Machine Learning Department
Carnegie Mellon University
School of Computer Science

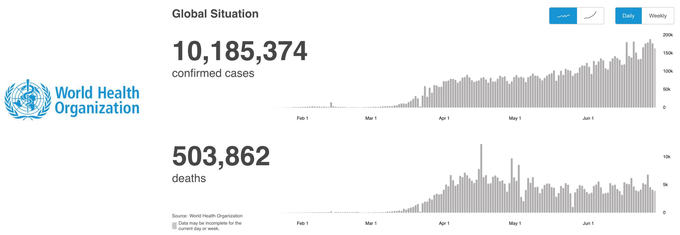
Predicting Mortality Risk in Viral and Unspecified Pneumonia to Assist Clinicians with COVID-19 ECMO Planning

Carnegie Mellon University
Heinz College

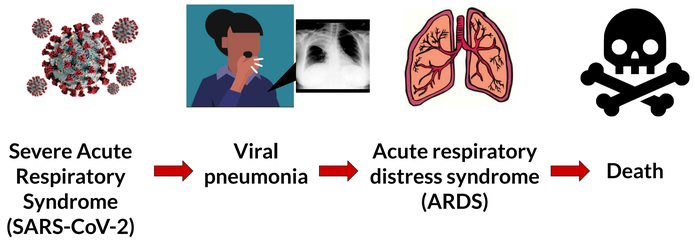
Helen Zhou, Cheng Cheng*, Zachary C. Lipton, George H. Chen, Jeremy C. Weiss*

THE PROBLEM

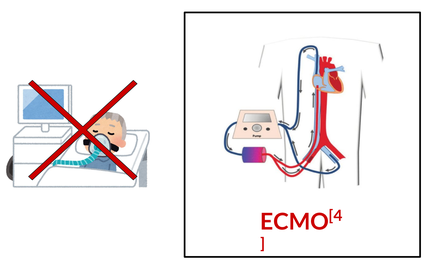
COVID-19 has spread globally, resulting in **millions of infections** and **hundreds of thousands of deaths**.[1]



Concerning patient trajectory:



When mechanical ventilation is insufficient to oxygenate the lungs, **ECMO** can temporarily sustain the patient.



While ECMO is more effective when planned in advance, ***applicable risk scores remain unavailable.***[2,3]

Goal: to develop a **risk score** for patients eligible for ECMO to assist with advanced planning.

METHODS

Cohort: critical care patients with viral or unspecified pneumonia, without contraindications for ECMO

Data: two publicly available critical care databases, eICU (n = 3617) and MIMIC-III (n = 937)

Target: in-ICU mortality. Secondary outcomes include vasopressor use and ventilator use.

Model: $\lambda(t|X_i) = \lambda_0(t)\exp(X_i \cdot \beta)$

- Cox proportional hazards model w/ L1 regularization
- 10-fold cross val. & grid search
- MissForest imputation

Experimental setup:

- eICU: 70-30 train-test
- MIMIC: for model evaluation

DISCUSSION & FUTURE WORK

- PEER score achieves greater or comparable concordance to baselines on the eICU and MIMIC test sets
- 18 features, easy to calculate
- Clear separation in survival curves of high & low-risk groups
- However, our cohort is defined not by COVID-19 positive pneumonia patients but instead by viral or unspecified pneumonia patients who are ECMO-eligible
- Ethical considerations beyond the scope of this work
- More broadly, we hope to provide this risk score as a potential resource for future SARS-like diseases that require ECMO consideration

RESULTS

The Viral or Unspecified Pneumonia ECMO-Eligible Risk Score (PEER Score)

Hazard Ratios

Feature	Hazards Ratio (95% confidence interval)
Age (years)	1.22 (1.04 - 1.43)
Heart rate (beats per minute)	1.13 (0.984 - 1.30)
Systolic blood pressure (mmHg)	0.928 (0.755 - 1.14)
Diastolic blood pressure (mmHg)	0.996 (0.745 - 1.33)
Mean arterial pressure (mmHg)	0.926 (0.673 - 1.27)
Glasgow Coma Scale	0.930 (0.803 - 1.08)
White blood cells (thousands/μL)	0.984 (0.871 - 1.11)
Platelets (thousands/μL)	0.924 (0.790 - 1.08)
Red blood cell dist. width (%)	1.24 (1.08 - 1.43)
Neutrophils (%)	0.972 (0.853 - 1.11)
Blood urea nitrogen (mg/dL)	1.07 (0.937 - 1.23)
Aspartate aminotransferase (units/L)	1.12 (1.06 - 1.18)
Direct bilirubin (mg/L)	1.03 (0.935 - 1.13)
Albumin (g/dL)	0.954 (0.820 - 1.11)
Troponin (ng/mL)	1.06 (0.985 - 1.14)
Prothrombin time (sec)	1.05 (0.909 - 1.20)
pH	0.856 (0.750 - 0.977)
Arterial oxygen saturation (mmHg)	0.787 (0.723 - 0.856)

