Multi-horizon predictive modeling for ECMO resource allocation in COVID-19 pandemic

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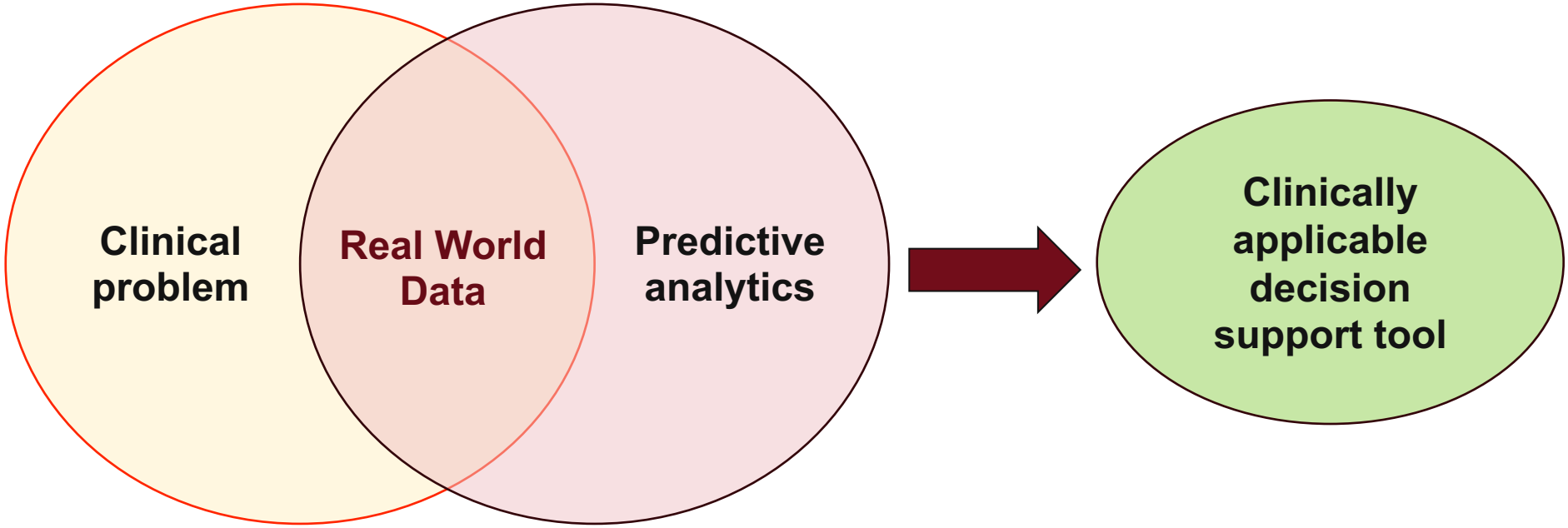
Translational Biomedical Informatics

"The development of storage, analytic, and interpretive methods to optimize the transformation of increasingly voluminous biomedical data, and genomic data, into proactive, predictive, preventive, and participatory health"



COVID-19 models

ARTIFICIAL INTELLIGENCE

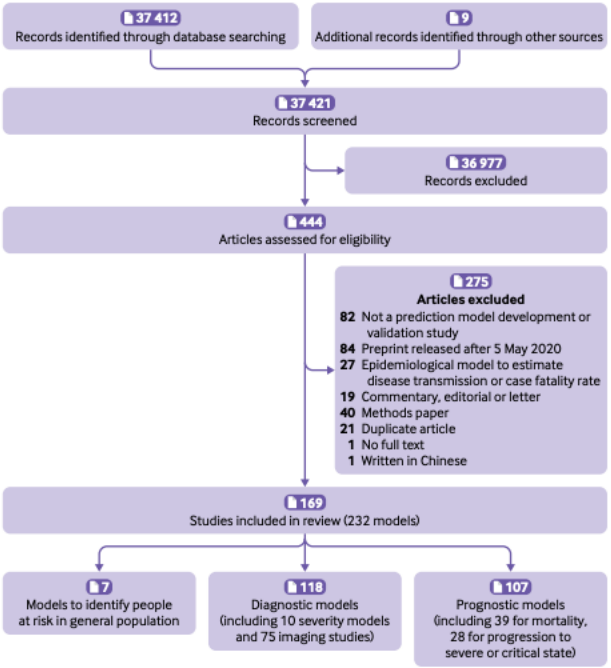
Hundreds of AI tools have been built to catch covid. None of them helped.

Some have been used in hospitals, despite not being properly tested. But the pandemic could help make medical AI better.

By Will Douglas Heaven July 30, 2021

Prediction models for diagnosis and prognosis of covid-19: systematic review and critical appraisal

BMJ 2020 ; 369 doi: https://doi.org/10.1136/bmj.m1328 (Published 07 April 2020)



Seven models identified patients at risk in the general population (using proxy outcomes for covid-19)

Thirty three diagnostic models were identified for detecting covid-19, in addition to 75 diagnostic models based on medical images, 10 diagnostic models for severity classification, and 107 prognostic models for predicting, among others, mortality risk, progression to severe disease

Proposed models are poorly reported and at high risk of bias, raising concern that their predictions could be unreliable when applied in daily practice

Two prediction models (one for diagnosis and one for prognosis) were identified as being of higher quality than others and efforts should be made to validate these in other datasets

"The pandemic has made it clear to many researchers that the way AI tools are built needs to change"
"Frankenstein data sets"

SARS-CoV2 “COVID-19” pandemic

- Unforeseen strains on global healthcare systems
- ECMO – life sustaining therapy in cardiopulmonary failure
  - Extensive expertise and resources
  - Significant risks and morbidities
- Guidelines discourage commissioning new ECMO centers

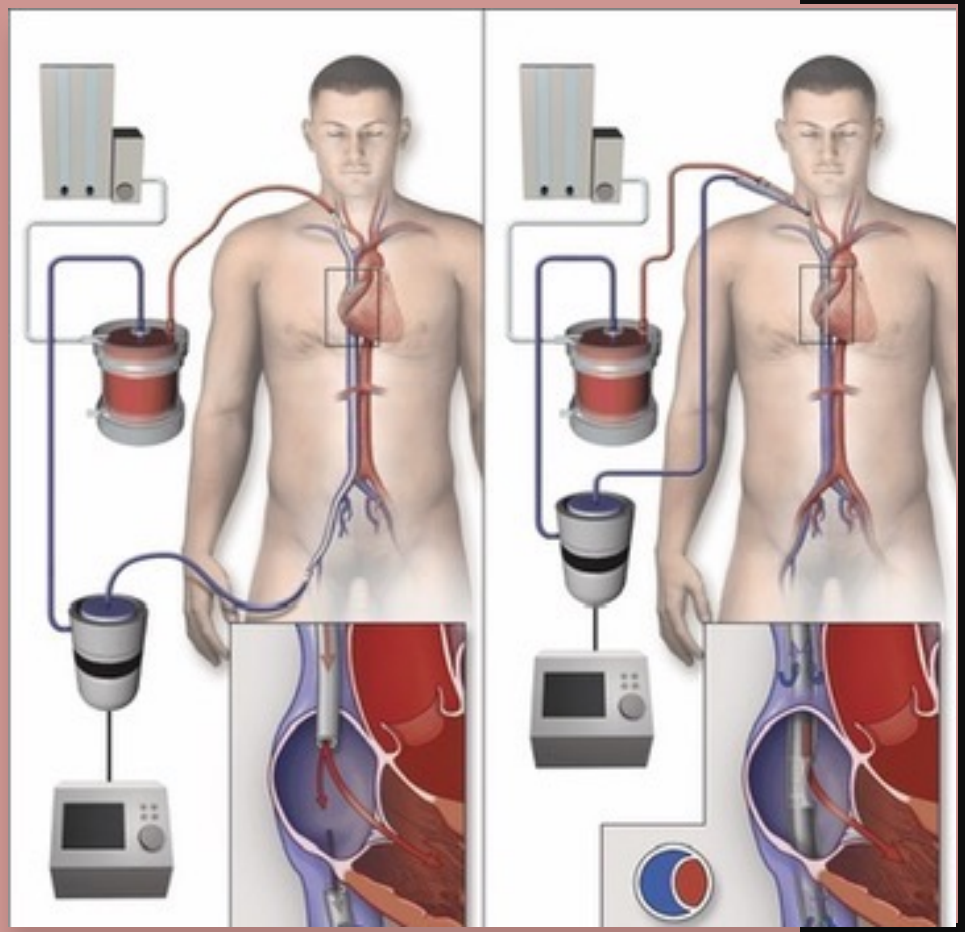


THE most resource intensive ICU therapy

Extracorporeal Membrane Oxygenation
ECMO

- The most complex, highest-risk and resource-intensive modality in intensive care units (ICU)
  - 1 – 5 year mortality rates 45% - 57%
  - Inpatient costs US$22,305 - 334,608/day (2019)

