

Predicting Positive Blood Cultures Early in Hospitalization Using Time Locked Electronic Health Record Data

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Abstract

Background

Blood cultures are essential for diagnosing serious infections, yet most do not yield a pathogen. We developed and internally validated a time locked electronic health record model to identify adults at highest risk for positive blood cultures among patients cultured within 24 hours of admission.

Methods

We performed a retrospective cohort study using data from MIMIC-IV version 3.1. Prediction was anchored at culture time, and only information available before that moment was used. We used subject level splitting, gradient boosted trees, validation set calibration, and clustered bootstrap confidence intervals. Secondary analyses tested robustness to variations in workflow features, prior history, measurement intensity, early death, and repeated admissions.

Results

Our cohort included 51,424 admissions from 36,275 subjects; 2,163 admissions (4.2%) were culture positive. The test set included 10,251 admissions from 7,255 subjects, with a culture positive prevalence of 4.04%. Our primary model achieved an AUROC 0.754 (95% CI, 0.726–0.778), AUPRC of 0.157 (95% CI, 0.129–0.193), and a Brier score of 0.037 (95% CI, 0.033–0.040). Culture positivity rose to 30.1% in the top 1%, 19.9% in the top 5%, and 10.8% in the top 20% of predicted risk groups.

Conclusions

Among adults already cultured early in hospitalization, a time locked electronic health record model can enrich for positive blood cultures. The model can have applications in post culture prioritization before results are finalized.

Background

Bloodstream infections are a major source of morbidity and mortality [1]. Blood cultures are central for diagnosis and antimicrobial decision making in patients with suspected sepsis or other serious infections, and current sepsis guidelines recommend obtaining cultures before antibiotics when this can be done without detrimental delay [2].

Blood cultures also have important limitations. Most do not yield a pathogen, and contaminated cultures can lead to unnecessary antibiotics, additional testing, longer length of stay, and greater unnecessary resource deployment [3–5]. These limitations create an operational need to identify, among patients already cultured, those who are most likely to have true pathogen positive results who may need faster microbiology follow up, stewardship review for appropriate antibiotics, or other downstream attention [3–7].

Prediction tools for bacteremia have been studied for more than a decade. Earlier work, including the Shapiro rule, focused on identifying lower risk emergency department patients in whom cultures might not be necessary [8]. Later reviews noted that heterogeneous populations and limited external validation create operational uncertainty concerning implementation [9, 10]. Recent emergency department machine learning tools and the Ottawa Bloodstream Infection Model show that clinically useful prediction is achievable, yet the window between culture draw and result confirmation has yet to be explored [11, 12].

In our study we focused on adults who had blood cultures obtained within the first 24 hours of hospital admission and anchored machine learning prediction to the time cultures were drawn. Our goal was not to decide whether a culture should be drawn, but to identify which cultures were most likely to become pathogen positive before knowing the result. We used only the chart information available before index culture time (t_0), including historical data and dynamic variables available 24 hours

before t0 to reflect the clinical window when laboratory prioritization, rapid diagnostics, and stewardship review could have additional impact [3, 6].

Methods

Study design and data source

We performed a retrospective cohort study using MIMIC-IV version 3.1, a deidentified electronic health record (EHR) dataset from Beth Israel Deaconess Medical Center [13, 14]. The analysis used only deidentified data and involved no patient contact. Reporting follows guidance for prediction model studies [15].

Cohort and prediction time

Our cohort includes adult admissions in which blood cultures were obtained within 24 hours of hospital admission. Prediction was anchored to the time of the patient's index culture drawn at time t0. Predictors were drawn from information available before t0 using the variable "storetime" in MIMIC-IV.

The model estimates risk at or immediately after blood cultures were obtained. Laboratory, vital signs, medication, and other dynamic variables were eligible only when the timestamp used for feature construction preceded t0; post t0 measurements / results first available after t0 were excluded.

Outcome and Predictors

Outcome and Predictors

The primary outcome was positive blood cultures in the admission window. Contaminant episodes were counted as negative. Contaminant organisms were identified from organism labels in the dataset and include skin flora such as coagulase negative staphylococci or *Staphylococcus epidermidis* type organisms, *Corynebacterium*, *Diphtheroids*, *Cutibacterium*, *Propionibacterium*, *Micrococcus*, and similar organisms [4, 5]. A tightened contaminant rule classified contaminant organisms as pathogen positive only when the same organism was recovered from more than one culture during admission testing. In the final dataset, 345 contaminant cultures were identified; the tightened rule then found only 291 contaminant events (Supplementary Table 1).

Predictors used in modelling included demographics, admission context, ICU status at t0, prior admissions / procedures, prior culture data, device history including catheters and implants, pre-culture antibiotic exposure, medication burden, routine laboratory values, and physiologic measurements such as vital signs.