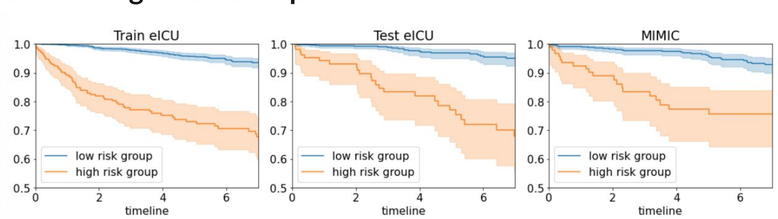
We also created a nomogram for manual calculation of the PEER score.

Concordance

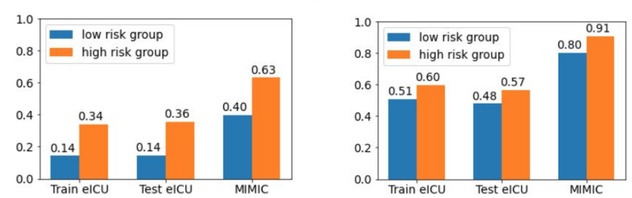
Score	Train eICU concordance	Test eICU concordance	MIMIC concordance
PEER (ours)	**0.77 (0.72 - 0.81)**	**0.77 (0.69 - 0.83)**	**0.66 (0.57 - 0.74)**
CURB-65 (Lim et al., 2003)	0.66 (0.61 - 0.70)	0.62 (0.55 - 0.69)	0.59 (0.52 - 0.66)
PSI/PORT (Fine et al., 1997)	0.71 (0.66 - 0.76)	0.71 (0.63 - 0.78)	0.62 (0.55 - 0.69)
SMART-COP (Charles et al., 2008)	0.69 (0.64 - 0.73)	0.73 (0.67 - 0.80)	**0.66 (0.59 - 0.72)**
GOQ (Gong et al., 2020)	0.67 (0.63 - 0.71)	0.62 (0.54 - 0.70)	0.58 (0.50 - 0.66)

Low and High Risk Groups

Kaplan-Meier Survival curves:



Secondary outcomes:



vasopressor use | ventilator use

[1] WHO Coronavirus Disease (COVID-19) Dashboard. (n.d.). June 30, 2020.
[2] T. Liang et al. Handbook of COVID-19 prevention and treatment.*The First Affiliated Hospital, Zhejiang University School of Medicine. Compiled According to Clinical Experience*, 2020.
[3] American College of Cardiology. ACC's COVID-19 Hub, 2020.
[4] Tarig, Fadelelmoula. "Extracorporeal membrane oxygenation therapy in adult patients: a narrative review of literature." May, 2020.

**equal contribution*

Machine Learning Department
Carnegie Mellon University
School of Computer Science

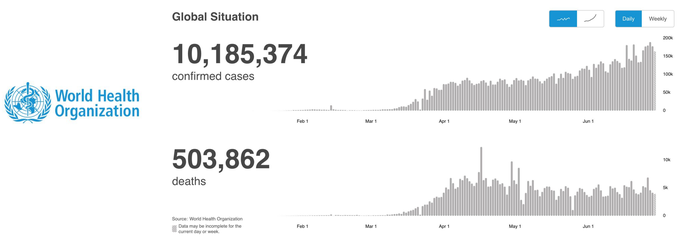
Predicting Mortality Risk in Viral and Unspecified Pneumonia to Assist Clinicians with COVID-19 ECMO Planning

Carnegie Mellon University
Heinz College

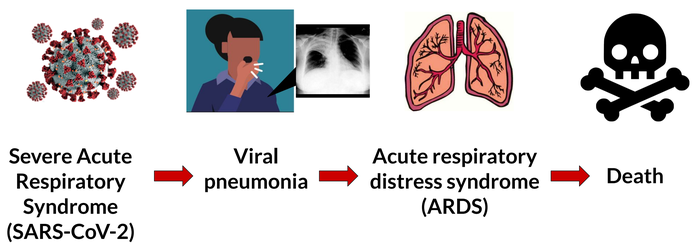
Helen Zhou, Cheng Cheng*, Zachary C. Lipton, George H. Chen, Jeremy C. Weiss*

THE PROBLEM

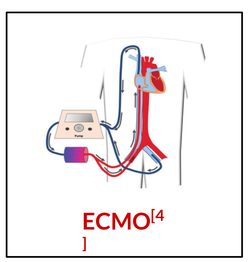
COVID-19 has spread globally, resulting in **millions of infections** and **hundreds of thousands of deaths**.[1]



Concerning patient trajectory:



When mechanical ventilation is insufficient to oxygenate the lungs, **ECMO** can temporarily sustain the patient.