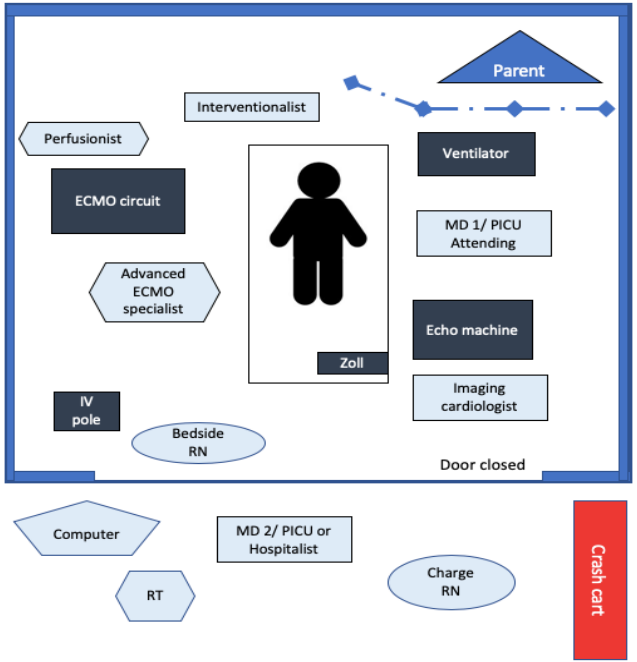
- ECMO mortality prediction scores, neither designed nor validated for patient triage or resource allocation



THE most resource intensive ICU therapy



Local ECMO initiation schematic



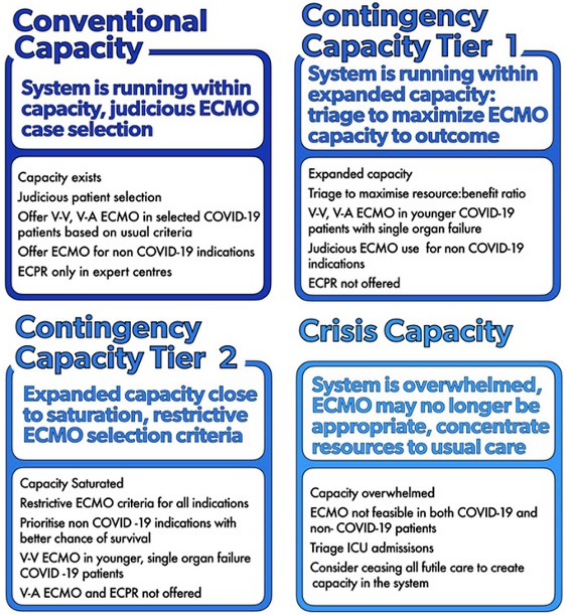
ECMO during the COVID-19 pandemic: when is it unjustified?

Darryl Abrams[1,2], Roberto Lorusso[3], Jean-Louis Vincent[4] and Daniel Brodie[1,2*]

Extracorporeal Membrane Oxygenation for Critically Ill Patients with COVID-19–related Acute Respiratory Distress Syndrome: Worth the Effort?

Planning and provision of ECMO services for severe ARDS during the COVID-19 pandemic and other outbreaks of emerging infectious diseases

Kollengode Ramanathan, David Antognini, Alain Combes, Matthew Paden, Bishoy Zakhary, Mark Ogino, Graeme MacLaren, Daniel Brodie, Kiran Shekar**



COVID-19 Cases on ECMO in the ELSO Registry:

Total COVID-19 Cases	COVID-19 Confirmed Cases
	17,674

Total counts of COVID-19 confirmed patients.

Patients who initiated ECMO at least 90 days ago	COVID-19 Confirmed	COVID-19 In-hospital Mortality
	16,255	48%

COVID-19 ECMO counts by ELSO Chapter

North America	11,211
Europe	3,529
Asia Pacific	571
Latin America	1,271
SWAAC	1,185

Reports counts of ECMO-supported suspected or confirmed COVID-19 cases by ELSO Chapter (provided the chapter has at least 5 cases reported)

Extracorporeal membrane oxygenation for coronavirus disease 2019-related acute respiratory distress syndrome

Short, Briana[a,b]; Abrams, Darryl[a,b]; Brodie, Daniel[a,b]

Author Information

Current Opinion in Critical Care: October 19, 2021 - Volume - Issue -
doi: 10.1097/MCC.0000000000000901

Resource allocation, patient triage, unexpected volumes

Regional experience

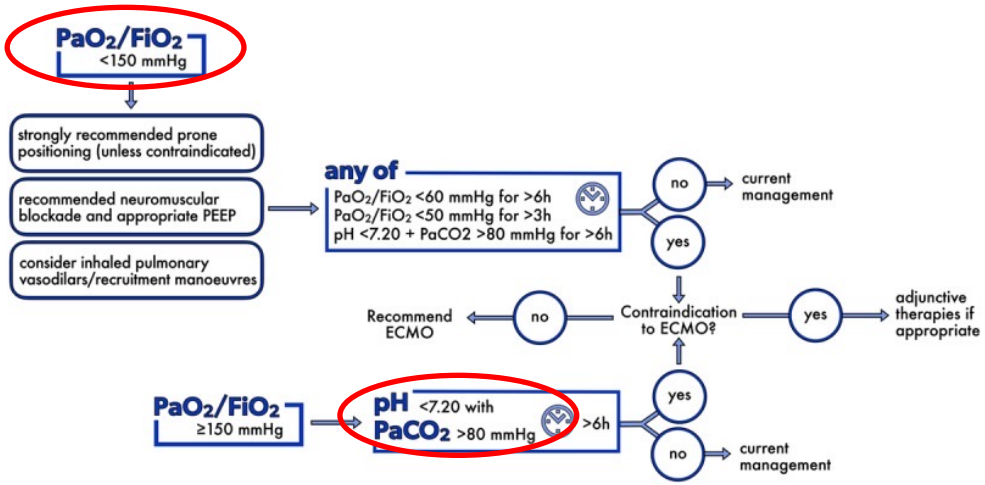
Gaps in current knowledge

No tools to early identify patients at risk of needing ECMO

Current recommendations limited to criteria to initiate ECMO based on immediately pre-ECMO labs and therapeutic requirements

Tools available for **resource allocation** limited to:

- Scores of severity of ICU illness
- Immediate pre-ECMO markers of respiratory failure