Missing data, leakage safeguards, and modeling

No predictor was allowed to use information that was available after the culture time t0. Organism name text fields, death related variables, and post culture variables were excluded before fitting. Missing numeric values were handled natively by our tree-based model (XGBoost), and missing categorical values were encoded as a distinct category. Outcome composition and missingness for predictors are summarized in our supplemental material (Supplementary Table 1).

We used subject level training, validation, and test split so that each patient appeared in only one partition. This yielded 32,987 training admissions from 23,216 subjects, 8,186 validation admissions from 5,804 subjects, and 10,251 test admissions from 7,255 subjects. The test set was absent from tuning; the validation set was used for early stopping and calibration.

Modeling was done with XGBoost [16] using fixed hyperparameters with AUROC / AUPRC as evaluation metrics. Our learning rate was 0.05, maximum tree depth 4, minimum child weight 5, subsample 0.8, column subsample 0.8, L2 regularization 1.0.

We had up to 3,500 boosting rounds and early stopping after 50 rounds without validation improvement. Predicted probabilities were calibrated on the validation set using Platt scaling.

We assessed discrimination with AUROC / AUPRC, prediction error with the Brier score, and calibration with intercept and slope [17]. Confidence intervals were estimated by clustered bootstrap resampling, with 400 resamples for performance metrics and 200 for predictor importance. Predictor importance was summarized using mean SHAP values [18].

Analyses

The main analyses included the primary model (which had a curated feature set eliminating leakage prone fields and redundant variables) and comparator models with varying feature set sizes. This was followed by modelling which removed workflow/support features, prior positive blood culture history, early deaths, measurement intensity features (how often measurements were obtained before t0), and a sample with first admissions only. Assessment of additional comparator models are shown in Supplementary Table 2.

Results

Cohort characteristics

Cohort characteristics are shown in Table 1. The final cohort included 51,424 admissions from 36,275 unique subjects; 2,163 admissions (4.2%) were blood culture positive. The test set included 10,251 admissions from 7,255 subjects, with 414 pathogen positive admissions (4.04%).

Table 1
Cohort Characteristics

Statistic	Overall	Train	Validation	Test
Admissions, n	51424	32987	8186	10251
Unique subjects, n	36275	23216	5804	7255
Positive blood culture, n (%)	2163 (4.2%)	1379 (4.2%)	370 (4.5%)	414 (4.0%)
Age, median [IQR]	63.0 [51.0, 75.0]	63.0 [51.0, 75.0]	63.0 [51.0, 75.0]	64.0 [51.0, 75.0]
Female, n (%)	23584 (45.9%)	15051 (45.6%)	3734 (45.6%)	4799 (46.8%)
ICU at t0, n (%)	13162 (25.6%)	8456 (25.6%)	2041 (24.9%)	2665 (26.0%)
Admitted from ED, n (%)	23580 (45.9%)	15050 (45.6%)	3800 (46.4%)	4730 (46.1%)
Time to culture, median [IQR], h	7.6 [3.5, 14.1]	7.6 [3.5, 14.2]	7.5 [3.5, 13.8]	7.8 [3.4, 14.2]
Prior positive blood culture history, n (%)	11514 (22.4%)	7383 (22.4%)	1772 (21.6%)	2359 (23.0%)
Recent hospitalization (within 90 d), n (%)	19654 (38.2%)	12667 (38.4%)	3128 (38.2%)	3859 (37.6%)
Vascular access present before t0, n (%)	2183 (4.2%)	1377 (4.2%)	350 (4.3%)	456 (4.4%)
Urinary drainage device before t0, n (%)	3935 (7.7%)	2539 (7.7%)	607 (7.4%)	789 (7.7%)
Endocarditis history, n (%)	723 (1.4%)	411 (1.2%)	123 (1.5%)	189 (1.8%)
Prosthetic valve or cardiac device history, n (%)	2273 (4.4%)	1458 (4.4%)	362 (4.4%)	453 (4.4%)
IVDU history, n (%)	2556 (5.0%)	1625 (4.9%)	384 (4.7%)	547 (5.3%)
Chronic wound or pressure ulcer history, n (%)	3002 (5.8%)	1974 (6.0%)	388 (4.7%)	640 (6.2%)
WBC before t0, median [IQR]	9.8 [6.5, 14.4]	9.9 [6.5, 14.4]	9.8 [6.3, 14.3]	9.8 [6.5, 14.4]
BUN before t0, median [IQR]	20.0 [13.0, 34.0]	20.0 [13.0, 34.0]	19.0 [12.0, 33.0]	20.0 [13.0, 34.0]
Lactate before t0, median [IQR]	1.7 [1.2, 2.5]	1.7 [1.2, 2.5]	1.7 [1.2, 2.6]	1.7 [1.3, 2.6]
Bicarbonate before t0, median [IQR]	24.0 [21.0, 26.0]	24.0 [21.0, 26.0]	24.0 [21.0, 26.0]	24.0 [21.0, 26.0]
Sodium before t0, median [IQR]	138.0 [135.0, 140.0]	138.0 [135.0, 140.0]	138.0 [135.0, 140.0]	138.0 [135.0, 141.0]
Shock Index before t0, median [IQR]	0.8 [0.6, 0.9]	0.8 [0.6, 0.9]	0.8 [0.6, 0.9]	0.8 [0.6, 0.9]
Heart rate before t0, median [IQR]	90.0 [76.0, 104.0]	89.0 [76.0, 104.0]	90.0 [76.0, 104.0]	89.5 [77.0, 104.0]
Temperature before t0, median [IQR]	36.9 [36.6, 37.6]	36.9 [36.6, 37.6]	36.9 [36.6, 37.5]	36.9 [36.6, 37.5]

