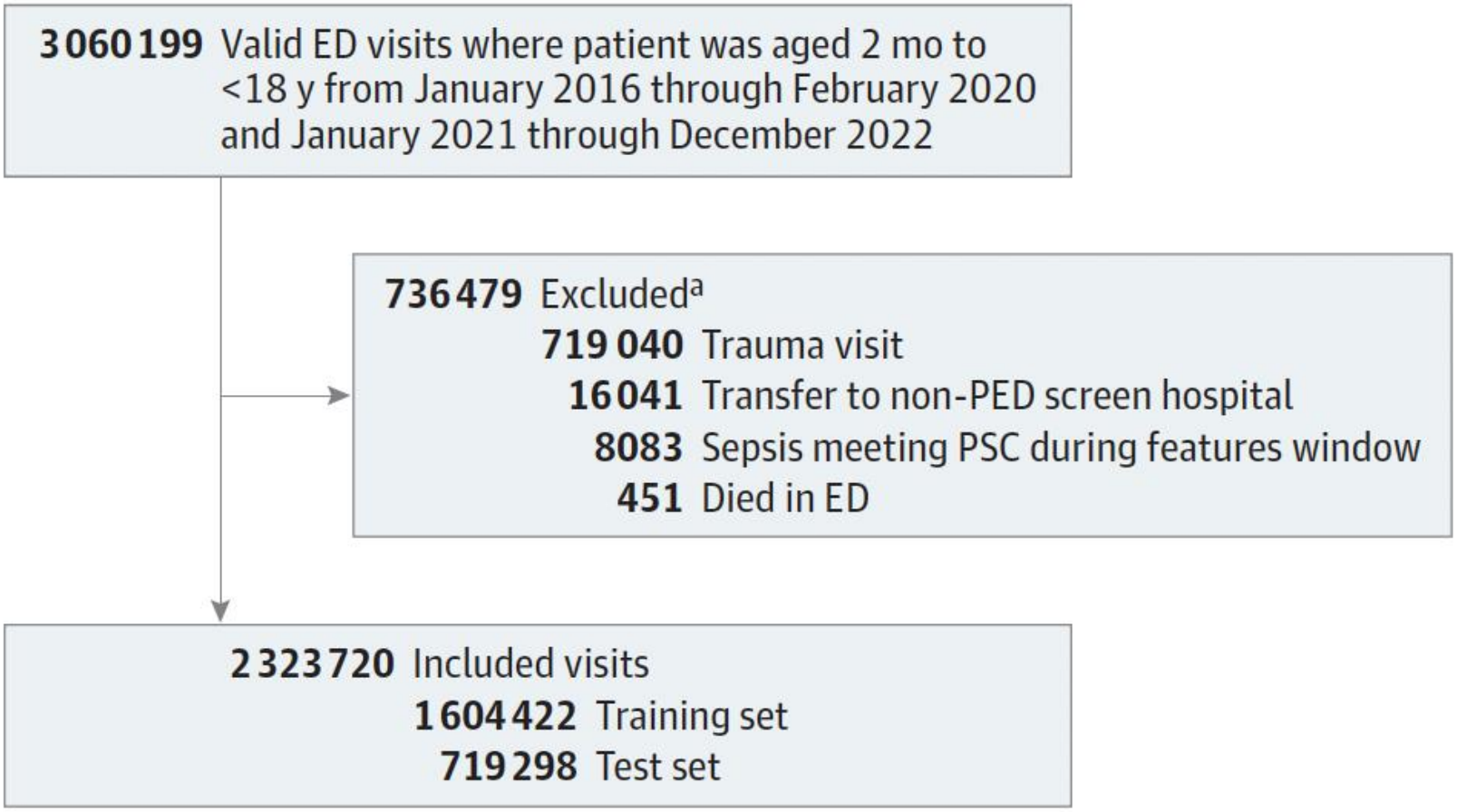
PECARN
Pediatric Emergency Care Applied Research Network

Figure 1. Flow Diagram



Results: Visits and Outcomes

Table 1. Phoenix Sepsis Criteria (PSC) Outcomes in the Study Cohort Excluding Individuals With Sepsis in the First 4 Hours of Emergency Department Care

Dataset	Visits with outcome, No. (%) [95% CI][a]	Range across health systems, %
Training (n = 1 604 422)		
PSC sepsis	5634 (0.35) [0.34-0.36]	0.17 to 0.50
PSC shock	2446 (0.15) [0.15-0.16]	0.08 to 0.26
Test (n = 719 298)		
PSC sepsis	2639 (0.37) [0.35-0.38]	0.22 to 0.61
PSC shock	1062 (0.15) [0.14-0.16]	0.09 to 0.21

[a] The outcome definition of suspected infection and sepsis or death included 16 of 8273 patients (5634 in the training cohort and 2639 in the test cohort) with PSC sepsis (0.19%) who did not meet sepsis organ dysfunction prior to death.

