Summer Discussion MI2

August 26, 2021

Sickest-first policy & Predictive Models for Liver Transplant Candidates in the US

Hoang Thien Ly

Outline

1/ Transplant problem and sickest-first policy

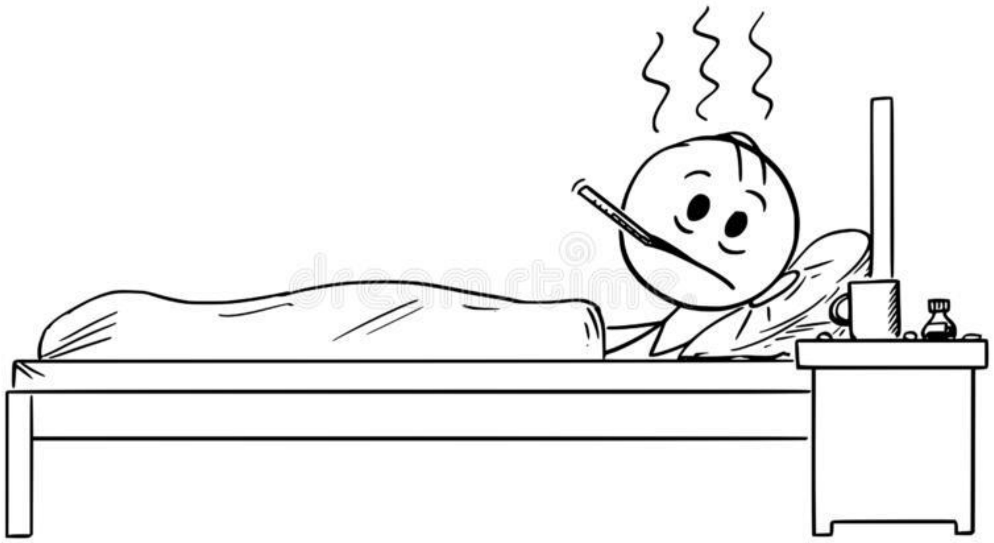
2/ MELD-Score and optimistic results

3/ Applying ML Techniques