Median age was 63 years (IQR, 51.0–75.0), 45.9% of admissions were female, 25.6% of the sample were in the ICU at time of culture, 45.9% were in the emergency department and admitted. Median time from admission to culture was 7.6 hours (IQR, 3.5–14.1). Prior positive blood culture history was present in 22.4% of admissions, 38.2% had a recent hospitalization (within 90 days), 4.2% had vascular access before culture, 7.7% had a urinary drainage device before culture. Endocarditis history was present in 1.4%, 4.4% had a prosthetic valve or cardiac device history, and injection drug use was present in 5.0% of the sample.

Primary model performance

Primary and secondary model performances are summarized in Table 2. In the test set, the primary model achieved AUROC 0.754 (95% CI, 0.726–0.778), AUPRC 0.157 (95% CI, 0.129–0.193), and Brier score of 0.037 (95% CI, 0.033–0.040). Calibration was good, with intercept – 0.108 and slope 1.012 (Supplementary Fig. 1). The precision recall curve can be found in Supplementary Fig. 2.

Table 2
Model Performance

Analysis	Test admissions, n	Test subjects, n	Test prevalence, %	AUROC (95% CI)	AUPRC (95% CI)	Brier (95% CI)	Calibration intercept	Calibration slope
Primary model (PM)	10251	7255	4	0.754 (0.726–0.778)	0.157 (0.129–0.193)	0.037 (0.033–0.040)	-0.108	1.012
PM without workflow/support features	10251	7255	4	0.730 (0.703–0.756)	0.151 (0.120–0.186)	0.037 (0.034–0.040)	-0.075	1.024
PM without prior positive blood culture history	10251	7255	4	0.662 (0.633–0.690)	0.081 (0.068–0.102)	0.038 (0.035–0.042)	-0.117	0.996
PM without prior/history features	10251	7255	4	0.666 (0.638–0.694)	0.082 (0.070–0.102)	0.038 (0.035–0.042)	0.493	1.205
PM without measurement-intensity features	10251	7255	4	0.752 (0.727–0.777)	0.152 (0.124–0.188)	0.037 (0.033–0.040)	-0.142	1
Sensitivity cohort: exclude death within 24 h of t0	10183	7198	4	0.751 (0.733–0.772)	0.161 (0.132–0.202)	0.036 (0.033–0.039)	-0.078	1.022
Sensitivity cohort: exclude death within 6 h of t0	10238	7243	4	0.750 (0.738–0.773)	0.154 (0.126–0.185)	0.037 (0.033–0.040)	-0.109	1.01
Sensitivity cohort: first admission per subject only	7255	7255	3.7	0.742 (0.710–0.771)	0.161 (0.128–0.204)	0.034 (0.031–0.038)	-0.189	0.991

Performance remained relatively informative in secondary modeling. Removing workflow/support features yielded AUROC 0.730 and AUPRC 0.151. Removing prior positive blood culture history reduced performance to AUROC 0.662 and AUPRC 0.081; removing the broader prior/history yielded AUROC 0.666 and AUPRC 0.082. The model without measurement intensity features performed similarly to the primary model (AUROC 0.752, AUPRC 0.152), suggesting performance was not driven by intensity of pre-culture workup. Results were stable after excluding early deaths and restricting data to first admissions only. Additional comparator models are shown in Supplementary Table 2.

Key predictors

Figure 1A and Table 3 summarize the strongest contributors to the primary model. Mean absolute SHAP values indicate average contribution magnitude and should not be interpreted as causal or as indicating direction. Prior positive culture history was dominant. Other influential predictors included time from admission to culture, admitted from emergency department status, prior admissions count, admission type, blood urea nitrogen, prior procedures, medication orders in the past 24 hours, lymphocyte percentage, bicarbonate, white blood cell count, anti MRSA antibiotic exposure, platelets, sodium, and distinct prior diagnosis codes.