Machine Learning Models

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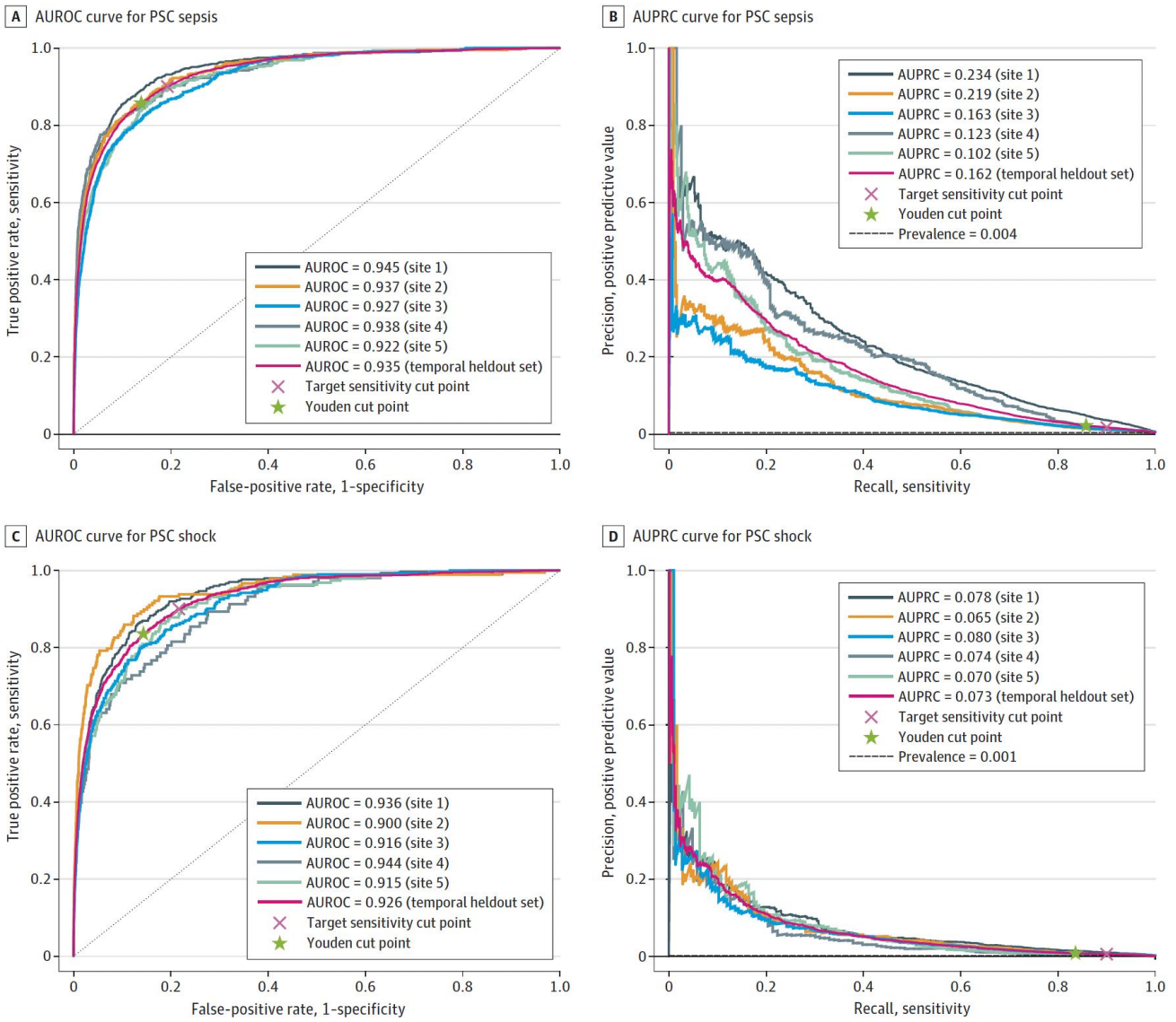
Precision-recall curve gives a more realistic sense of the challenge of predicting rare outcomes



For PSC sepsis (A and B) and PSC shock (C and D), the gradient tree boosting algorithm area under the receiver operator characteristic (ROC) curves and area under the precision-recall curves (AUPRC) are shown for the temporal validation dataset.