- Process of cleaning datasets
- Models and obtained results from a paper

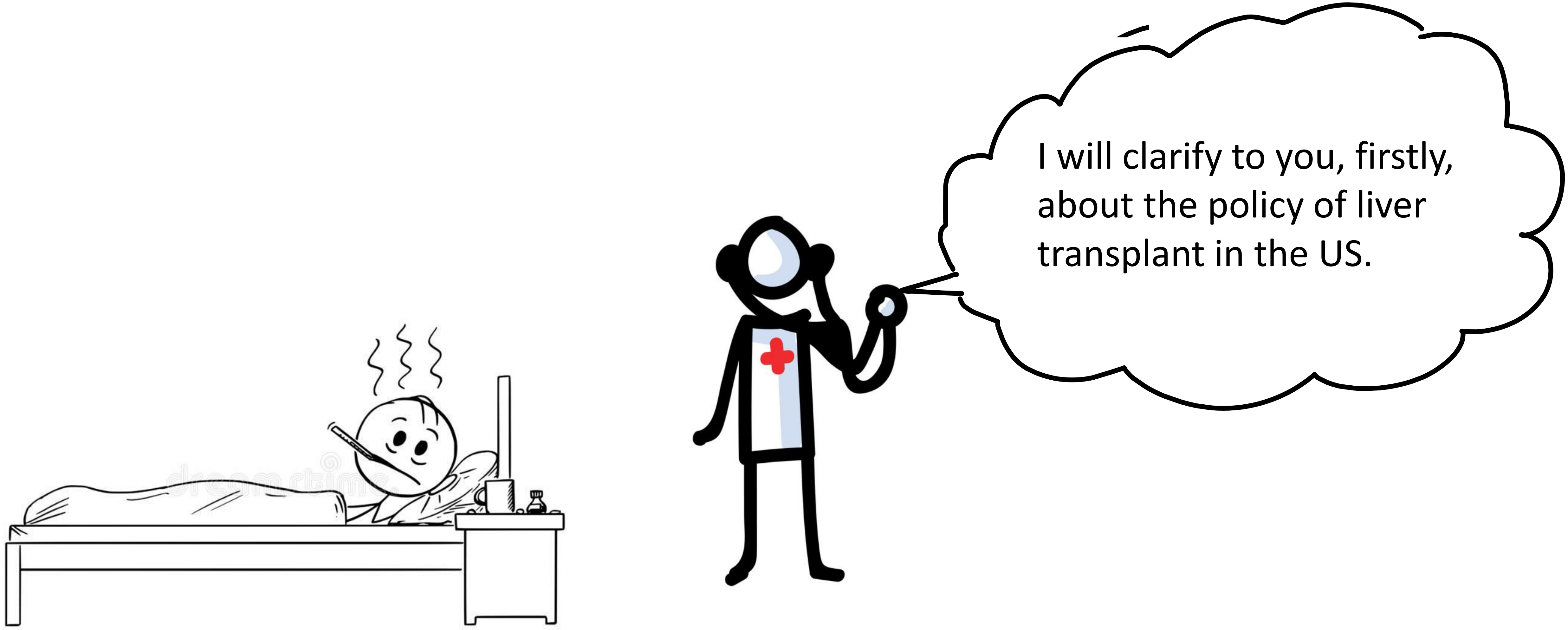
4/ Related works and Q&A section

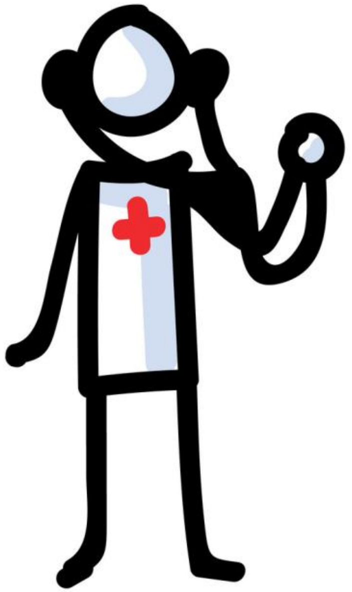
Transplant problem & policy



I am patient with end-stage liver disease. I need a liver-transplantation.