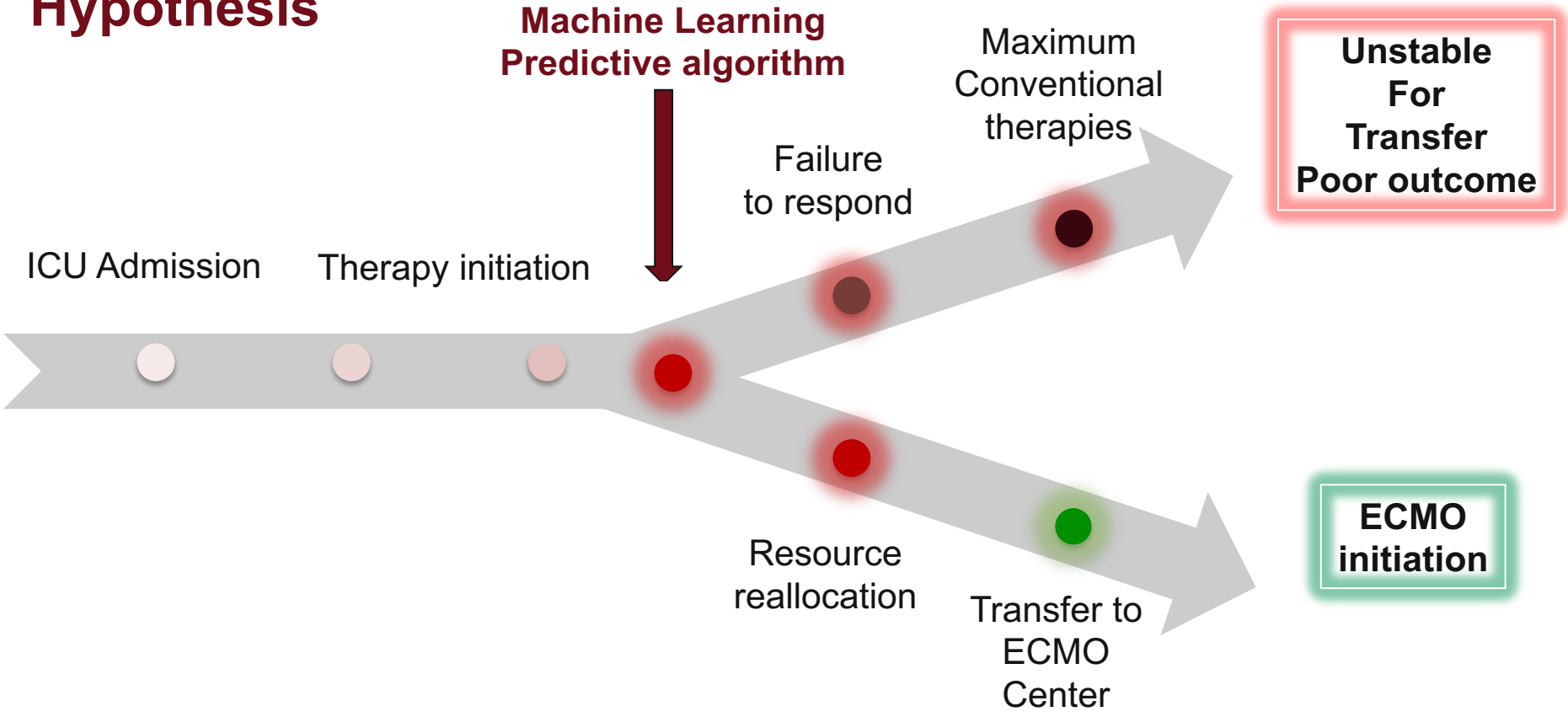


Big data approach?

Machine learning?

Translational Biomedical Informatics?

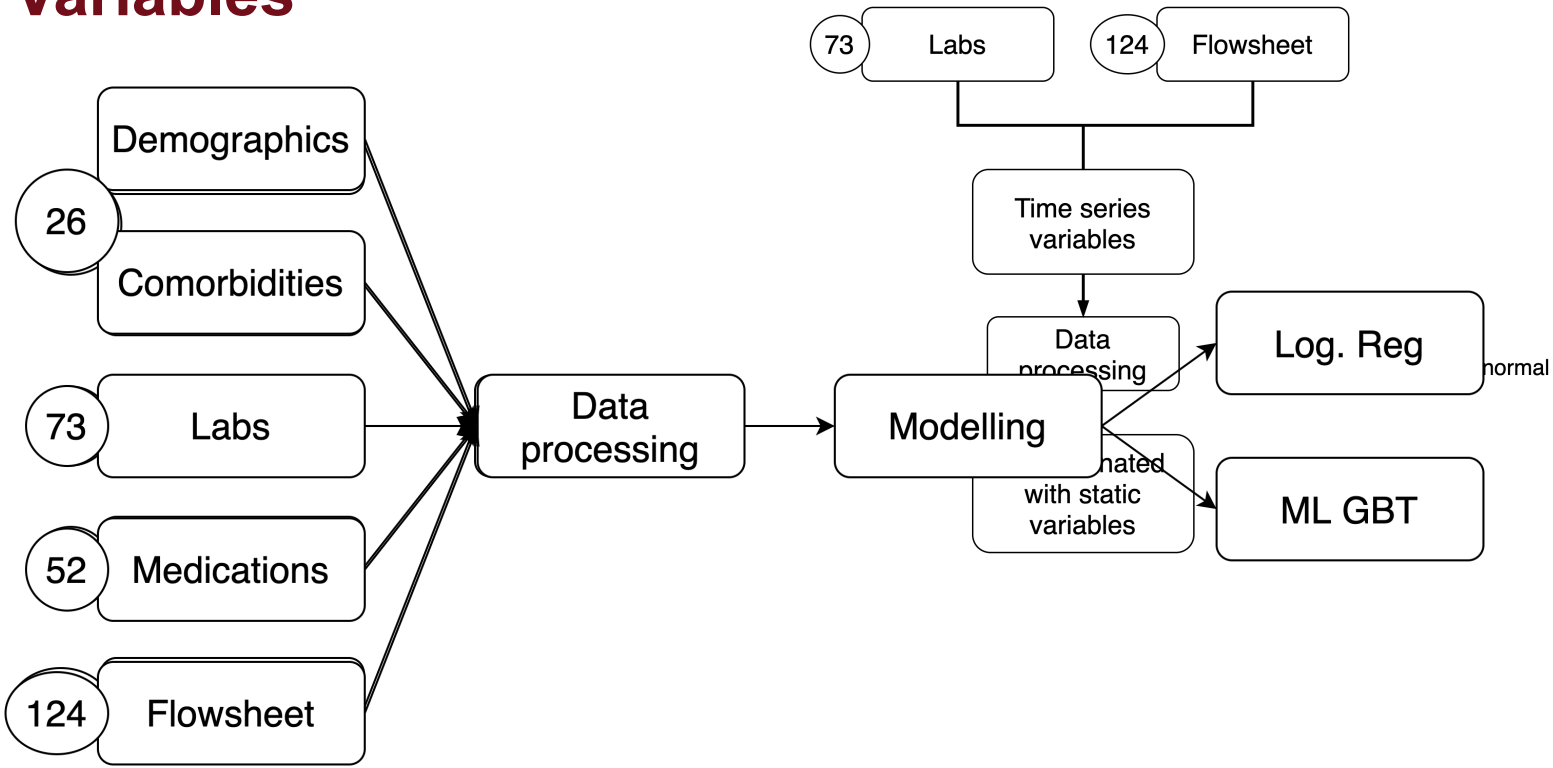
Hypothesis


Machine Learning
Predictive algorithm
Maximum
Conventional
therapies
Unstable
For
Transfer
Poor outcome
Failure
to respond
ICU Admission
Therapy initiation
Resource
reallocation
Transfer to
ECMO
Center
ECMO
initiation