Table 3
Key Predictors of Positive Blood Cultures

3A. Primary model						
Rank	Predictor	Clinical domain	Variable type	Pattern in culture positive admissions	Mean absolute SHAP	95% bootstrap CI
1	Prior positive blood culture history	Prior history / healthcare exposure	Binary indicator	More common among positives	0.561	0.558–0.564
2	Time to culture, h	Workflow / treatment context	Continuous timing variable	Higher among positives	0.072	0.072–0.073
3	Admitted from ED	Workflow / treatment context	Binary indicator	Less common among positives	0.068	0.067–0.069
4	Prior admissions count	Prior history / healthcare exposure	Count	Similar in positives and negatives	0.065	0.064–0.068
5	Admission type: ED observation	Demographics / encounter	Categorical indicator	Less common among positives	0.061	0.057–0.065
6	BUN before t0	Laboratory	Continuous laboratory value	Higher among positives	0.057	0.056–0.058
7	Prior procedures within 90 days	Prior history / healthcare exposure	Count	Similar in positives and negatives	0.056	0.055–0.057
8	Admission type: Urgent admission	Demographics / encounter	Categorical indicator	More common among positives	0.053	0.052–0.054
9	Medication orders in prior 24 h	Workflow / treatment context	Count	Higher among positives	0.048	0.047–0.049
10	Lymphocytes (%), before t0	Laboratory	Continuous laboratory value	Lower among positives	0.044	0.042–0.046
11	Days since last discharge	Prior history / healthcare exposure	Continuous timing variable	Lower among positives	0.042	0.041–0.043
12	Bicarbonate before t0	Laboratory	Continuous laboratory value	Lower among positives	0.042	0.041–0.043
13	WBC before t0	Laboratory	Continuous laboratory value	Higher among positives	0.039	0.038–0.041
14	Any anti-MRSA antibiotic before t0	Workflow / treatment context	Binary indicator	More common among positives	0.037	0.036–0.038
15	Chloride before t0	Laboratory	Continuous laboratory value	Similar in positives and negatives	0.037	0.036–0.038
16	Platelets before t0	Laboratory	Continuous laboratory value	Lower among positives	0.035	0.034–0.036
17	Sodium before t0	Laboratory	Continuous laboratory value	Lower among positives	0.034	0.034–0.035

3A. Primary model						
18	Hours from first antibiotic to t0	Workflow / treatment context	Continuous timing variable	Higher among positives	0.031	0.030–0.032
19	Alkaline phosphatase before t0	Laboratory	Continuous laboratory value	Higher among positives	0.030	0.029–0.031
20	Number of distinct prior diagnosis codes	Prior history / healthcare exposure	Count	Higher among positives	0.030	0.029–0.030
3B. Model without prior positive blood culture history						
Rank	Predictor	Clinical domain	Variable type	Descriptive pattern in culture positive admissions	Mean absolute SHAP value	95% bootstrap CI
1	Prior procedures within 90 days	Prior history / healthcare exposure	Count	Similar in positives and negatives	0.094	0.093–0.096
2	Admitted from ED	Workflow / treatment context	Binary indicator	Less common among positives	0.089	0.088–0.090
3	Any IV antibiotic before t0	Workflow / treatment context	Binary indicator	More common among positives	0.085	0.084–0.085
4	Any anti-MRSA antibiotic before t0	Workflow / treatment context	Binary indicator	More common among positives	0.078	0.076–0.079
5	Bicarbonate before t0	Laboratory	Continuous laboratory value	Lower among positives	0.077	0.076–0.079
6	Medication orders in prior 24 h	Workflow / treatment context	Count	Higher among positives	0.077	0.076–0.078
7	Admission type: ED observation	Demographics / encounter	Categorical indicator	Less common among positives	0.074	0.070–0.079
8	Platelets before t0	Laboratory	Continuous laboratory value	Lower among positives	0.069	0.068–0.071
9	WBC before t0	Laboratory	Continuous laboratory value	Higher among positives	0.066	0.065–0.068
10	Chloride before t0	Laboratory	Continuous laboratory value	Similar in positives and negatives	0.064	0.062–0.065
11	BUN before t0	Laboratory	Continuous laboratory value	Higher among positives	0.058	0.056–0.060
12	Days since last discharge	Prior history / healthcare exposure	Continuous timing variable	Lower among positives	0.051	0.049–0.052
13	Alkaline phosphatase before t0	Laboratory	Continuous laboratory value	Higher among positives	0.048	0.046–0.050
14	Sodium before t0	Laboratory	Continuous laboratory value	Lower among positives	0.041	0.041–0.042