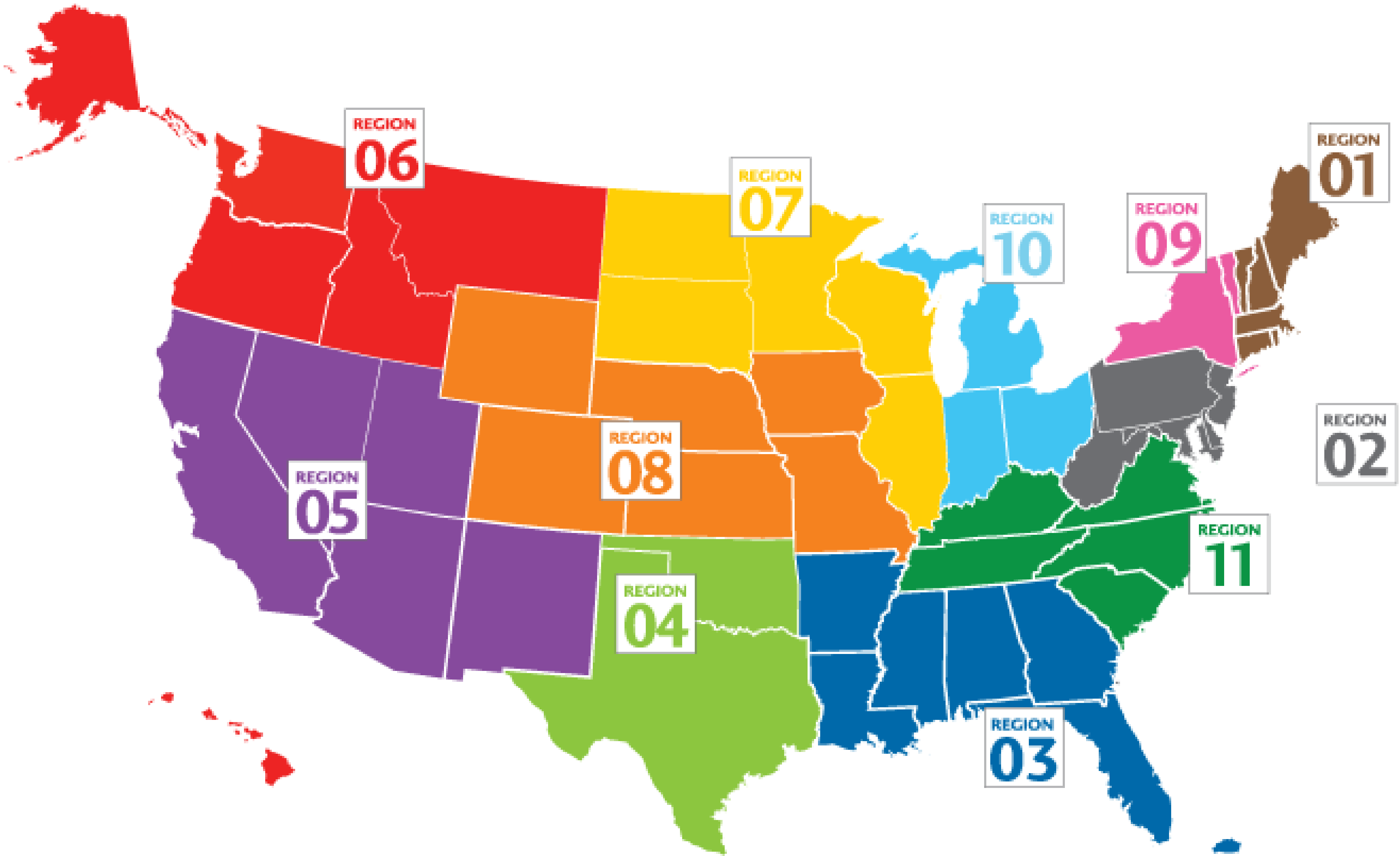

Alright. Beforehand, we need to explain to you and decide whether you may benefit from a transplant.


I will clarify to you, firstly, about the policy of liver transplant in the US.

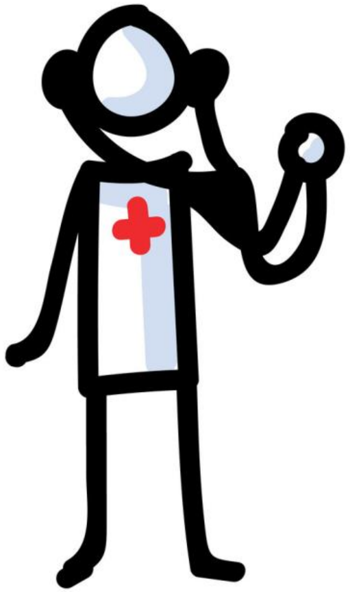


- One national waiting list for the entire US. You can register at medical centers in different regions.

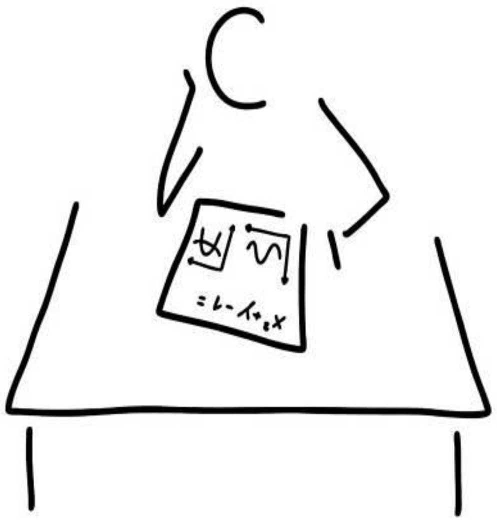
- Waiting time cannot be predictable and may vary from regions of the country and from the illness levels.



UNOS.org (United Network for Organ Sharing)



- The deceased donor livers are assigned to matches among patients according to sickest-first policy.
- When get top of the waiting list, we consider compatibility of patient to donor liver to lower risk of failure:
  + Blood type,
  + Body size,
  + Geographical considerations…



- November 12, 2019:
  12 965 patients are on waiting list for liver transplantation.