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	AUROC	Sensitivity	Specificity	PPV	NNE
PSC Sepsis					
$LR_{90\%}$	0.923	0.900	0.779	0.015	68
LR_{Youden}		0.844	0.854	0.021	48
$XGBoost_{90\%}$	0.936	0.900	0.807	0.017	59
$XGBoost_{Youden}$		0.858	0.861	0.022	45
PSC Shock					
$LR_{90\%}$	0.923	0.900	0.778	0.006	168
LR_{Youden}		0.848	0.840	0.008	128
$XGBoost_{90\%}$	0.926	0.900	0.783	0.006	164
$XGBoost_{Youden}$		0.836	0.857	0.009	117

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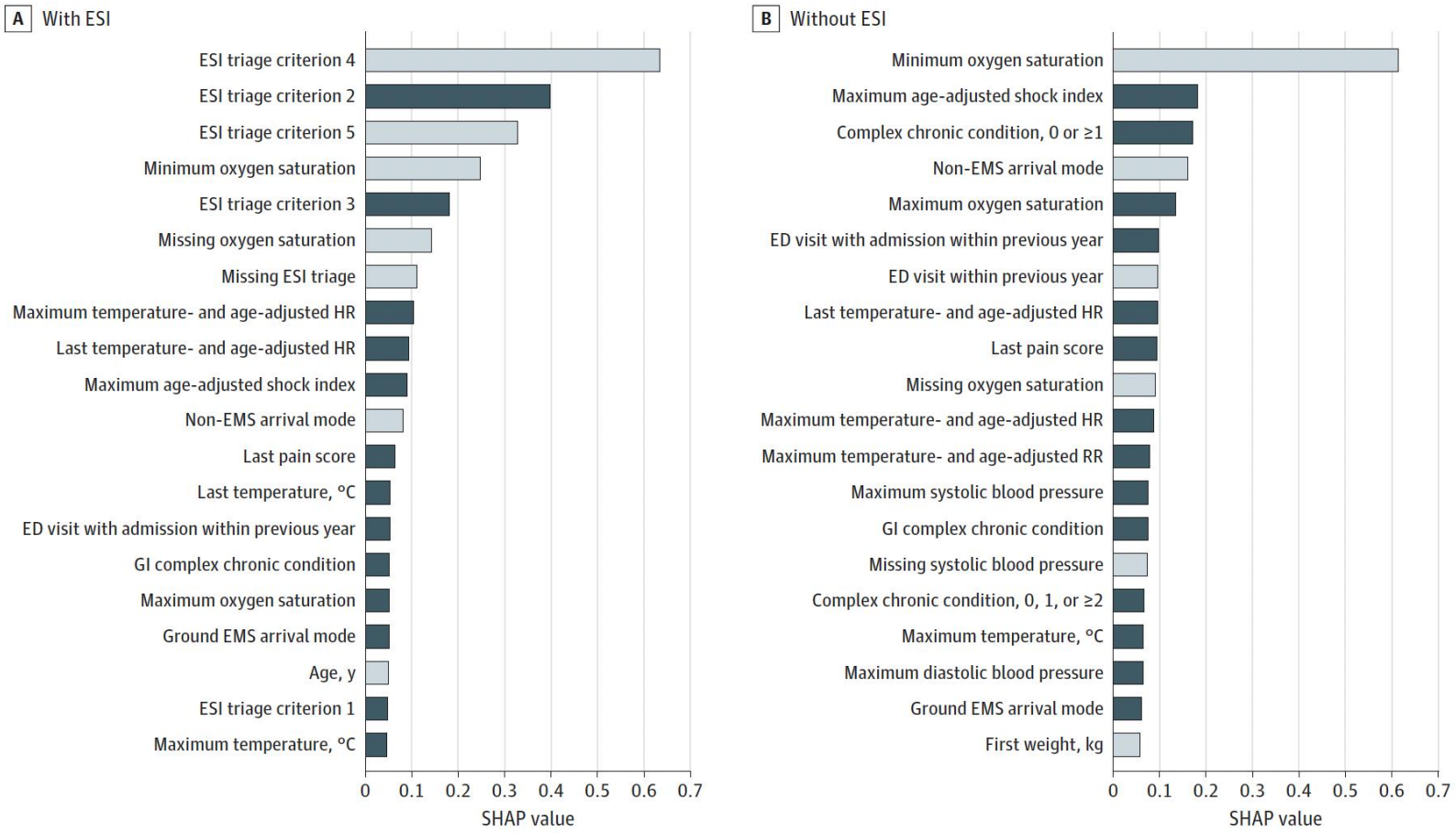
Important predictive features included ESI category; age and temp adjusted vital signs; oxygen saturation; age-adjusted shock index; and markers of medical complexity