3A. Primary model						
15	Hours from first antibiotic to t0	Workflow / treatment context	Continuous timing variable	Higher among positives	0.037	0.036–0.038
16	Lymphocytes (%), before t0	Laboratory	Continuous laboratory value	Lower among positives	0.036	0.034–0.038
17	INR before t0	Laboratory	Continuous laboratory value	Higher among positives	0.036	0.034–0.037
18	RDW-CV before t0	Laboratory	Continuous laboratory value	Higher among positives	0.032	0.030–0.034
19	Lactate before t0	Laboratory	Continuous laboratory value	Higher among positives	0.032	0.030–0.033
20	RBC count before t0	Laboratory	Continuous laboratory value	Lower among positives	0.032	0.031–0.033

Table 3 also reports descriptive patterns in pathogen positive admissions. For example, prior positive blood culture history and anti MRSA antibiotic exposure were more common among culture positive admissions, whereas bicarbonate, platelets, sodium, and lymphocyte percentage were lower.

Figure 1B and Table 3 are useful clinically because they show the refit model without prior positive blood culture history. The remaining predictors cluster into recent healthcare exposure, early treatment intensity, and laboratory markers, including bicarbonate, platelets, white blood cell count, chloride, blood urea nitrogen, sodium, lymphocyte percentage, international normalized ratio, red cell distribution width and lactate.

Risk enrichment

The other main clinical message is shown in Fig. 2. Baseline positive culture prevalence in the test set was 4.0%. Observed positive culture rate increased to 30.1% in the top 1% of predicted risk (31/103), 19.9% in the top 5% (102/513), 15.5% in the top 10% (159/1,025), and 10.8% in the top 20% (221/2,050).

The top 20% risk group captured 53.4% of positive cultures. These findings support the model as a prioritization tool for already cultured patients. The full risk enrichment across cumulative predicted risk groups is shown in Supplementary Table 3.

Discussion

Three practical signals stood out from this study: prior positive blood culture history, recent healthcare exposure, and evidence of acute illness. Among adults cultured within 24 hours of admission, our model identified subgroups with substantially higher positive pathogen rates than the overall cohort. About one in three admissions in the top 1% of predicted risk and one in five in the top 5% had a positive blood culture, compared with about one in twenty-five overall.

Our results fit the broader culture prediction literature while targeting post culture prioritization, whereas prior models focused on whether cultures might be omitted in lower risk patients [8–12]. Once cultures are drawn the question becomes whether the episode is high enough risk to justify earlier laboratory follow up, pharmacy / stewardship review, infectious diseases input, or other rapid diagnostics. This reframes the goal to diagnostic stewardship, which seeks not only to reduce low yield testing but also to direct resources toward patients most likely to benefit [3, 6, 7].

Recurrent bloodstream infection is well described and is commonly used to guide antibiotic choices [19, 20], so it is unsurprising that prior positive blood culture history was the strongest predictor. Even so, the model did not collapse without

that feature. The refit model still used recent healthcare exposure, admission context, early antibiotic treatment, medication burden, and laboratory abnormalities with some success indicating that variables have a role to play.

Predictors beyond prior positive blood culture history

The variables outside of prior positive blood cultures are also clinically coherent.

Prior procedures (within 90 days), prior admissions, and days since last discharge included in our primary model capture healthcare exposure, barrier disruption, device exposure and peri procedural complications. These variables could also flag unresolved infections as well as clinical deterioration of patients [21].

Other familiar risk factors, including vascular access, urinary drainage devices, endocarditis history, prosthetic valve or cardiac device history, chronic wounds, and injection drug use, were included as candidates but did not rank among the top 20 SHAP features. This does not mean they are clinically unimportant; several were uncommon or may have been absorbed by broader signals such as prior procedures, prior positive cultures, antibiotic exposure, and abnormal laboratory values.

Admission pathway and treatment context variables also played a prominent role. These include variables like : Admitted from ED status, ED observation admission type, urgent admission type. These pathway related variables capture the context of culture acquisition including triage acuity and early clinical concern [2, 22].

Intravenous or anti MRSA antibiotic exposure before t0, hours from first antibiotic to culture, and medication order burden reflect how clinicians recognized and responded to illness before or at culture acquisition. Preculture antibiotics may reduce culture yield when exposure is sufficient, but in this already cultured population they also mark clinician concern or treatment escalation [23]. Other clinical workflow predictors, such as time to culture, medication order burden, antibiotic timing, and admission pathway, are not purely biologic. They play a key role as part of the information state available when the model would be used and allow us to estimate risk from that real world clinical context [22].

