
The Artificial Intelligence Clinician learns optimal treatment strategies for sepsis in intensive care

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25% of ICU death is associated with Septic Shock^[1]

Sepsis is infection which leads to life-threatening acute organ dysfunction.

Treatment of sepsis depends highly on the condition of patient and currently there are no tool for this highly personalized treatment.

[1] Rhee C, Klompas M. Sepsis trends: increasing incidence and decreasing mortality, or changing denominator?. *J Thorac Dis.* 2020;12(Suppl 1):S89-S100.

Two challenges in sepsis treatment

- Management of the intravenous (IV) fluids

Too much will lead to **organ failure** whereas too less will **not retain the capillary volume**.

- Management of the vasopressors

Too much will lead to **heart failure** whereas too less will **not correct the heart activity**.

MDP has been used to model the optimal trajectory

A policy iteration approach has been used to identify the optimal amount of IV fluid and vasopressors in any patient state.

Two dataset has been used for training and testing phase

- MIMIC-III
 - 17083 patients
- eRi
 - 79073 patients

The dataset has been filtered out based on,

- SOFA score
- Sample Collection time
- Sepsis type
- Availability of age and mortality information

48 variable defines a patient's state

Patient state contains

- Demographics
- Vital Sign
- Lab result
- Amount of fluid , vasopressor received
- Fluid balance

Duration of a patient stay in hospital is considered as the trajectory.

Goal of RL agent is optimization of mortality

Two conditions for end of trajectory

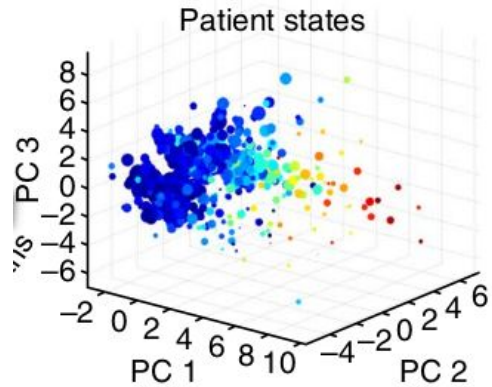
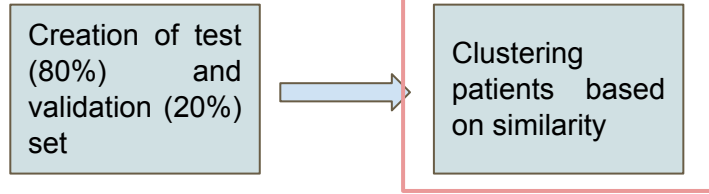
- **Hospital Mortality:** The patient died during the stay in hospital
- **90D Mortality:** The patient died between 0 and 90th day of surgery.

Reward = $\begin{cases} -100 & \text{if the patient died at the end of trajectory} \\ 100 & \text{else} \end{cases}$