Methods

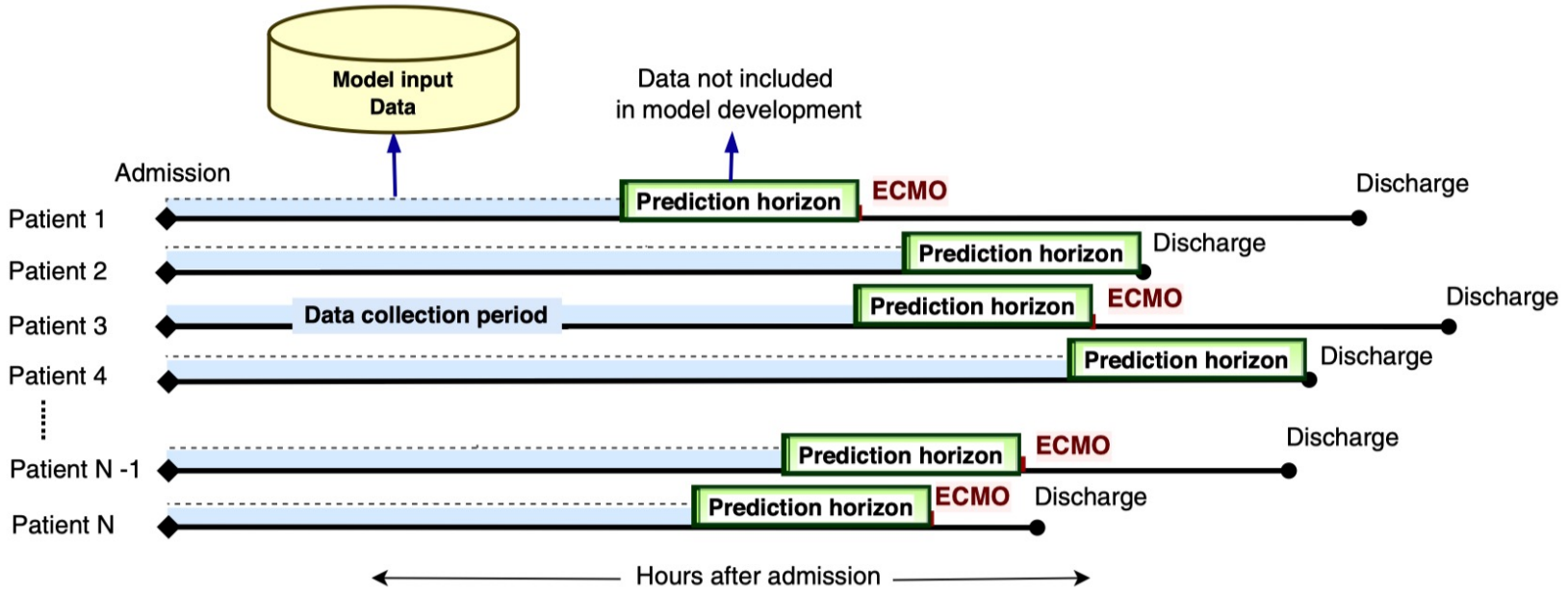
- Institutional data registry:
  - All COVID-19 patients
  - 15 hospitals – BJC
  - March 3rd 2020 – October 1st 2021
- **Inclusion criteria:**
  - SARS-CoV-2 viral PCR positive
  - Admitted to ICU ≥ 24 hours
- **Exclusion criteria:**
  - Age < 3 years
  - Institutional ECMO exclusion criteria:
    - Age > 70 years
    - BMI > 45 Kg/m^2
- **Outcome:**
  - ECMO during hospitalization
  - ECMO confirmed to be directly related to COVID-19 infection - detailed chart review
- **Comparatives:**
  - Logistic regression (**LR**) models of all considered variables
  - Severity of illness score: **SOFA**
  - ECMO decision making variable: **PF ratio**
  - ECMO mortality prediction score: PREdiction of Survival on ECMO Therapy (**PRESET**)

Variables


73
Labs
124
Flowsheet
Time series variables
Demographics
26
Comorbidities
73
Labs
52
Medications
124
Flowsheet
Data processing
Modelling
Data processing
Log. Reg
ML GBT
with static variables

Modeling

Multi-horizon approach “ForecastECMO”
– predict ECMO use at 2 hour intervals from admission



Prediction horizons 0- 96 hours prior to ECMO initiation

Modeling

GBT models: Prediction horizons 0- 96 hours prior to ECMO initiation
Training and evaluation: 10 random shuffles of 10-fold stratified cross validation

ForecastECMO

XGBoost: 212 included variables

Clinical GBT

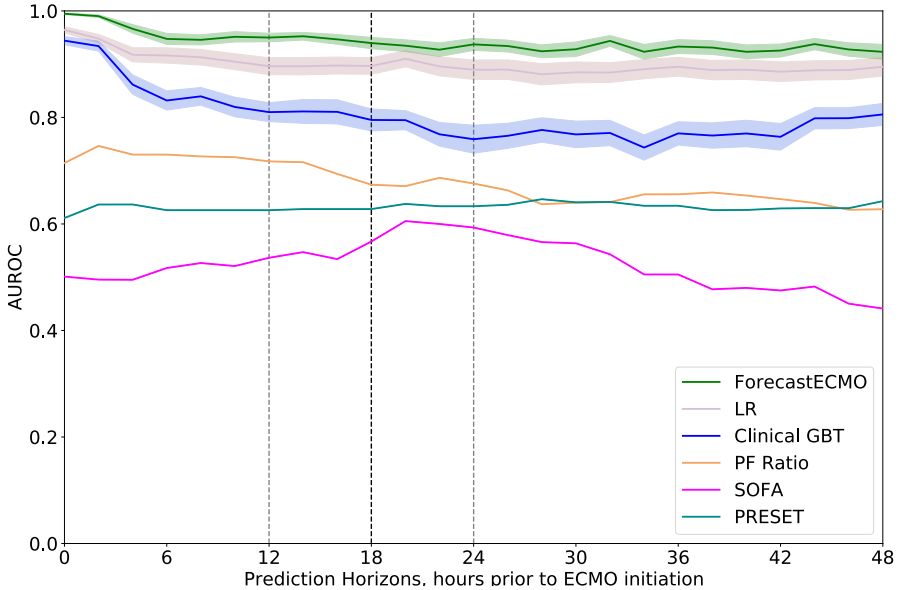
XGBoost 30 a priori clinical variables; relevance to ECMO decision making