Routine laboratory and physiologic measures remained important after prior positive culture history was removed. Lower bicarbonate, sodium, platelet count, lymphocyte percentage, higher white blood cell count, blood urea nitrogen, lactate, international normalized ratio, and red cell distribution width are plausible markers of physiologic stress, inflammation and organ dysfunction / acute illness severity especially in septic patients [2, 24].

Lower bicarbonate and higher lactate are plausible markers of metabolic stress, tissue hypoperfusion, lactic acidosis, renal dysfunction, or shock physiology. Surviving Sepsis Campaign guidance includes lactate measurement and lactate-guided resuscitation in appropriate patients, while also emphasizing clinical context [2].

Lower platelet count and higher international normalized ratio can reflect sepsis-associated coagulopathy [25]. Higher blood urea nitrogen is a marker for possible renal hypoperfusion, dehydration, catabolism, or acute kidney injury [26]. Higher white blood cell count reflects systemic inflammatory response [24]. Lower lymphocyte percentage is biologically plausible because sepsis is associated with lymphocyte apoptosis and impaired lymphocyte recovery [27]. Hyponatremia is a notable marker for inflammatory stress wherein excess antidiuretic hormone is released and its effect compounded by fluid shifts or renal dysfunction [28]. Red cell distribution is reactionary to oxidative stress and chronic disease burden and is a known marker in sepsis [29].

Together these lab variables are not specific for bloodstream infection, but their combined pattern is consistent with sepsis in which clinicians obtain early cultures [24].

The model was robust to several artifacts. Performance was similar after removing measurement intensity features, suggesting results were not driven mainly by testing volume. Results were also stable after excluding early deaths and restricting data to first admissions.

This study has limitations. It was restricted to adults cultured within the first 24 hours of admission, so it should not be applied to patients never cultured, hospital acquired infections, or pediatric populations without refitting and validation. Since we used MIMIC-IV our data originates from a single center critical care focused pool [13, 14]. External validation is essential because of culturing practices, contamination rates, patient mix, laboratory workflows, assay sensitivity, and documentation patterns vary across hospitals. Many of our laboratory features were also incomplete, which may have impacted modelling and skewed the impact of measurement intensity features. Also, missingness patterns may differ elsewhere. Finally, the outcome was pathogen positive blood culture rather than organism specific and syndrome specific applications which remain future work.

The most plausible implementation of this type of work is post order prioritization after blood culture collection to facilitate efficient resource use. High risk episodes could be routed to earlier stewardship or pharmacy review and have earlier infectious diseases input. Prioritized use of limited rapid diagnostic testing can also be an application especially cost/ availability is restricted like rapid molecular assays, culture independent tests, or sequencing approaches [30, 31].

The same enrichment framework could be applied in other research contexts to support patient population selection and validation of emerging non culture related pathogen detection technologies such as DNA sequencing, RNA sequencing and metagenomic methods used in similar diagnostics such as iDTECT and methods used in the Next GeneSiS and mNGS-DISCOVER approaches by enrolling or prioritizing patients by predicted risk and increasing sample yield of true positive cultures [32–35].

The next step should be external and prospective validation with assessment of whether risk-based prioritization improves turnaround time, treatment decisions, or resource use.

Conclusion

Among adults who had a blood culture obtained within the first hospital day, a time locked structured electronic health record model identified a subgroup with much higher likelihood of pathogen positive blood cultures than the overall cohort. A history of positive cultures were strongly associated with repeat positive testing with significantly improved model predictability. The model is best viewed as a practical prioritization tool after culture acquisition. External and prospective validation are needed.

Abbreviations

AUROC

area under the receiver operating characteristic curve

AUPRC

area under the precision-recall curve

BUN

blood urea nitrogen

CI

confidence interval

ED

emergency department

EHR

electronic health record

ICU

intensive care unit

INR

international normalized ratio

IQR

interquartile range

IV

intravenous
MIMIC-IV
Medical Information Mart for Intensive Care IV
MRSA
methicillin-resistant *Staphylococcus aureus*
RDW-CV
red cell distribution width-coefficient of variation
SHAP
Shapley additive explanations
t0
index blood culture time
WBC
white blood cell count

Declarations

Ethics approval and consent to participate

This study used the MIMIC-IV de-identified electronic health record dataset. It is available to credentialed users via PhysioNet under a data use agreement. The study was conducted in accordance with the Declaration of Helsinki. The Institutional Review Board of Beth Israel Deaconess Medical Center approved use of the MIMIC-IV research resource and grants a waiver of informed consent. Our investigators had no direct patient contact and no access to identifiable patient information.

Availability of data and materials

MIMIC-IV version 3.1 is available to credentialed users through PhysioNet under a data-use agreement. Repository link for analytics code available upon request.