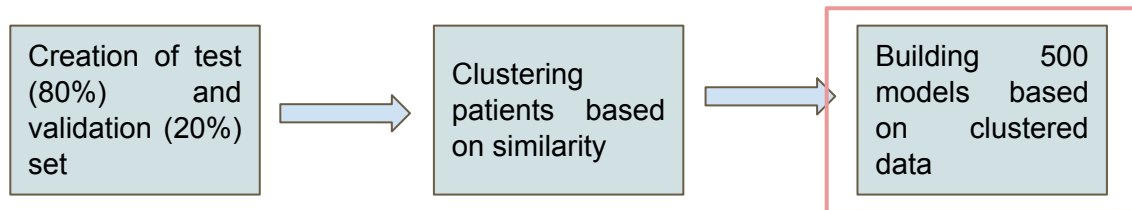
Modeling Stages

Creation of test
(80%) and
validation (20%)
set

Modeling Stages



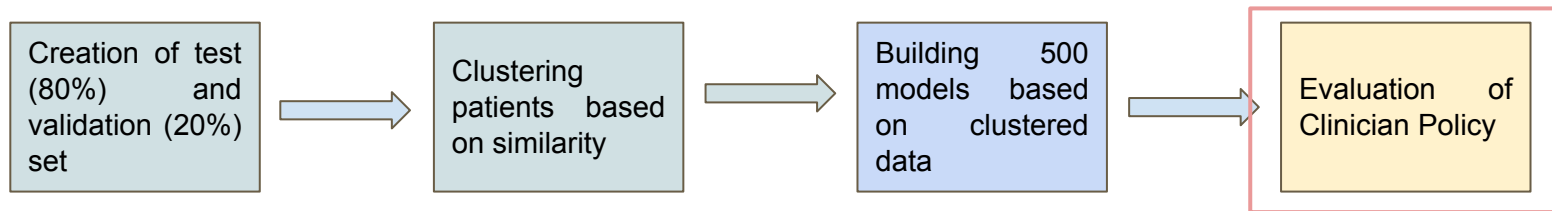
Modeling Stages



$$\pi^*(s) \leftarrow \operatorname{argmax}_a Q^{\pi^*}(s, a) \quad \forall s$$

$$V^\pi(s) = \sum_a \pi(s, a) \sum_{s'} T(s', s, a) [R(s') + \gamma V^\pi(s')]$$

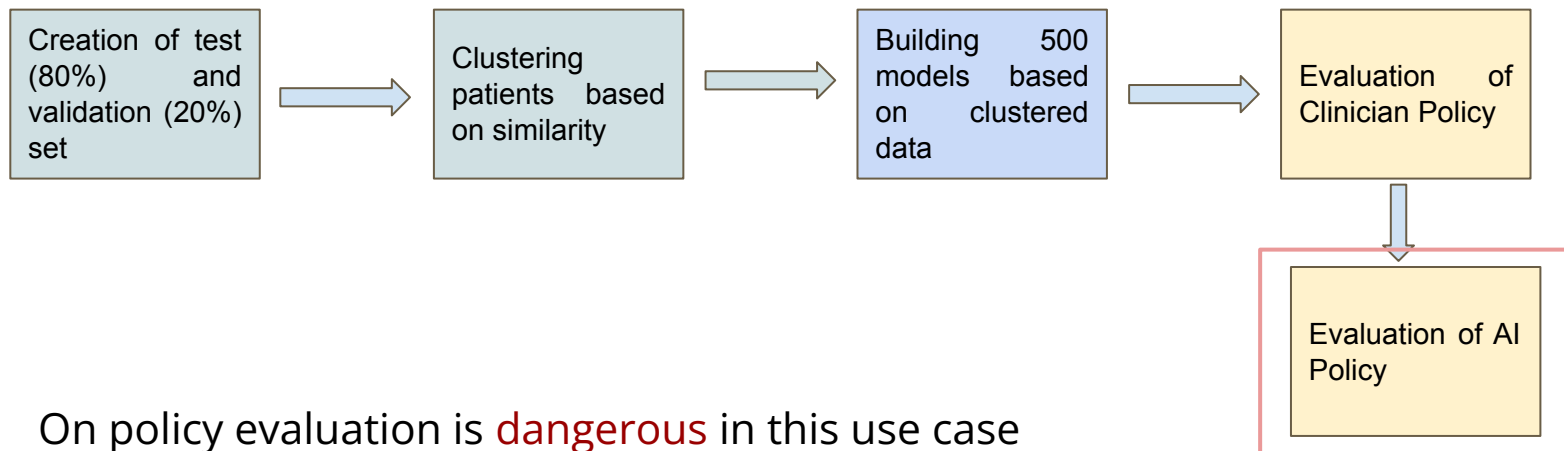
Modeling Stages



Clinicians policy was evaluated using Q function

$$Q^\pi(s, a) \leftarrow Q^\pi(s, a) + \alpha \cdot (r + \gamma \cdot Q^\pi(s', a') - Q^\pi(s, a))$$

Modeling Stages



On policy evaluation is **dangerous** in this use case

Off Policy Evaluation (OPE)

Two approaches for OPE

- Model based evaluation
 - Estimation bias
 - Availability of data
- Importance sampling
 - High variance

Weighted Importance Sampling (WIS) is used for OPE

The data is generated by a different policy (Clinician policy)

We want to estimate the expectation of AI policy on that data

$$v_g \doteq \mathbb{E}_g [\bar{Y}_k]$$

$$\rho_k \doteq \frac{g(Y_k)}{l(Y_k)}$$

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$$v_g \doteq \mathbb{E}_g [\tilde{Y}_k] \quad \rho_k \doteq \frac{g(Y_k)}{l(Y_k)}$$