Results

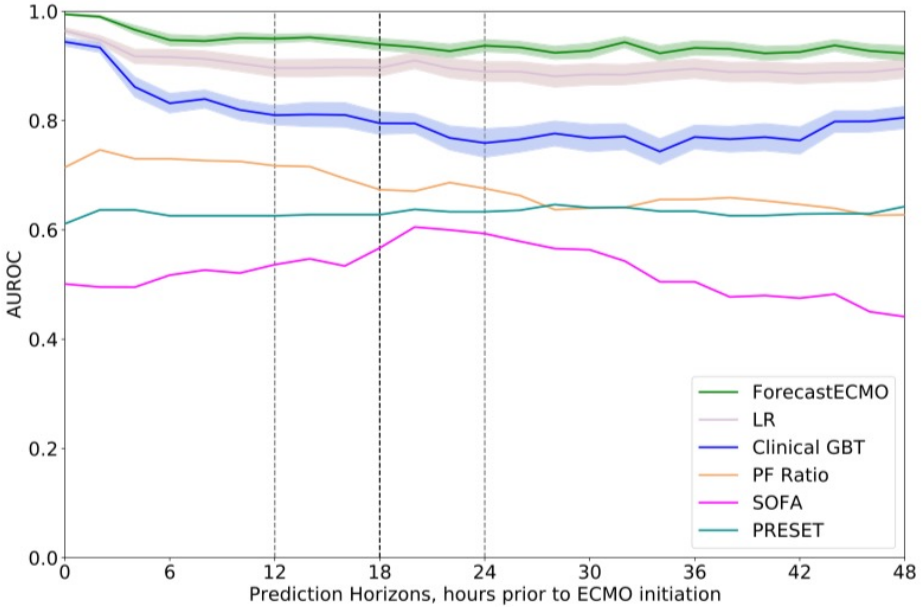
Features	Total cohort, $n = 6247$	Development cohort		Holdout cohort	
		ECMO, $n = 67$	Non-ECMO, $n = 2251$	ECMO, $n = 68$	Non-ECMO, $n = 3861$
Age (years)	54 [26, 64]	54 [44, 59]*	58 [45, 65]*	55 [43, 61]*	48 [13, 63]*
Male sex, *n* (%)	3550 (57)	46 (69)	1255 (56)*	45 (66)	2204 (57)
Caucasian, *n* (%)	3965 (64)	38 (57)*	1348 (60)*	42 (62)	2537 (66)
Height (cm)	168 [157, 178]	170 [163, 180]	170 [163, 178]	175 [168, 183]*	165 [145, 176]*
Weight (kg)	76 [56, 95]	85 [79, 105]*	84 [67, 100]*	88 [77, 109]*	71 [44, 91]*
BMI (kg/m^2)	26 [20, 32]	30 [26, 35]*	28 [24, 34]*	29 [26, 34]*	25 [19, 31]*
Tobacco use, *n* (%)	1207 (19)	5 (7)*	500 (22)*	5 (7)*	697 (18)*
SOFA[a]	9 [6, 13]	12 [10, 13]*,**	11 [7, 14]*	9 [6, 12]*,**	12 [9, 14]*
Lowest PF ratio[a]	112 [66, 204]	56 [48, 69]*	107 [65, 201]*	55 [50, 63]*	126 [71, 218]*
Hospital mortality, *n* (%)	1079 (17)	32 (48)*	391 (17)*	26 (38)*	630 (16)*
CCI	4 [1, 7]	2 [1, 4.5]*	4 [2, 8]*	3 [1, 4]	3 [1, 7]
Chronic pulmonary disease, *n* (%)	2305 (37)	18 (27)*	899 (40)*	13 (19)*	1375 (36)*
Diabetes, *n* (%)	2994 (48)	36 (54)	1388 (62)	30 (44)	1540 (40)
Malignancy, *n* (%)	1537 (25)	6 (9)*	594 (26)*	10 (15)	927 (24)
Renal disease, *n* (%)	1369 (22)	13 (19)	568 (25)	9 (13)	779 (20)
Hospital length of stay (days)	8 [4, 18]	24 [13, 42]*,**	8 [4, 17]*	38 [27, 53]*,**	8 [4, 18]*
Mechanical ventilation (days)[a]	2 [0, 7]	10 [2, 22]*,**	3 [1, 10]*	21 [6, 37]*,**	4 [1, 15]*
CRRT, *n* (%)	386 (6)	16 (24)*	145 (6)*	14 (21)*	211 (5)*
Remdesivir, *n* (%)	764 (12)	27 (40)*,**	372 (17)*	26 (38)*,**	339 (9)*
Neuromuscular blockade, *n* (%)	631 (10)	45 (67)*	188 (8)*	56 (83)*	342 (9)*
Nitric oxide/Iloprost, *n* (%)	511 (8)	41 (61)*	196 (9)*	45 (67)*	229 (6)*
Dopa. <5 μg/kg/min, Dobu., milrinone or levosimendan, *n* (%)[a]	592 (10)	15 (22)*	145 (6)*	11 (16)*	421 (11)*
Dopa. 5–15 μg/kg/min, Epi/NorEpi <0.1 μg/kg/min, Vaso, Phenyl, *n* (%)[a]	3219 (52)	67 (100)*	1138 (51)*	68 (100)*	1946 (49)*
Dopa >15 μg/kg/min, Epi/NorEpi >0.1 μg/kg/min, *n* (%)[a]	2154 (35)	63 (94)*	726 (32)*	65 (96)*	1300 (33)*