Competing interests

SFM is a founder of Alcini, LLC, and an advisor to Danaher and Lilac Biosciences

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Authors' contributions

R.G and SF.M contributed to conceptualization.

R.G contributed to methodology, data curation, analysis, visualization, and writing of the original draft.

N.G., M.R., H.S., and S.M. contributed to validation, writing, review and editing.

SF.M. provided supervision.

All authors reviewed and approved the final manuscript.

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Figures

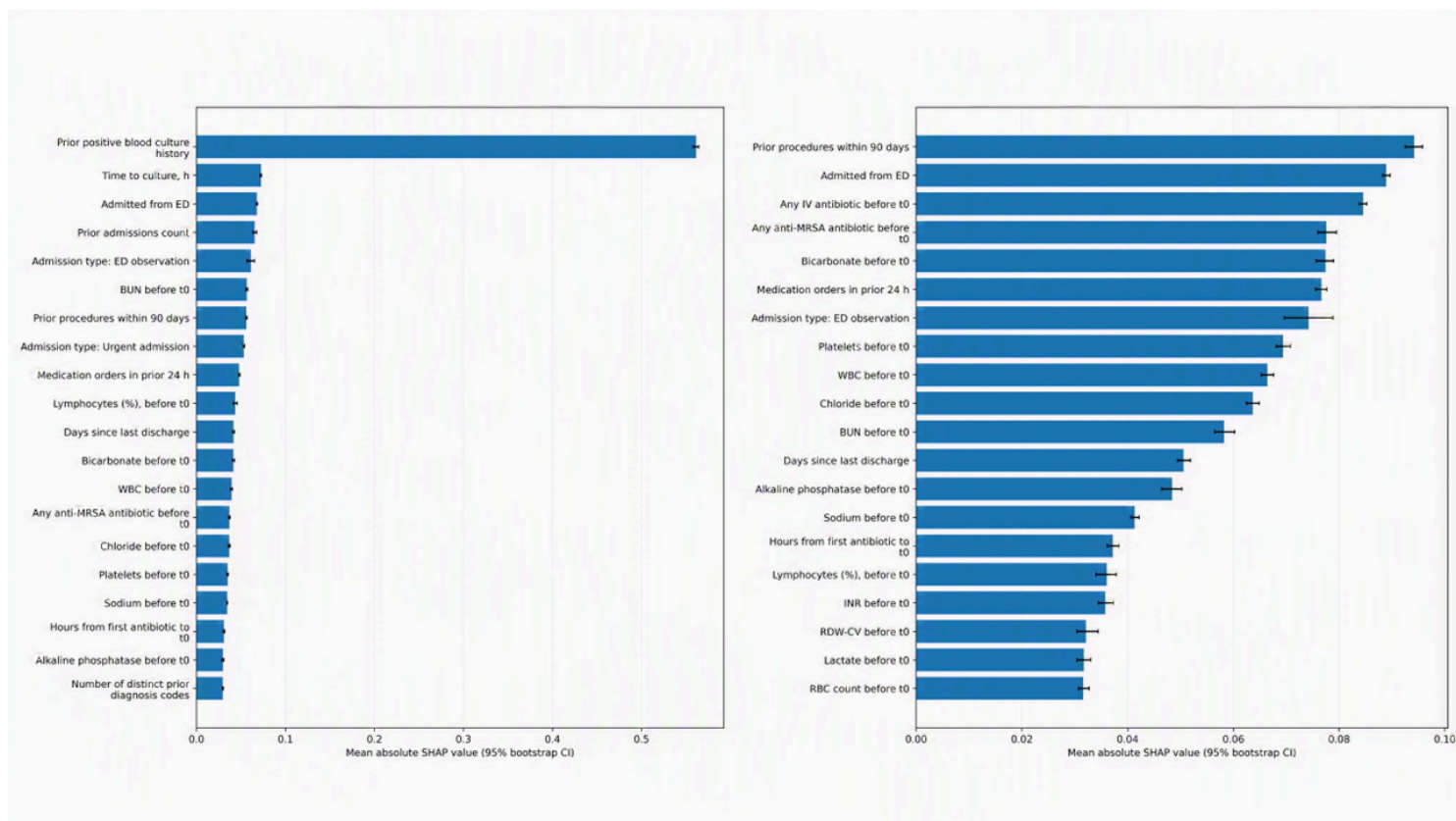


Figure 1

Top predictors of positive blood cultures. 1A (left) 20 highest ranked predictors in the primary model. 1B (right) 20 top ranked predictors in the model refit without prior positive blood culture history. Bars represent mean absolute SHAP values with 95% bootstrap confidence intervals. Higher values indicate greater average contribution to the model's risk estimate. Abbreviations: BUN, blood urea nitrogen; ED, emergency department; INR, international normalized ratio; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; RBC, red blood cell; RDW-CV, red cell distribution width-coefficient of variation; SHAP, Shapley additive explanations; t0, blood culture time.

