Development and Validation of Machine Learning Models to Predict Serious Infection and Sepsis Interventions in Children: A Multi-Centre Prospective Study

Dr Flora Silvester [1]; Eloise Blanquet [1]; Carlo Schillaci [6], Jacob Shaw [6]; Dr Ranjit Singh [1,6]; Melissa Mead [6]; Emily Jin [1]; Lawrence Adams [1]; Vitaliy Oliynyk [1]; Aleksandra Foy [1]; Dr Ewan Carr [2]; Dr Sylvester Gomes [1].

INSTITUTIONS: [1] Guys and St Thomas's Hospital; [2] Department of Biostatistics & Health Informatics, King's College, London; [3] Manchester University Foundation Trust & Clinical Data Science Unit; [4] Cambridge University Foundation Trust; [5] University College Hospital, London. **Patient & Public** [6]

INTRODUCTION

Early identification of children at risk for serious infection and sepsis in emergency departments is challenging. Existing criteria lack specificity for UK settings and do not support early risk prediction. Machine learning, a subset of artificial intelligence, offers potential to improve risk stratification by capturing complex patterns in routine data.

OBJECTIVES

To develop and validate multi-site machine learning models to predict serious infections, sepsis interventions, and outcomes in children attending emergency departments.

METHODS

Prospective observational cohort study across four UK NHS Trusts (October 2024-March 2026). Children <16 years presenting to paediatric emergency departments were included, excluding trauma. We developed multivariable prediction models using elastic net, random forest, and XGBoost algorithms with 30 demographic and clinical predictors from triage and blood tests. Internal-external validation used repeated leave-one-site-out cross-validation. Performance assessed using Brier score, AUC, and calibration. **Primary outcome:** Admission for intravenous antibiotics > 48 hours. **Secondary outcomes:** Critical care interventions (antibiotics with fluid resuscitation > 20 ml/kg and/or vasoactive agents, non-elective ventilation), ICU admission/death.

PATIENT & PUBLIC INVOLVEMENT

The study PPI group includes young people and adults, including former sepsis patients and their parents. Members met to discuss study progress, challenges, and application of public views and personal experiences. They helped translate Phase One findings into everyday language for wider public use. A Young Persons Advisory Group also provided oversight of study design, enhanced research questions, ensured ethical data use, reviewed analyses, and supported dissemination.

INTERIM RESULTS

Single site models (~14,000 attendances; 1.8% primary outcome prevalence), evaluated using nested 10-fold cross-validation, showed modest discrimination using triage information and demographics alone (AUROC 0.66-0.69). However, performance improved substantially after adding physiological observations and diagnostic groupings (AUROC 0.87–0.89) across models. Penalised regression showed excellent calibration; tree-based models demonstrated some miscalibration (Figure 1). Key predictors included temperature, heart rate, oxygen saturation, capillary refill time, triage severity, age, diagnostic groupings (Figure 2).

Figure 1. Calibration for Random Forest Model

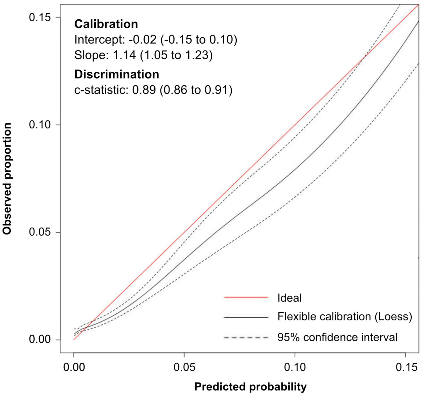
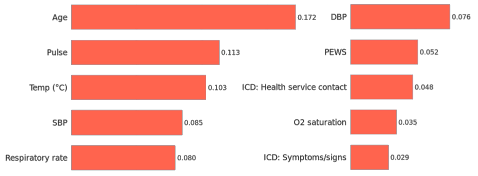


Figure 2. Feature importance for triage model (top 10)



CONCLUSIONS

Machine learning models demonstrated **strong discrimination and moderate calibration** for identifying children at increased risk of sepsis interventions. Adding physiological observations substantially improved performance, outperforming triage-based approaches. Multi-site validation results will inform future clinical decision support tools for paediatric sepsis.

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Corresponding author: sylvester.gomes1@nhs.net