Model performance

Accuracy



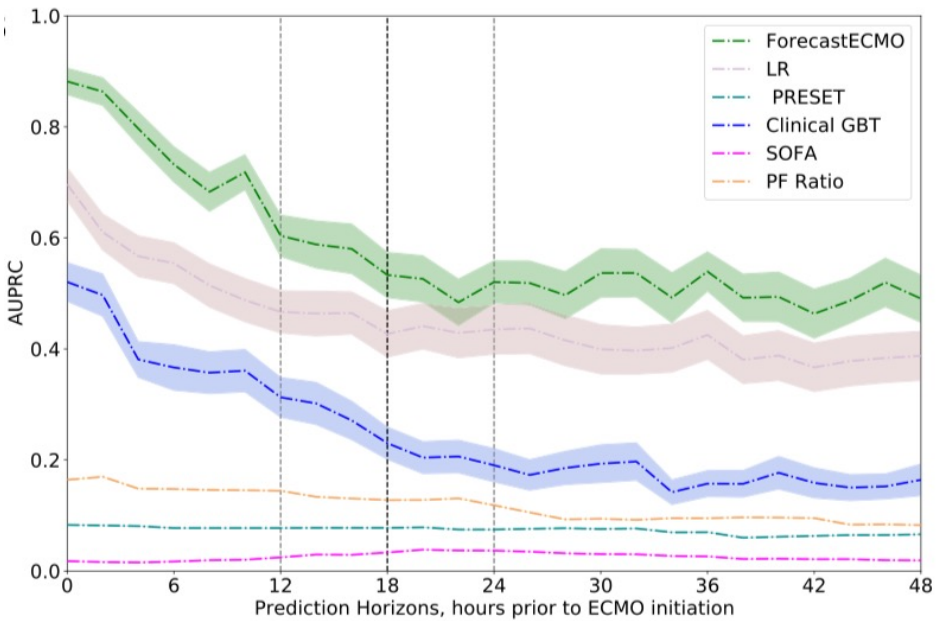
Development



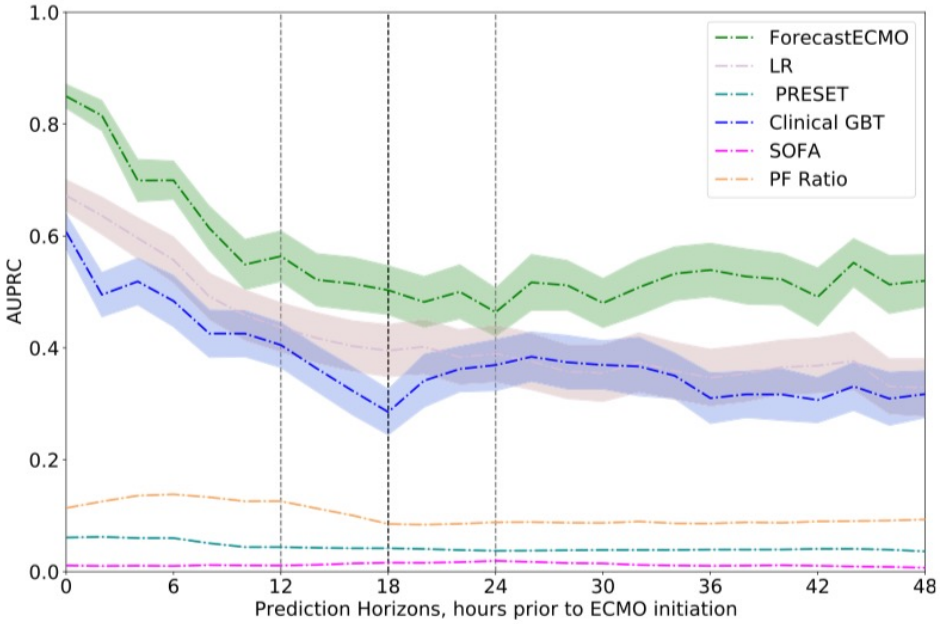
Holdout

Model performance

Precision



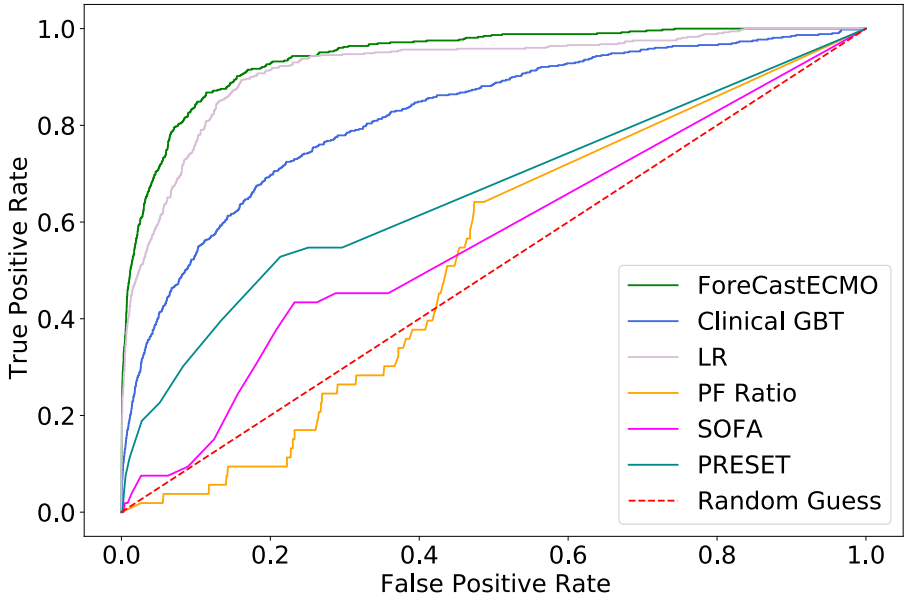
Development



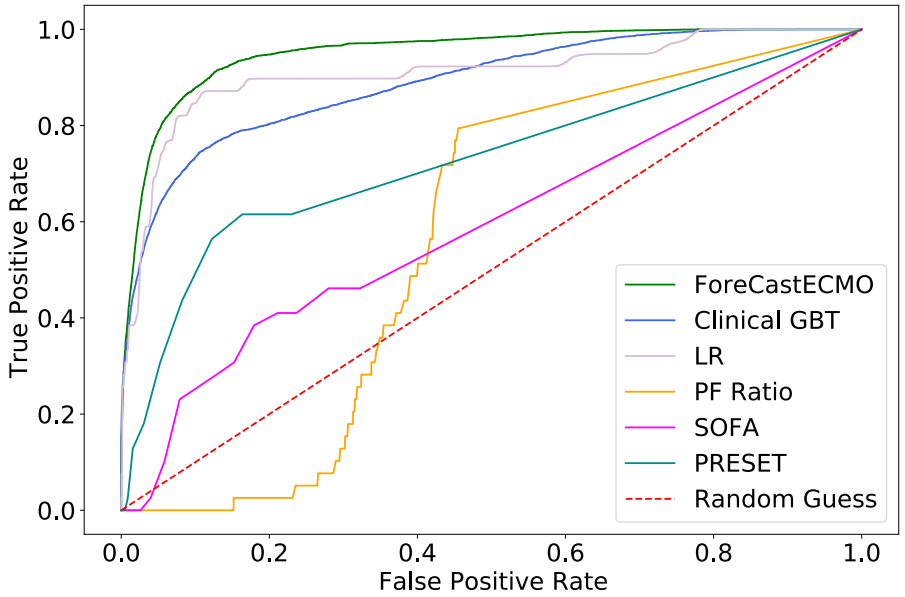
Holdout

Model performance – 18 hours

AUROC



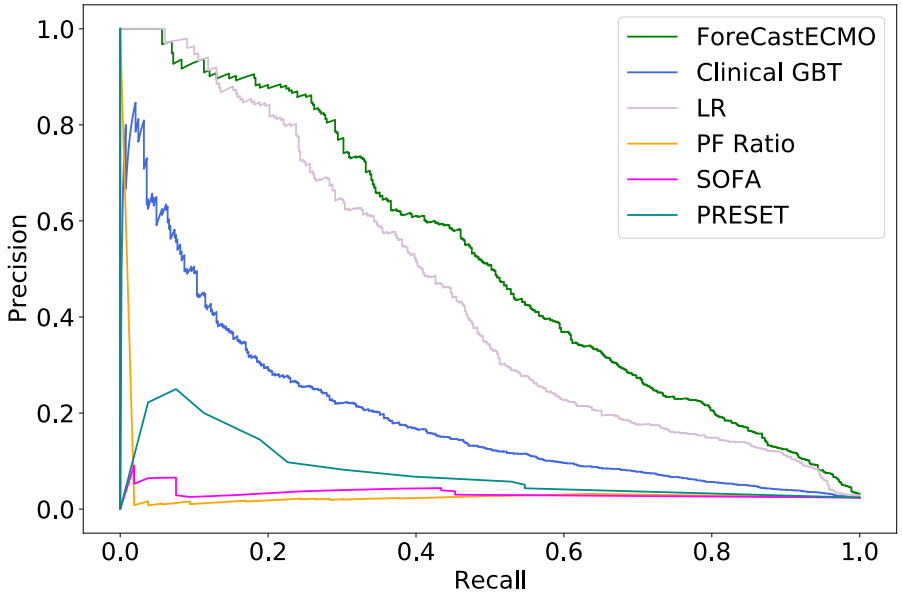
Development



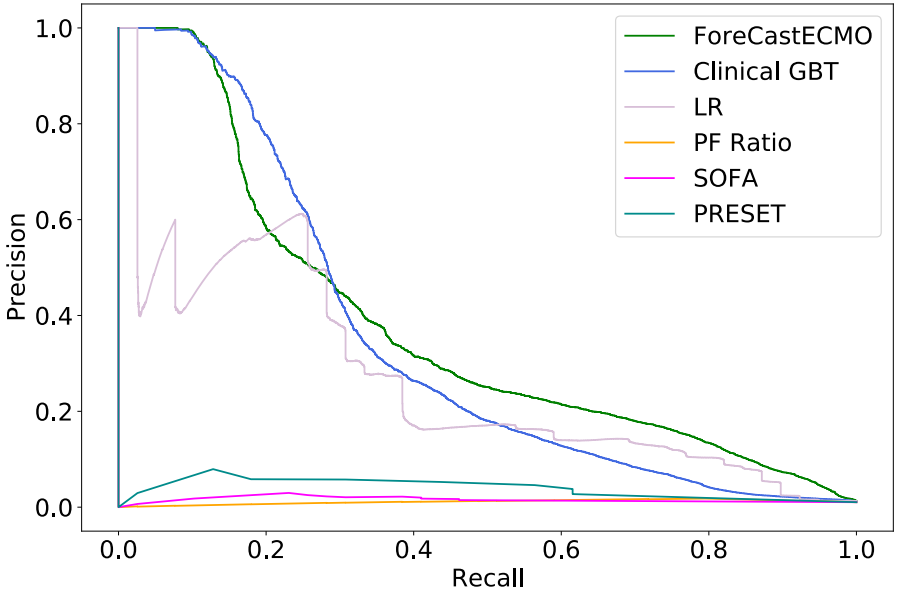
Holdout

Model performance – 18 hours

AUPRC



Development



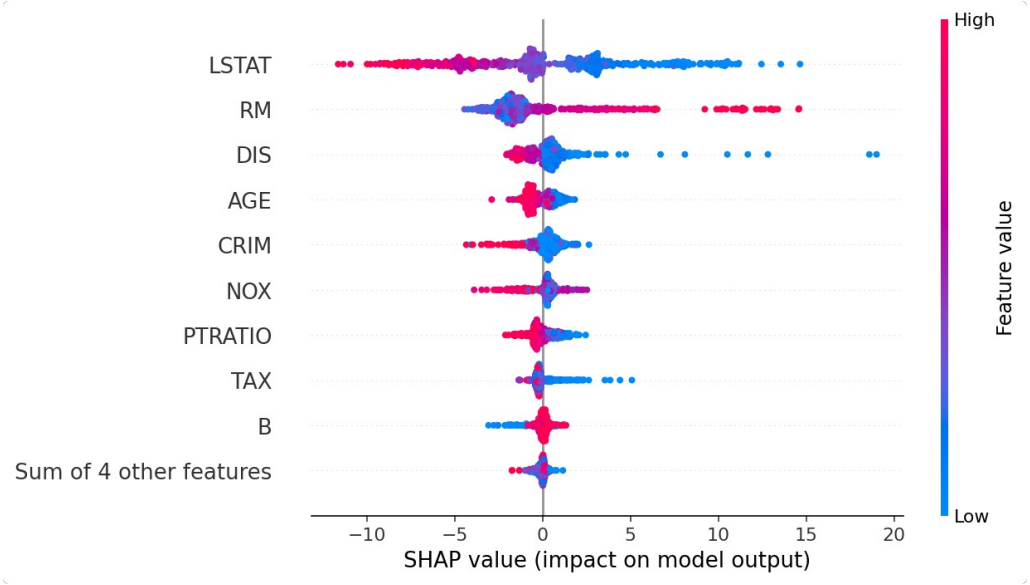
Holdout

What is a good alert tool?