- In 2018:
  12 700 patients were added to the list.
  8 250 liver transplants were performed.
  609 patients died while waiting.
  627 patients were removed due to being too sick.

Problem of assessing disease severity of a patient

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MELD-score and its variants

- The Model for End-stage Liver Disease (MELD-score) estimates the chance of surviving during the next 3 months of patients with chronic liver disease.
- MELD-score is ranged from 6 to over 40
- The higher the score, the sicker the patient is, and the higher his/her position is in waiting list
- It has variants: MELD, MELD-Na, MELD-exception (for liver cancer, or hepatopulmonary syndrome,…) and PELD (for pediatric patients)

MELD-score and its variants

3-Month Mortality Based on MELD Scores

MELD Score	Mortality Probability
40	71.3% mortality
30-39	52.6% mortality
20-29	19.6% mortality
10-19	6.0% mortality
9 or less	1.9% mortality

https://www.hepatitisc.uw.edu/go/management-cirrhosis-related-complications/liver-transplantation-referral/calculate-meld-score

MELD-score and its variants

1 Year Survival Rate Based on MELD Scores

MELD Score	Waiting list	Post Transplant
Score 10	90% survival	83% survival
Score 15	81% survival	80% survival
Score 20	63% survival	78% survival
Score 25	42% survival	74% survival
Score 30	21% survival	71% survival

Calculating the MELD Score [UndergroundMed]

MELD-score and its variants

As conditions change, MELD changes.
The table below shows how often MELD score gets updated.

MELD Score	**Recalculation**
25 or higher	Every week
19-24	Every 30 days
11-18	Every three months
10 or less	Once a year

https://www.upmc.com/services/transplant/liver/process/waiting-list/meld-score

Formula of MELD-Score

$$\text{MELD} = 3.78 \times \ln[\text{Bili (mg/dL)}] + 11.2 \times \ln[\text{INR}] + 9.57 \times \ln[\text{Creati (mg/dL)}] + 6.43$$

$$\text{MELD-Na} = \text{MELD} + 1.32 \times (137 - \text{Na}) - [0.033 \times \text{MELD} * (137 - \text{Na})]$$

Bilirubin: how well liver clears substance “bile” (żółć))

INR: how well liver makes proteins needed for blood to clot (krzepnięcie krwi)

Creatinine: how well kidneys work

Na: serum sodium, recently added, how well body regulates fluid balance. Ranged from 125 to 137

Formula of MELD-Score

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$$\text{MELD-Na} = \text{MELD} + 1.32 \times (137 - \text{Na}) - [0.033 \times \text{MELD} * (137 - \text{Na})]$$

- If Bili, INR, Creati < 1, use 1
- If Creati > 4, use 4

Optimistic results from MELD-Score

The MELD-based allocation system was immediately successful, leading to the first ever reduction in the number of waiting list candidates and a 15% reduction in mortality among those on the waiting list.

Freeman, R., Wiesner, R., Edwards, E., Harper, A., Merion, R., Wolfe, R.: Results of the first year of the new liver allocation plan. Liver Transplant, **10**, 7-15 (**2004**)

Drawbacks of MELD-Score based system

- The log-transformed values of Bili, INR, Creati at 1.0 can be problematic, as a large percentage waiting list candidates possess Creati levels below, and values below this threshold can reflect different levels of kidney function.

Sharma, P., Schaubel, D., Sima, C., Merion, R., Merion, R., Lok, A.: Re-weighting the model for end-stage liver disease score components. Gastroenterology, **135**, 1574-1581 (**2008**)

- Correlation between MELD and outcome is not equally strong for all patients. For some patients, MELD may not accurately reflect the severity of their condition.

It’s high time for ML Models!!