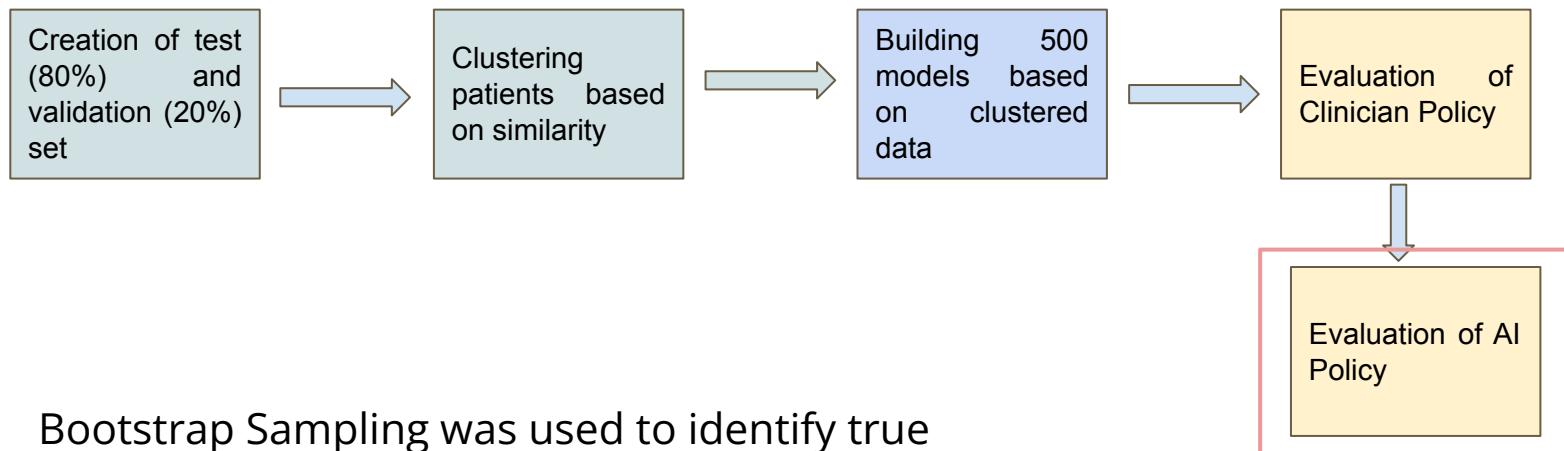
$$\tilde{v}_g \doteq \frac{\sum_{k=1}^n \rho_k Y_k}{n}$$

Weighted Importance Sampling (WIS) is used for OPE

WIS decreases variance with possibility of increased bias

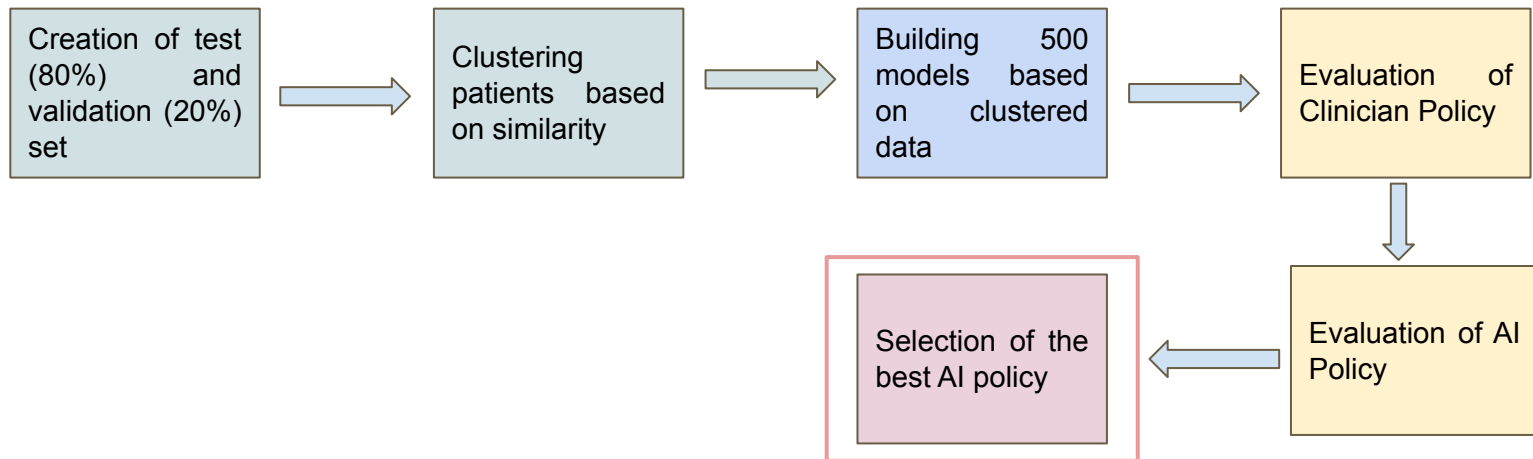
$$\hat{v}_g \doteq \frac{\sum_{k=1}^n \rho_k Y_k}{\sum_{k=1}^n \rho_k}.$$