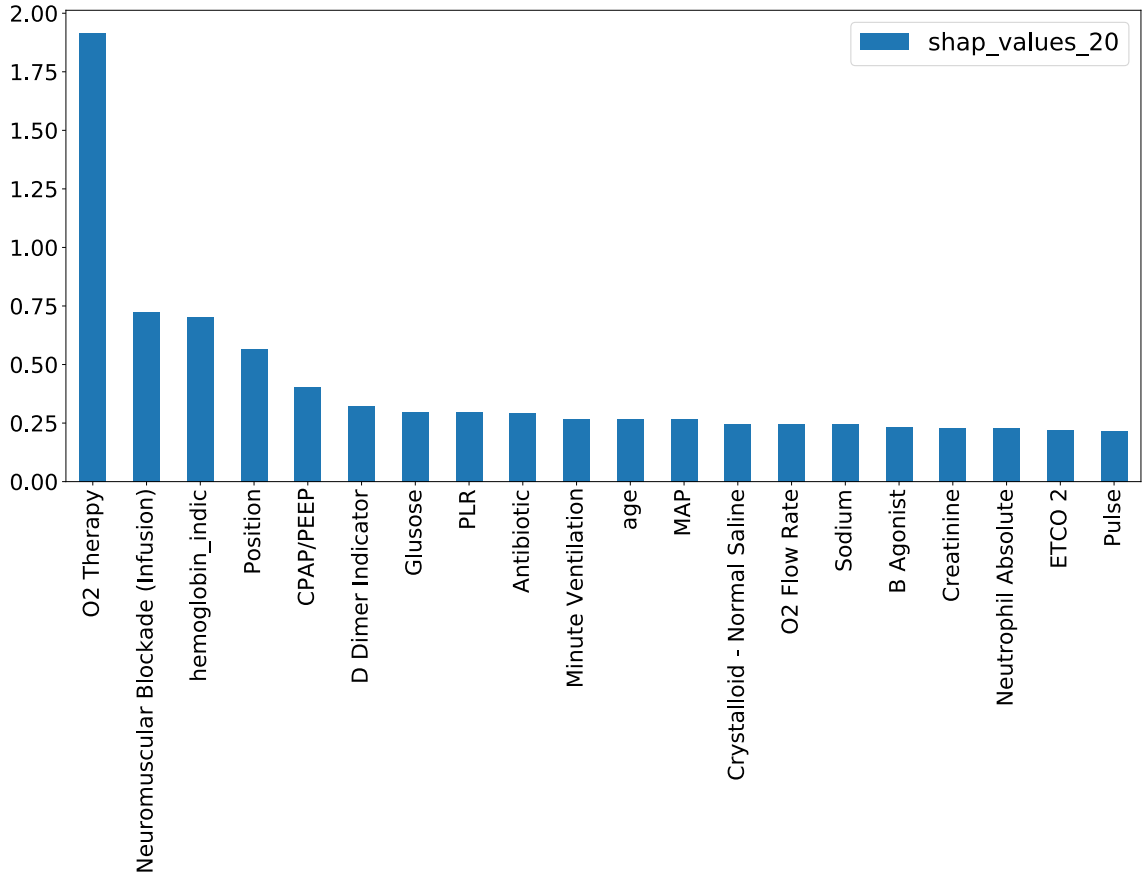
	Development Incidence: 2.89%		Holdout Incidence: 1.73%	
	AUROC	AUPRC	AUROC	AUPRC
ForecastECMO	**0.94 [0.93–0.95]**	**0.546 [0.51–0.582]**	**0.952 [0.951–0.953]**	**0.376 [0.37–0.382]**
PF ratio	0.52	0.032	0.564	0.011
SOFA score	0.56	0.032	0.59	0.015
PRESET score	0.66	0.077	0.726	0.039
LR	0.92 [0.91–0.93]	0.474 [0.435–0.512]	0.908 [0.908–0.908]	0.262 [0.261–0.262]
Clinical GBT	0.82 [0.8–0.83]	0.248 [0.218–0.277]	0.889 [0.887–0.89]	0.345 [0.341–0.382]

SHAP
(SHapley Additive exPlanations)