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ML methods from a paper of 2021

Predicting Mortality in Liver Transplant Candidates

Jonathon Byrd, Sivaraman Balakrishnan, Xiaoqian Jiang, and Zachary C. Lipton

J. Byrd (✉) · S. Balakrishnan · Z. C. Lipton
Carnegie Mellon University, Pittsburgh, PA 15213, USA
e-mail: jabyrd@cmu.edu

S. Balakrishnan
e-mail: siva@stat.cmu.edu

Z. C. Lipton
e-mail: zlipton@cmu.edu

X. Jiang
University of Texas Health Science Center at Houston, Houston, TX 77030, USA
e-mail: Xiaoqian.Jiang@uth.tmc.edu

A. Shaban-Nejad et al. (eds.), *Explainable AI in Healthcare and Medicine*,
Studies in Computational Intelligence 914,
https://doi.org/10.1007/978-3-030-53352-6_31

ML Pipeline

- Data: waiting list histories from June 30, 2004 to 2016
- Data division: 50-25-25% for train-val-test
- Out of sample test set.
- Metric: ROC AUC (concerning with giving livers to patients who most need them than accurately predicting mortality risk)
- Number of features: 50
  - 31 known at registration
  - 19 updated over time

Data preprocessing

- Cat features ← dummy variables
- Num features ← standardization (zero mean, unit variance in training set)
- MELD & MELD-Na Score ← by formulae
- Missing values:
  - Numerical time-series features: forward-filled by last known value
  - Other numerical missing values: by median from training set

→ **After pre-processing, data has 241 columns**

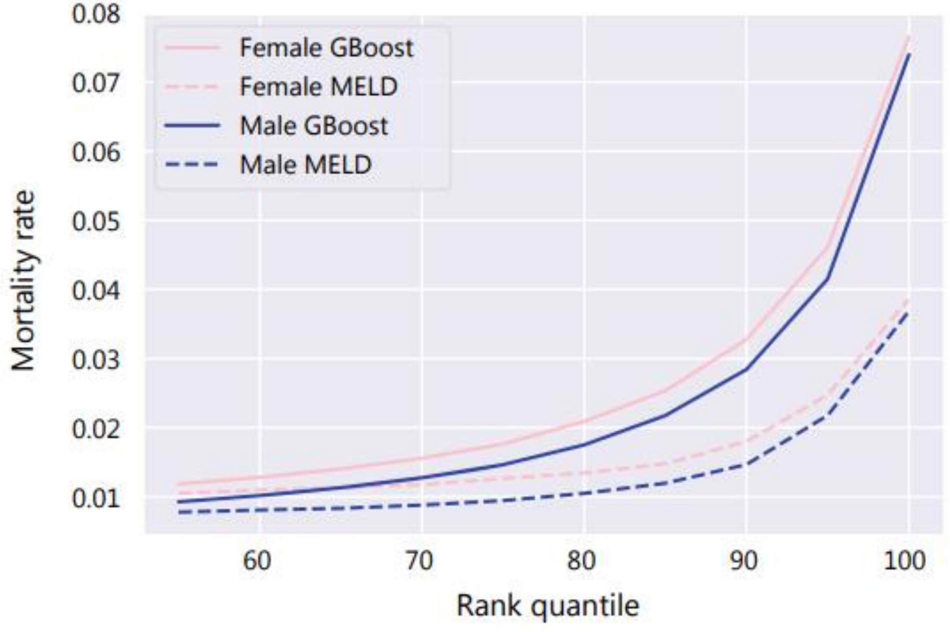
Training model

- Train models using four different feature sets:
  - **First set:** all available features
  - **Second set:** excludes demographic features: citizenship, education, gender, ethnicity, blood type, income (age, height, and weight are kept)
  - **Third set:** excludes diagnosis, functional status,… (can be manipulated by doctors)
  - **Fourth set:** only has: Bilirubin, INR, Creatinine, Na and dialysis twice in previous week
- Models: Logistic Regression and Gradient Boosting ensembles with decision trees
- Hyperparameters: detailed in the paper