Modeling Stages

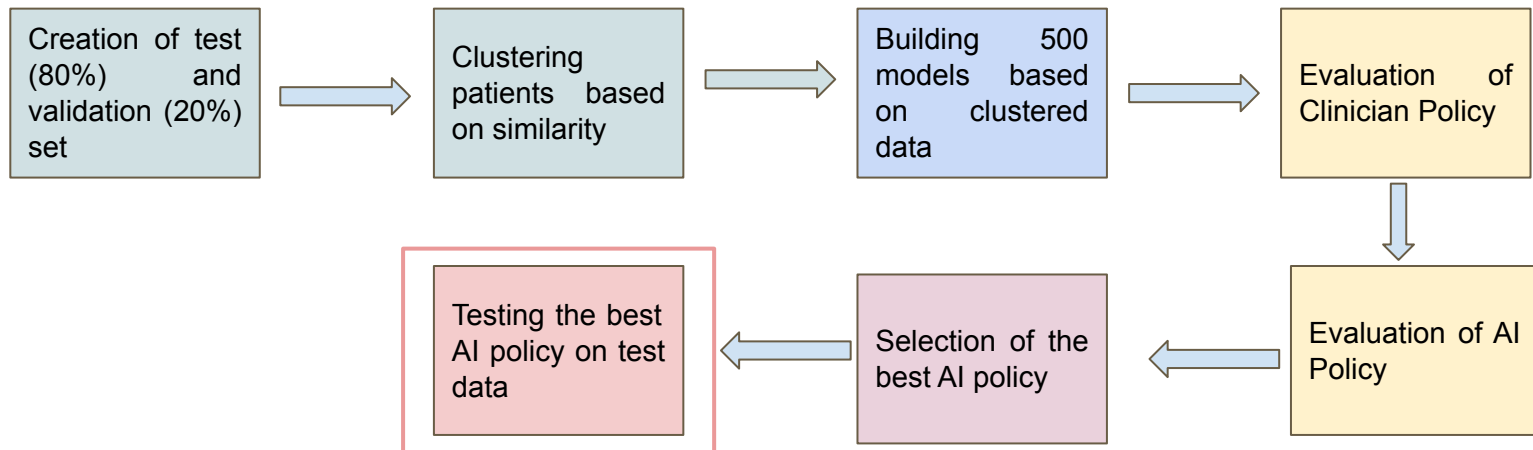


Bootstrap Sampling was used to identify true distribution in test set

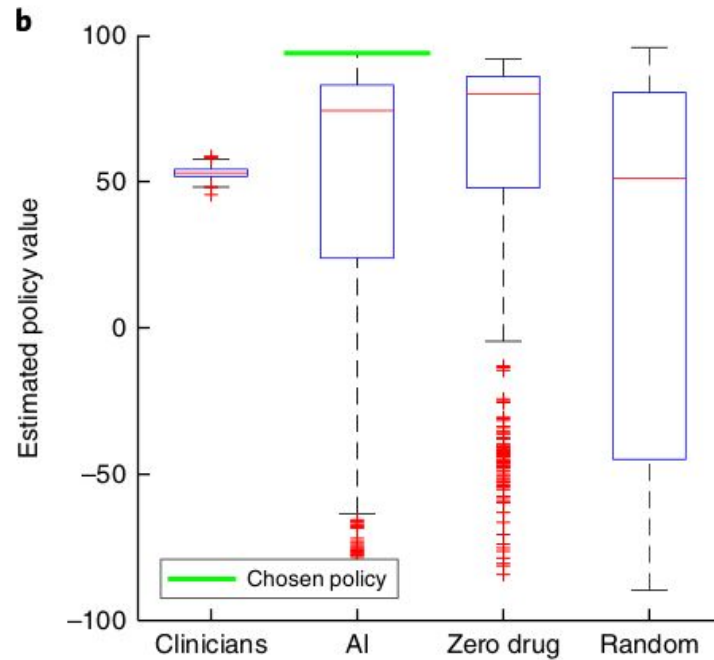
Modeling Stages



