ML Approaches to Paediatric Febrile Illness

Annex B - Cascade Model Supplementary Results

Results of the Cascade Approach Across Cross Validation Training Data

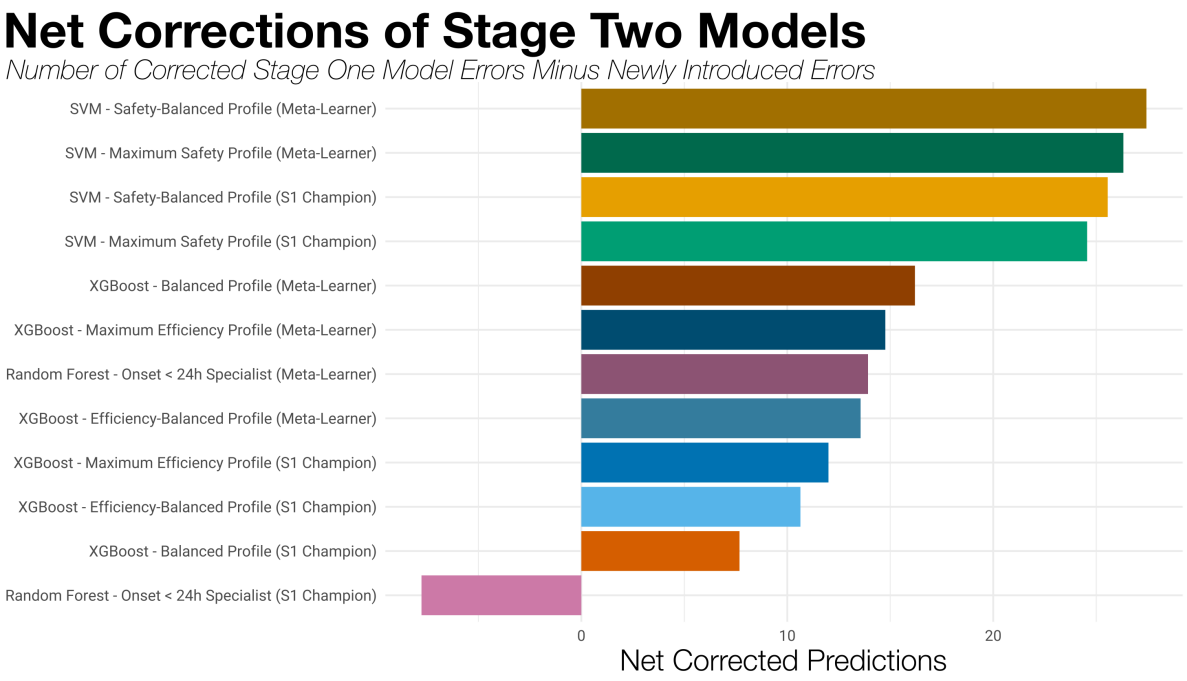

Figure 1: Net Corrections by Stage Two Models Across Each Cascade

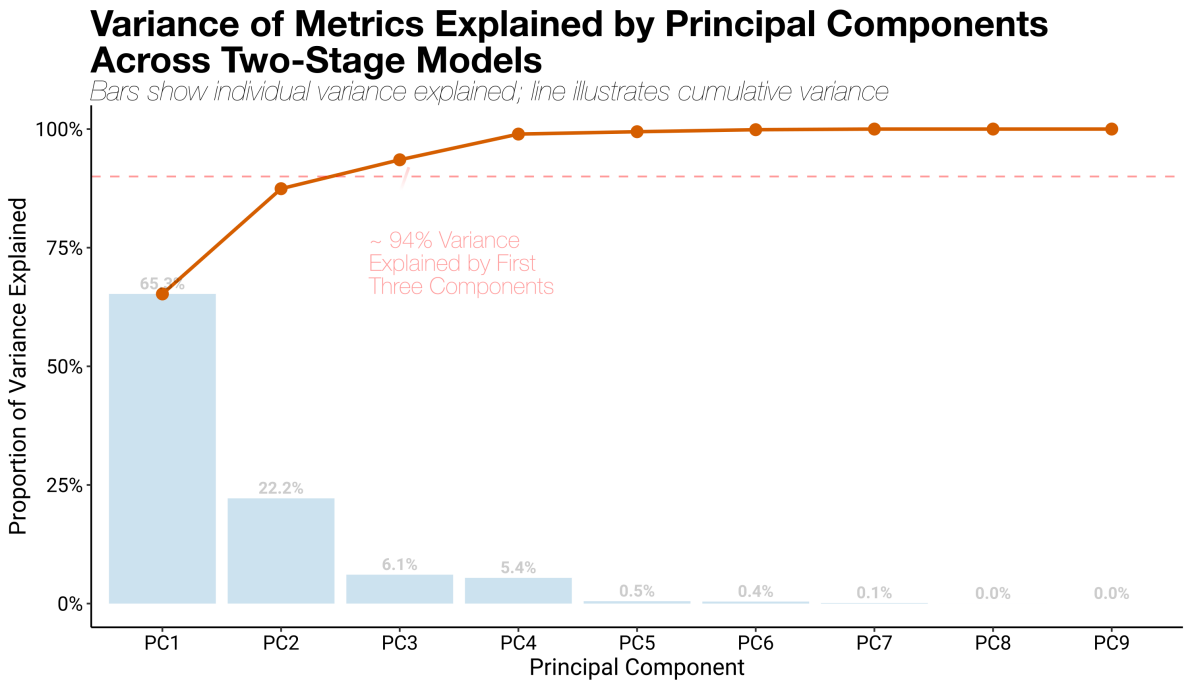

Figure 2: Scree Plot of Final Metric PCA

Table 1: Model Scores on First Three Principal Components of Final Results

Stage One Model	Stage Two Model	Policy	PC1	PC2	PC3	Desirability Score
XGBoost - Maximum Efficiency Profile	Meta-Leaner	Safeguard	-1.604	0.524	-1.468	3.016
Random Forest - Onset < 24h Specialist	Meta-Leaner	Safeguard	-1.901	2.742	0.135	2.542
XGBoost - Maximum Efficiency Profile	Meta-Leaner	Standard	-1.137	0.125	-1.248	2.243
XGBoost - Balanced Profile	Meta-Leaner	Safeguard	-1.862	1.558	-0.065	1.959
Random Forest - Onset < 24h Specialist	Meta-Leaner	Standard	-1.356	2.297	0.378	1.674
XGBoost - Efficiency-Balanced Profile	Meta-Leaner	Safeguard	-1.618	1.699	0.229	1.561
XGBoost - Maximum Efficiency Profile	S1 Champion	Safeguard	-0.112	-0.255	-1.152	1.423
XGBoost - Balanced Profile	Meta-Leaner	Standard	-1.444	1.215	0.123	1.290
SVM - Maximum Safety Profile	Meta-Leaner	Safeguard	-2.179	-1.161	-0.816	1.180