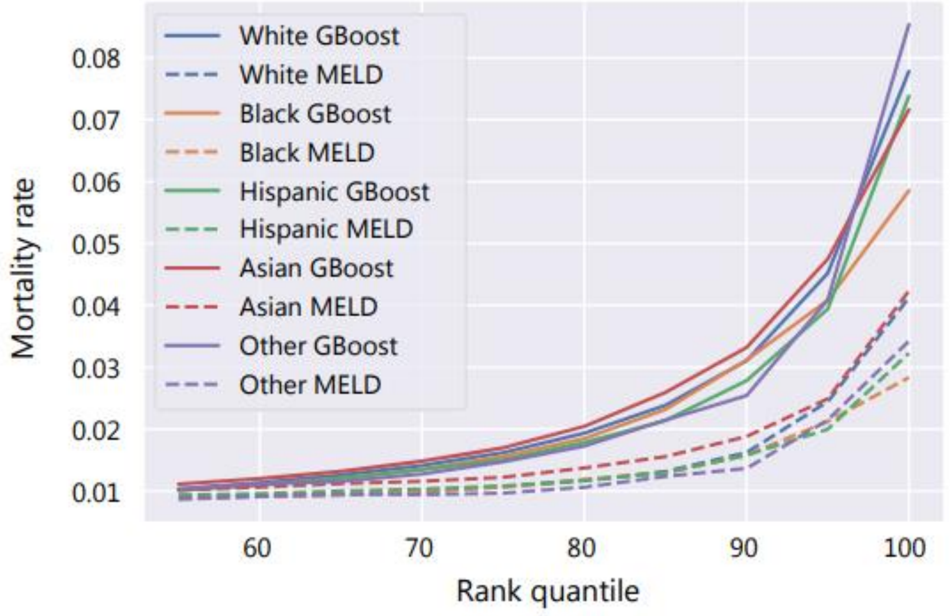
Obtained results

	All features	Non-demographic features	Selected features	MELD-Na features
Same-day mortality				
MELD	N/A	N/A	N/A	0.825, 0.791
MELD-Na	N/A	N/A	N/A	0.831, 0.793
Match MELD	N/A	N/A	N/A	0.750, 0.729
Logistic Regression (same-day)	0.888, 0.867	0.886, 0.864	0.876, 0.855	0.817, 0.782
Gradient Boosting (same-day)	**0.935, 0.920**	0.931, 0.918	0.873, 0.857	0.793, 0.735
Logistic Regression (3-month)	0.881, 0.851	0.880, 0.849	0.872, 0.839	0.820, 0.774
Gradient Boosting (3-month)	0.902, 0.873	0.901, 0.873	0.894, 0.864	0.832, 0.796
3-month mortality				
MELD	N/A	N/A	N/A	0.715, 0.674
MELD-Na	N/A	N/A	N/A	0.730, 0.686
Match MELD	N/A	N/A	N/A	0.685, 0.651
Logistic Regression (same-day)	0.786, 0.756	0.786, 0.752	0.778, 0.745	0.700, 0.662
Gradient Boosting (same-day)	0.783, 0.767	0.781, 0.765	0.808, 0.781	0.731, 0.690
Logistic Regression (3-month)	0.820, 0.772	0.818, 0.770	0.809, 0.759	0.734, 0.687
Gradient Boosting (3-month)	**0.834, 0.800**	0.832, 0.798	0.827, 0.789	0.734, 0.696

Obtained results



(a) Gender



(b) Ethnicity

Conclusions

- Gradient boosting ensembles outperform MELD and MELD-Na for AUC ROC
    - 0.935 (grad-boost) vs 0.831 (MELD-Na) for same-day prediction
    - 0.834 (grad-boost) vs 0.730 (MELD-Na) for 3-months prediction
- Removing demographic features (race, education, gender,…) and subjective features does not have a large effect on model performance
- Both model and MELD-Na slightly underestimate mortality in female patients, but no similar trends when comparing across ethnicities

References

- Predicting Mortality in Liver Transplant Candidates Explainable AI in Healthcare and Medicine, **2021**, Volume 914 ISBN : 978-3-030-53351-9 Jonathon Byrd, Sivaraman Balakrishnan, Xiaoqian Jiang, Zachary C. Lipton
- Waiting List, MELD Score, Liver Transplants - Dr. Robert S. Brown
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- https://columbiasurgery.org/liver/liver-transplant-waiting-list
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- https://www.organdonor.gov/learn/organ-donation-statistics
- UNOS.org

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Discussion Time