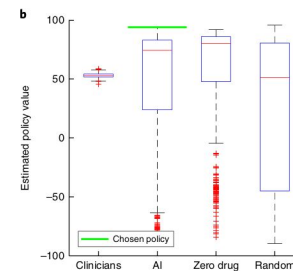
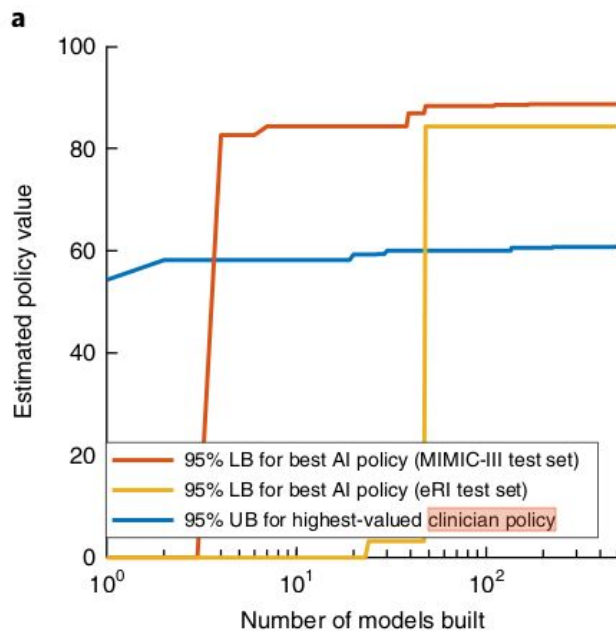
Modeling Stages



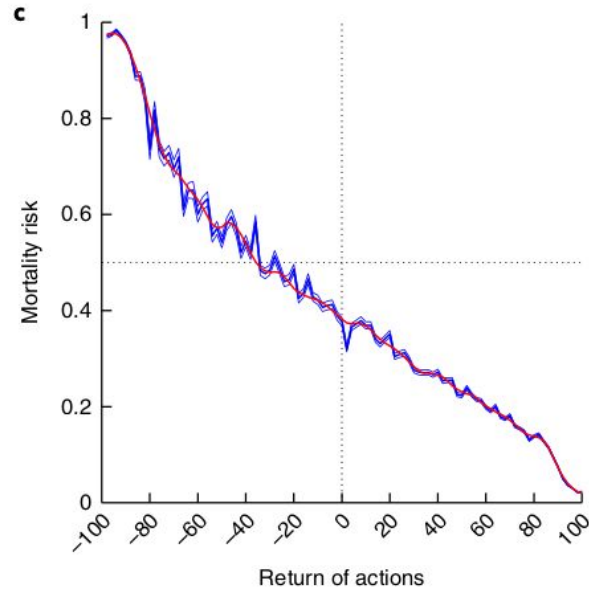
Best AI policy is better than clinician policy