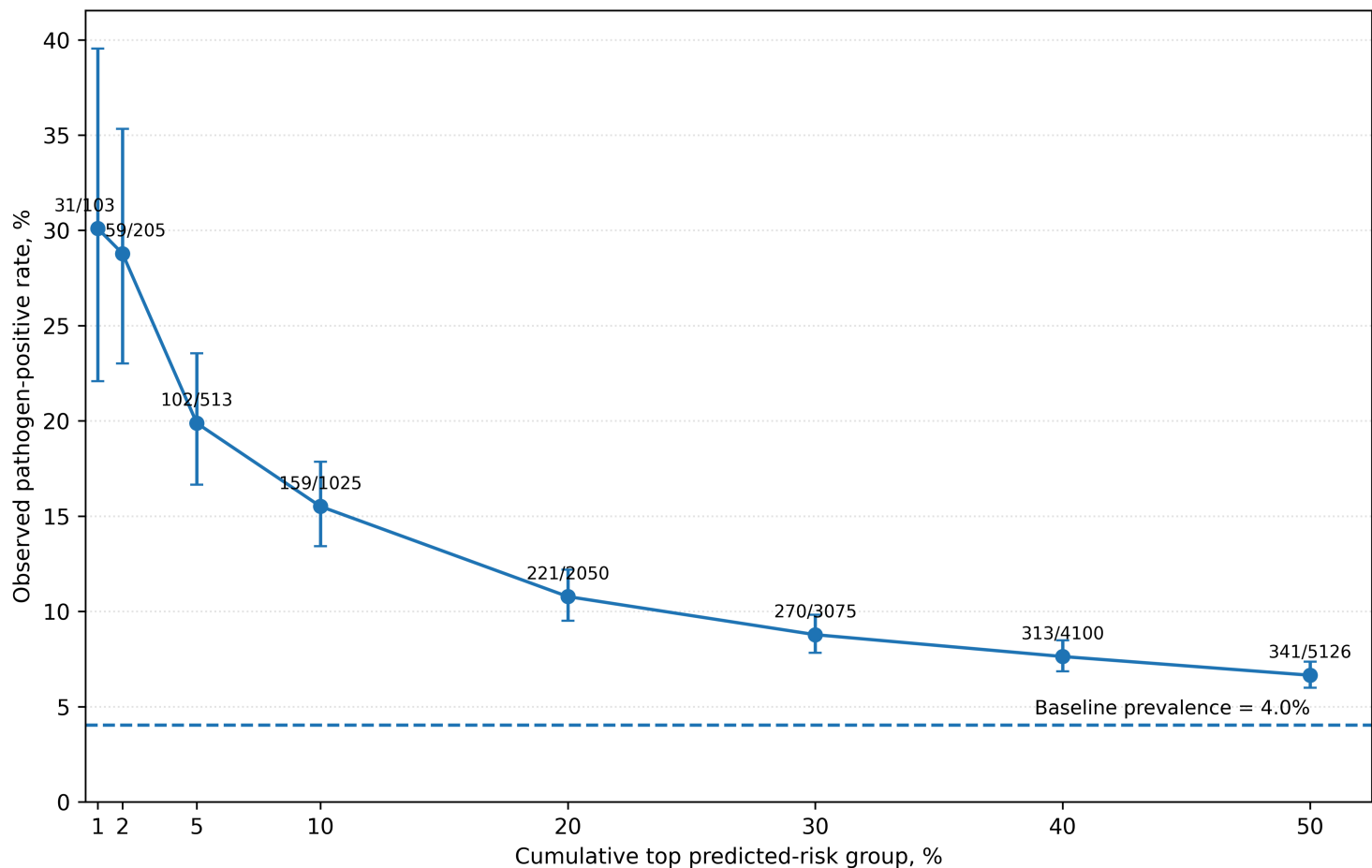


Figure 2

Risk enrichment across cumulative top risk groups. Shows the observed positive blood culture rate in cumulative top risk groups as defined by the model's predicted risk. Points represent the number of positive cultures over the number of admissions in each group. Error bars show 95% confidence intervals. The dashed line represents baseline culture positive prevalence in the test set.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [AdditionalFile1SupplementaryTable1Missingnessandoutcomecomposition.xlsx](#)
- [AdditionalFile2SupplementaryTable2Additionalcomparatormodels.xlsx](#)
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- [AdditionalFile5SupplementaryFigureS2Precisionrecallcurve.png](#)
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