XGBoost - Efficiency-Balanced Profile	Meta-Leaner	Standard	-1.186	1.341	0.425	0.864
SVM - Maximum Safety Profile	Meta-Leaner	Standard	-1.652	-1.586	-0.585	0.348
XGBoost - Maximum Efficiency Profile	S1 Champion	Standard	0.649	-0.894	-0.801	0.182
XGBoost - Efficiency-Balanced Profile	S1 Champion	Safeguard	0.079	0.609	0.730	-0.587
XGBoost - Balanced Profile	S1 Champion	Safeguard	2.035	0.245	0.045	-0.727
SVM - Maximum Safety Profile	S1 Champion	Safeguard	-0.886	-2.156	-0.258	-0.812
SVM - Safety-Balanced Profile	Meta-Leaner	Safeguard	-1.320	-0.720	0.717	-0.933
Random Forest - Onset < 24h Specialist	S1 Champion	Safeguard	6.260	1.105	-0.575	-1.024
SVM - Safety-Balanced Profile	Meta-Leaner	Standard	-0.987	-0.978	0.855	-1.440
SVM - Safety-Balanced Profile	S1 Champion	Safeguard	-0.609	-1.159	0.825	-1.683
SVM - Maximum Safety Profile	S1 Champion	Standard	-0.188	-2.724	0.052	-1.921
XGBoost - Balanced Profile	S1 Champion	Standard	2.803	-0.377	0.384	-1.942
XGBoost - Efficiency-Balanced Profile	S1 Champion	Standard	0.999	-0.137	1.136	-2.044
Random Forest - Onset < 24h Specialist	S1 Champion	Standard	7.223	0.329	-0.153	-2.541
SVM - Safety-Balanced Profile	S1 Champion	Standard	-0.007	-1.642	1.087	-2.627