ECMO[4]

While ECMO is more effective when planned in advance, ***applicable risk scores remain unavailable.***[2,3]

Goal: to develop a **risk score** for patients eligible for ECMO to assist with advanced planning.

METHODS

Cohort: critical care patients with viral or unspecified pneumonia, without contraindications for ECMO

Data: two publicly available critical care databases, eICU (n = 3617) and MIMIC-III (n = 937)

Target: in-ICU mortality. Secondary outcomes include vasopressor use and ventilator use.

Model:

- Cox proportional hazards model w/ L1 regularization
- 10-fold cross val. & grid search
- MissForest imputation

$$\lambda(t|X_i) = \lambda_0 \exp(X_i \cdot \beta)$$

Experimental setup:

- eICU: 70-30 train-test
- MIMIC: for model evaluation

DISCUSSION & FUTURE WORK

- PEER score achieves greater or comparable concordance to baselines on the eICU and MIMIC test sets
- 18 features, easy to calculate
- Clear separation in survival curves of high & low-risk groups
- However, our cohort is defined not by COVID-19 positive pneumonia patients but instead by viral or unspecified pneumonia patients who are ECMO-eligible
- Ethical considerations beyond the scope of this work
- More broadly, we hope to provide this risk score as a potential resource for future SARS-like diseases that require ECMO consideration

RESULTS

The Viral or Unspecified Pneumonia ECMO-Eligible Risk Score (PEER Score)

Hazard Ratios

Feature	Hazards Ratio (95% confidence interval)
Age (years)	1.22 (1.04 - 1.43)
Heart rate (beats per minute)	1.13 (0.984 - 1.3)
Systolic blood pressure (mmHg)	0.928 (0.755 - 1.14)
Diastolic blood pressure (mmHg)	0.996 (0.745 - 1.33)
Mean arterial pressure (mmHg)	0.926 (0.673 - 1.27)
Glasgow Coma Scale	0.930 (0.803 - 1.08)
White blood cells (thousands/μL)	0.984 (0.871 - 1.11)
Platelets (thousands/μL)	0.924 (0.79 - 1.08)
Red blood cell dist. width (%)	1.24 (1.08 - 1.43)
Neutrophils (%)	0.972 (0.853 - 1.11)
Blood urea nitrogen (mg/dL)	1.07 (0.937 - 1.23)
Aspartate aminotransferase (units/L)	1.12 (1.06 - 1.18)
Direct bilirubin (mg/L)	1.03 (0.935 - 1.13)
Albumin (g/dL)	0.954 (0.82 - 1.11)
Troponin (ng/mL)	1.06 (0.985 - 1.14)
Prothrombin time (sec)	1.05 (0.909 - 1.20)
pH	0.856 (0.750 - 0.977)
Arterial oxygen saturation (mmHg)	0.787 (0.723 - 0.856)

We also created a nomogram for manual calculation of the PEER score.

Concordance

Table 3: Concordances of the PEER score, CURB-65, PSI/PORT, SMART-COP, and GOQ. Bootstrapping with 1000 replicates was used to compute 95% confidence intervals (in parentheses).

Score	Train eICU concordance	Test eICU concordance	MIMIC concordance
PEER (ours)	**0.77 (0.72 - 0.81)**	**0.77 (0.69 - 0.83)**	**0.66 (0.57 - 0.74)**
CURB-65 [Lim et al., 2003b]	0.66 (0.61 - 0.70)	0.62 (0.55 - 0.69)	0.59 (0.52 - 0.66)
PSI/PORT [Fine et al., 1997]	0.71 (0.66 - 0.76)	0.71 (0.63 - 0.78)	0.62 (0.55 - 0.69)
SMART-COP [Charles et al., 2008]	0.69 (0.64 - 0.73)	0.73 (0.67 - 0.80)	**0.66 (0.59 - 0.72)**
GOQ [Gong et al., 2020b]	0.67 (0.63 - 0.71)	0.62 (0.54 - 0.70)	0.58 (0.50 - 0.66)

Low and High Risk Groups:

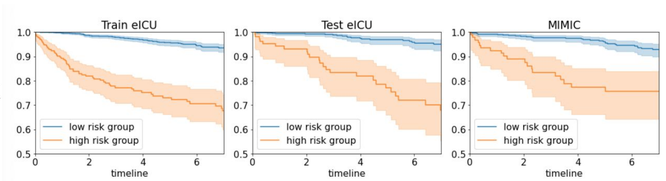


Figure 4.3: Kaplan-Meier survival curves of high vs. low risk groups in train eICU, test eICU, and MIMIC. Shaded regions are the 95% confidence intervals.