Figure 3. Extreme Gradient Boosting Feature Importance With and Without Emergency Severity Classification (ESI)



Top 20 features are shown (dark blue indicates a positive association with the sepsis outcome and light blue indicates an inverse association with the outcome). ED indicates emergency department; EMS, emergency medical services; GI, gastrointestinal; HR, hazard ratio; SHAP, Shapley Additive Explanations.

Limitations

Clinical Judgement Markers

Some organ dysfunction outcomes are influenced by care processes (e.g., missing O_2 sat may reflect absence of respiratory distress)

Complex Model

Challenges for implementation, especially related to explainability and acceptability

Alarm

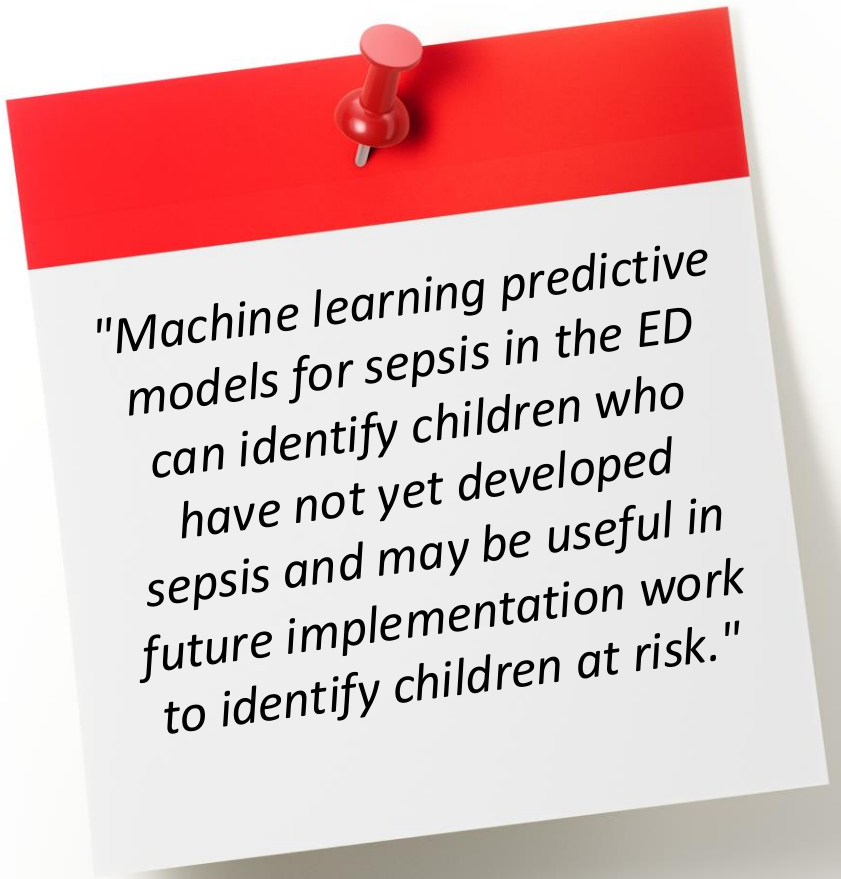
Inherent to rare outcomes; variable cutpoints will be needed to balance sensitivity and false positives

Generalizability

Limited to quaternary and affiliated community EDs; future work should include general EDs and prehospital settings.

Conclusions

- In a large multicenter EHR database, sepsis within 48 hours, when not present in the first 4 hours, was a rare outcome
- Developed and validated models with high areas under the receiver operating characteristic curve and meaningful positive likelihood ratios
- Findings illustrate the challenge of predicting the rare occurrence of pediatric sepsis in the ED setting
- Further work integrating EHR models with clinical judgement are needed



Thank you!

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