*Desirability metric created by summing z-score–standardized principal components, with PC1 and PC3 values inverted.

Table 2: Two-Stage Cascade Cross Validation Result Metrics

Stage One Model	Stage Two Model	Policy	Balanced Accuracy	Avg. Severe Sensitivity	PR AUC (Non-Severe)	Macro PR AUC	Macro Sensitivity	Macro Specificity	% Handoff Rate	% Severe Case Handoff Rate	S2 Net Corrections
Random Forest - Onset < 24h Specialist	Meta-Leaner	Safeguard	0.666	0.232	0.771	0.518	0.455	0.877	94.163	76.425	13.92
XGBoost - Efficiency-Balanced Profile	Meta-Leaner	Safeguard	0.663	0.224	0.765	0.511	0.450	0.875	96.313	78.546	13.56
XGBoost - Balanced Profile	Meta-Leaner	Safeguard	0.661	0.217	0.771	0.521	0.447	0.876	95.597	81.752	16.20
SVM - Maximum Safety Profile	Meta-Leaner	Safeguard	0.660	0.202	0.767	0.496	0.444	0.876	98.905	94.143	26.32
Random Forest - Onset < 24h Specialist	Meta-Leaner	Standard	0.660	0.199	0.771	0.518	0.443	0.877	94.163	76.425	13.92
XGBoost - Maximum Efficiency Profile	Meta-Leaner	Safeguard	0.659	0.199	0.771	0.509	0.441	0.876	95.544	93.078	14.76
XGBoost - Efficiency-Balanced Profile	Meta-Leaner	Standard	0.657	0.198	0.765	0.511	0.440	0.875	96.313	78.546	13.56
XGBoost - Balanced Profile	Meta-Leaner	Standard	0.656	0.191	0.771	0.521	0.437	0.875	95.597	81.752	16.20
SVM - Maximum Safety Profile	Meta-Leaner	Standard	0.654	0.170	0.767	0.496	0.432	0.876	98.905	94.143	26.32
XGBoost - Maximum Efficiency Profile	Meta-Leaner	Standard	0.653	0.170	0.771	0.509	0.430	0.876	95.544	93.078	14.76
SVM - Safety-Balanced Profile	Meta-Leaner	Safeguard	0.651	0.162	0.762	0.505	0.427	0.875	98.254	83.747	27.44
SVM - Safety-Balanced Profile	Meta-Leaner	Standard	0.647	0.143	0.762	0.505	0.420	0.875	98.254	83.747	27.44
XGBoost - Efficiency-Balanced Profile	S1 Champion	Safeguard	0.645	0.139	0.763	0.505	0.416	0.874	96.313	78.546	10.64
SVM - Safety-Balanced Profile	S1 Champion	Safeguard	0.644	0.131	0.769	0.498	0.415	0.874	98.254	84.046	25.56
XGBoost - Maximum Efficiency Profile	S1 Champion	Safeguard	0.644	0.141	0.766	0.503	0.414	0.874	95.544	93.005	12.00
SVM - Maximum Safety Profile	S1 Champion	Safeguard	0.644	0.124	0.768	0.500	0.412	0.875	98.905	94.237	24.56
SVM - Safety-Balanced Profile	S1 Champion	Standard	0.637	0.096	0.769	0.498	0.401	0.873	98.254	84.046	25.56
SVM - Maximum Safety Profile	S1 Champion	Standard	0.635	0.081	0.768	0.500	0.396	0.874	98.905	94.237	24.56
XGBoost - Maximum Efficiency Profile	S1 Champion	Standard	0.634	0.093	0.766	0.503	0.396	0.873	95.544	93.005	12.00
XGBoost - Efficiency-Balanced Profile	S1 Champion	Standard	0.634	0.084	0.763	0.505	0.394	0.873	96.313	78.546	10.64
XGBoost - Balanced Profile	S1 Champion	Safeguard	0.631	0.128	0.746	0.478	0.394	0.868	95.595	81.347	7.68
XGBoost - Balanced Profile	S1 Champion	Standard	0.622	0.081	0.746	0.478	0.376	0.867	95.595	81.347	7.68
Random Forest - Onset < 24h Specialist	S1 Champion	Safeguard	0.610	0.117	0.658	0.444	0.362	0.858	94.178	77.252	-7.76
Random Forest - Onset < 24h Specialist	S1 Champion	Standard	0.598	0.059	0.658	0.444	0.340	0.857	94.178	77.252	-7.76