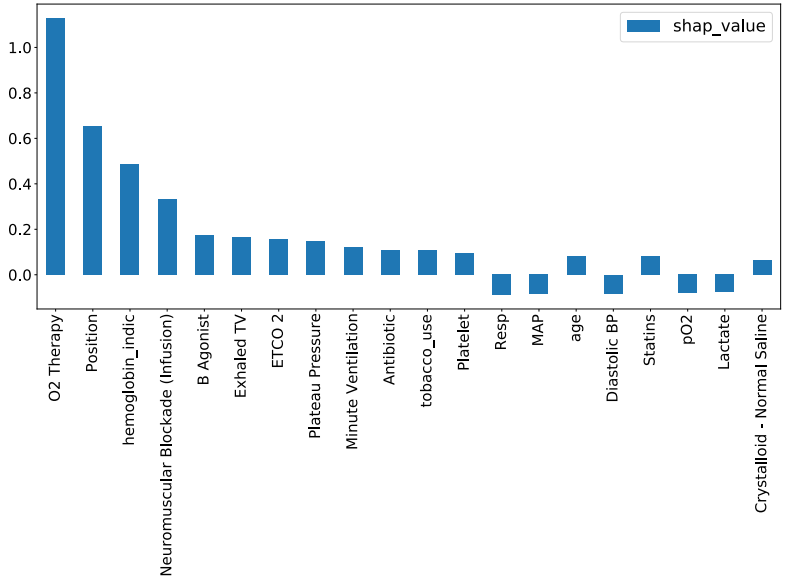
How features effect model performance

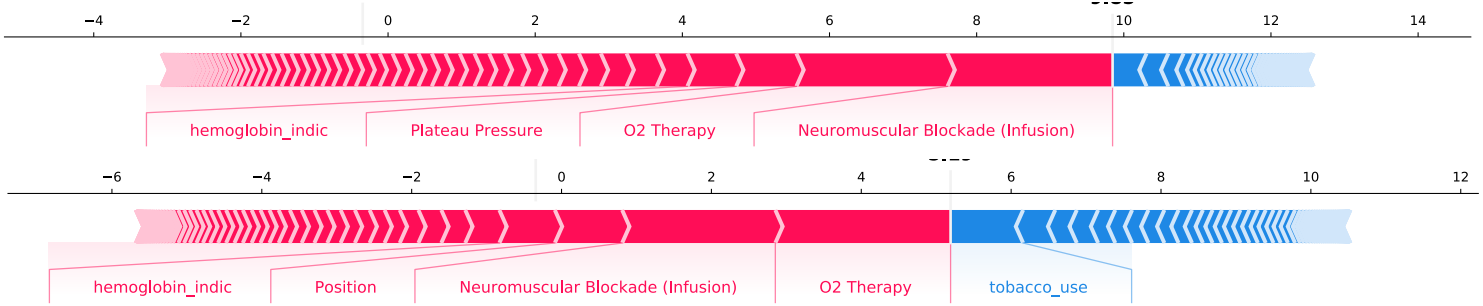


SHAP

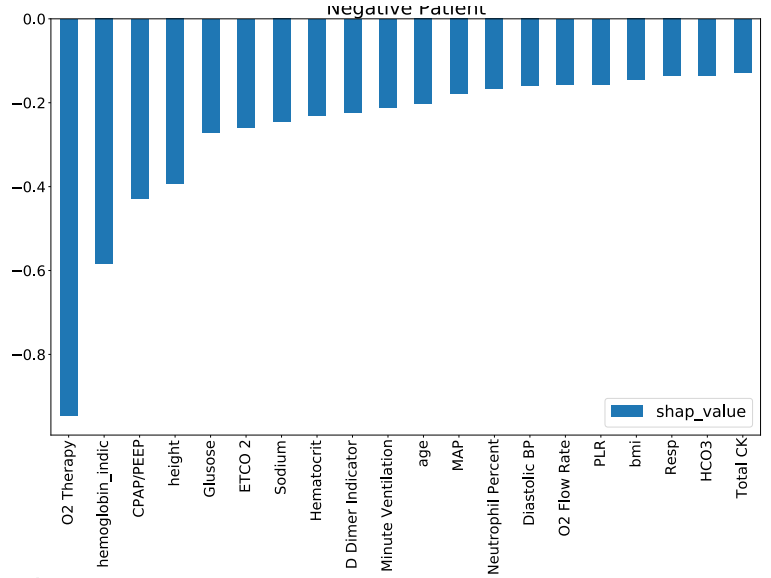

shap_values_20
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
O2 Therapy
Neuromuscular Blockade (Infusion)
hemoglobin_indic
Position
CPAP/PEEP
D Dimer Indicator
Glusose
PLR
Antibiotic
Minute Ventilation
age
MAP
Crystalloid - Normal Saline
O2 Flow Rate
Sodium
B Agonist
Creatinine
Neutrophil Absolute
ETCO 2
Pulse

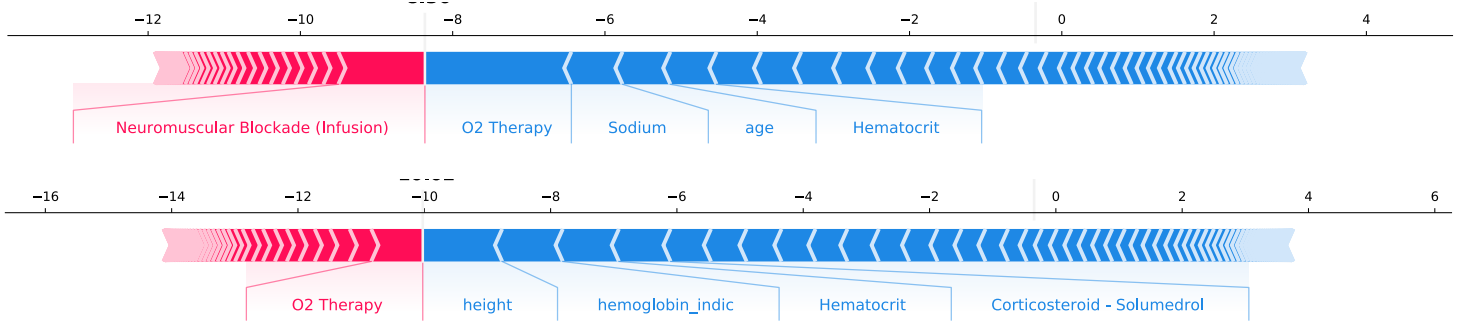
Positive cohort – patients supported on ECMO



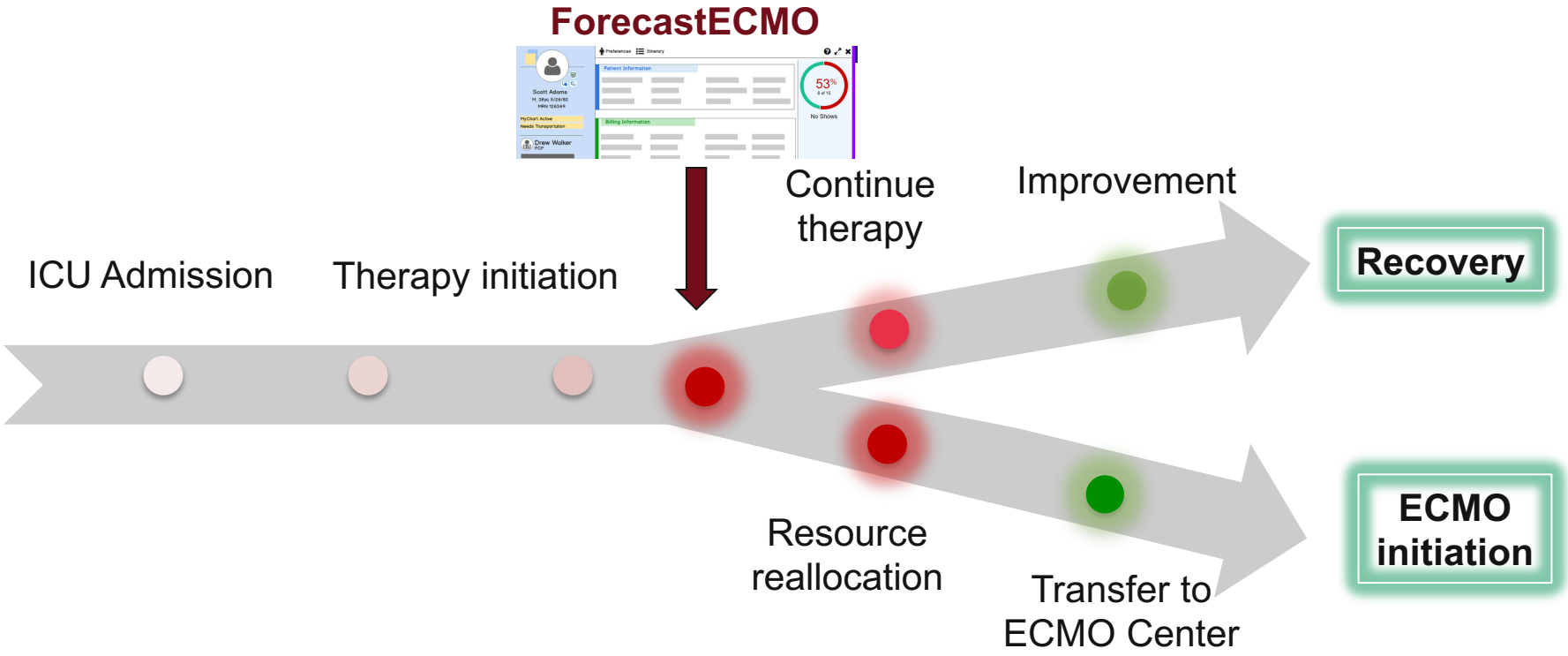


Negative cohort – patients not supported on ECMO





Machine learning models have the potential to serve as clinical decision support tools in **resource allocation** and **patient triage** in healthcare system stress



Real time EHR example



Factors Contributing to Score

Contribution	Factor	Value
30%	ECG/EKG order	**present in last 6 months**
22%	Imaging order	**present in last 6 months**
16%	Number of hospitalizations in last year	**1**
14%	Number of active Rx orders	**6**
12%	Current length of stay	**3.951 days**
6%	Future appointment	**scheduled**
<1%	Age	**1**

Factors Not Contributing to Score

Description

View model formula and coefficients

Predicted risk of an unplanned readmission in the next 30 days.

This score is available for currently admitted patients.

Thank you

Washington University in St Louis Institute of Informatics

BJC Healthcare Innovations lab

Big Ideas Competition

Bing Xue

Hanqing Yang

Neel Shah, MD

Thomas Kannampallil, PhD

Philip Payne, PhD

Chenyang Lu, PhD

Ahmed Said, MD PhD
Said_a@wustl.edu