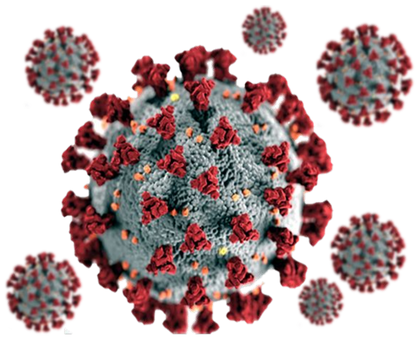
(a) vasopressor (b) ventilator

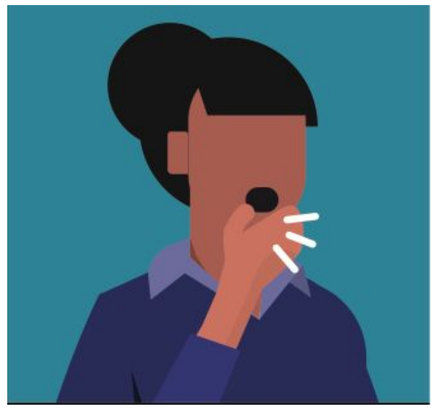
Figure 4.4: Proportion of high and low risk patients who received vasopressors or ventilators. High and low risk groups are derived from the PEER score.

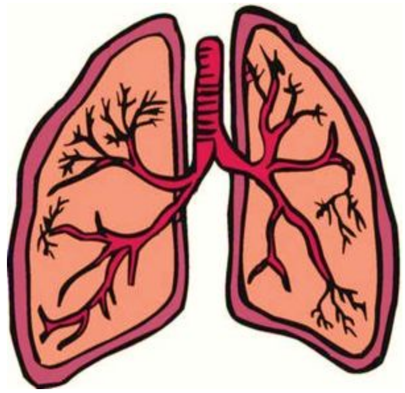
[1] WHO Coronavirus Disease (COVID-19) Dashboard. (n.d.). June 30, 2020.
[2] T. Liang et al. Handbook of COVID-19 prevention and treatment.*The First Affiliated Hospital, Zhejiang University School of Medicine. Compiled According to Clinical Experience*, 2020.
[3] American College of Cardiology. ACC's COVID-19 Hub, 2020.
[4] Tarig, Fadelelmoula. "Extracorporeal membrane oxygenation therapy in adult patients: a narrative review of literature." May, 2020.

**equal contribution*

Many concerning cases of COVID-19 progress from...







Severe Acute Respiratory Syndrome (SARS-CoV-2) → Viral pneumonia → Acute respiratory distress syndrome (ARDS) → Death

Feature	Hazards Ratio (95% confidence interval)
Age (years)	1.22 (1.04 - 1.43)
Heart rate (beats per minute)	1.13 (0.984 - 1.3)
Systolic blood pressure (mmHg)	0.928 (0.755 - 1.14)
Diastolic blood pressure (mmHg)	0.996 (0.745 - 1.33)
Mean arterial pressure (mmHg)	0.926 (0.673 - 1.27)
Glasgow Coma Scale	0.930 (0.803 - 1.08)
White blood cells (thousands/μL)	0.984 (0.871 - 1.11)
Platelets (thousands/μL)	0.924 (0.79 - 1.08)
Red blood cell dist. width (%)	1.24 (1.08 - 1.43)
Neutrophils (%)	0.972 (0.853 - 1.11)
Blood urea nitrogen (mg/dL)	1.07 (0.937 - 1.23)
Aspartate aminotransferase (units/L)	1.12 (1.06 - 1.18)
Direct bilirubin (mg/L)	1.03 (0.935 - 1.13)
Albumin (g/dL)	0.954 (0.82 - 1.11)
Troponin (ng/mL)	1.06 (0.985 - 1.14)
Prothrombin time (sec)	1.05 (0.909 - 1.20)
pH	0.856 (0.750 - 0.977)
Arterial oxygen saturation (mmHg)	0.787 (0.723 - 0.856)

Acute respiratory distress syndrome (ARDS)

ML for global health instructions

As a follow up to the previous email, please use this form to send us your the PDF of your poster as well as provide other information we need for planning: https://forms.gle/HZa9qcNLtGLMV2Yt6 After you submit, you will still be able to edit the form up to the deadline of *July 1, 2020*.

1. Format: Feel free to use a format of your choice. Keep in mind that you want to want your poster to be readable. So avoid clutter, focus on the most important things and use figures and tables where possible. Also ensure that your poster is only 1 page of PDF.

2. Poster session: Note that the actual poster session will happen on Zoom. You will have a Zoom room to yourself during which you can engage with visitors to your poster. More details on this to come.

3. Oral presenters: If you were selected for an oral presentation, note that you encouraged (but not required) to have a poster. It will give you an extended opportunity to talk about your work and network with attendees at the workshop.