Final Cascade Model Results on Held Out Test Data

Table 3: Final Cascade Model Confusion Matrix

	Truth				
	Onset within 24 hours	Onset greater than 24 hours	Probable Severe	Probable Non Severe	Non Severe
Onset within 24 hours	8	2	7	1	0
Onset greater than 24 hours	0	0	0	0	0
Probable Severe	9	4	308	96	30
Probable Non Severe	1	1	38	41	6
Non Severe	0	0	17	18	90

Final Cascade Model Sensitivity Analyses

Table 4: Breakdown of True Severe Case Predictions by Clinical Site

		Model Prediction for True Severe Cases		
Site	Total Severe Cases	Predicted: Onset < 24h	Predicted: Probable Severe	Predicted: Probable Non-Severe
Goyalmara, Bangladesh	8	5	3	0
Angkor, Cambodia	6	4	2	0
Dong Nai, Viet Nam	6	1	5	0
National, Viet Nam	5	0	3	2

Sites with zero severe cases in the test set are not shown.

Table 5: Breakdown of True Severe Case Predictions by Age Group

		Model Prediction for True Severe Cases		
Age Group	Total Severe Cases	Predicted: Onset < 24h	Predicted: Probable Severe	Predicted: Probable Non-Severe
Child (>=12m)	11	1	9	1
Infant (<12m)	14	9	4	1

Table 6: Breakdown of True Severe Case Predictions by Sex

		Model Prediction for True Severe Cases		
Sex	Total Severe Cases	Predicted: Onset < 24h	Predicted: Probable Severe	Predicted: Probable Non-Severe
Female	18	8	10	0
Male	7	2	3	2

Final Cascade Model Feature Importance

Table 7: Top 15 Weighted Feature Importance Scores Across Full Cascade Model

Rank	Feature	Mean Importance Score
1	Clinical Site (Overall)	0.060
2	TNFR1 (pg/ml)	0.040
3	Haemoglobin (mg/dL)	0.040
4	Heart Rate (bpm)	0.039
5	Respiratory Rate (breaths/min)	0.037
6	Age (Months)	0.034
7	Oxygen Saturation (%)	0.033
8	Interleukin-6 (pg/ml)	0.032
9	Missingness Indicator for: SIRS Score	0.031
10	VEGFR1 (pg/ml)	0.030
11	suPAR (ng/ml)	0.028
12	STREM1 (pg/ml)	0.028
13	SIRS Score	0.027
14	CHI3L1 (ng/ml)	0.027
15	Weight for Age Z-Score	0.027

*Weighted average of feature importance, giving equal weight to the Stage 1 model and the four Stage 2 specialist models combined. Root Mean Square (RMS) was used to average the magnitude of the scores at each stage. See Supplementary Materials for full data.