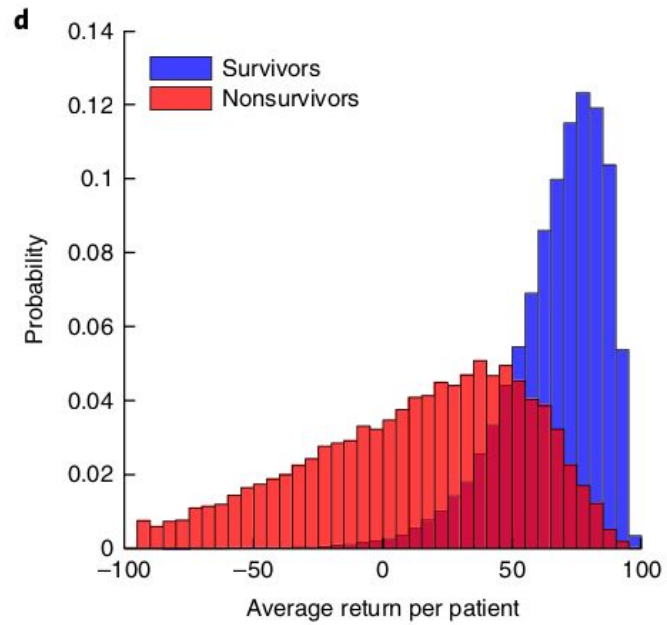


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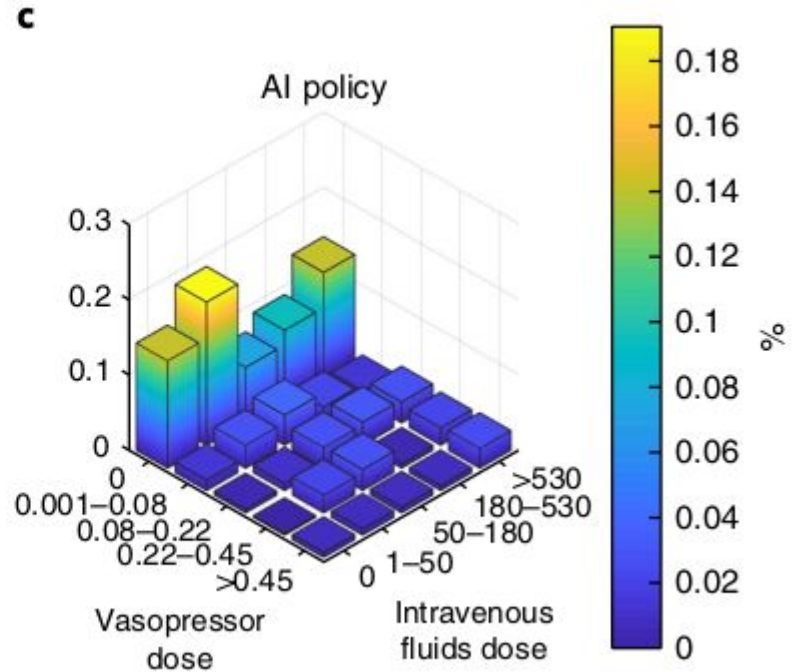
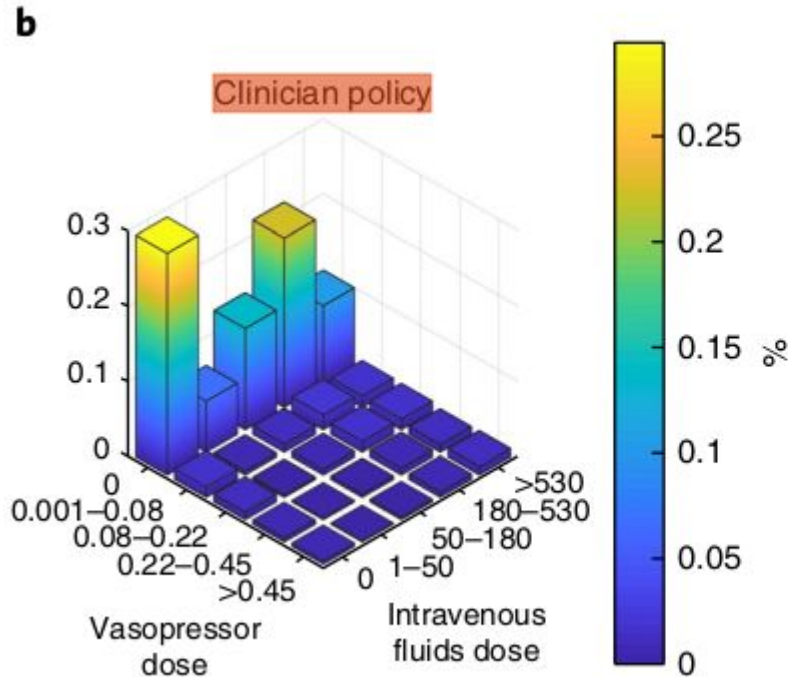


Mortality risk is inversely related to return of actions

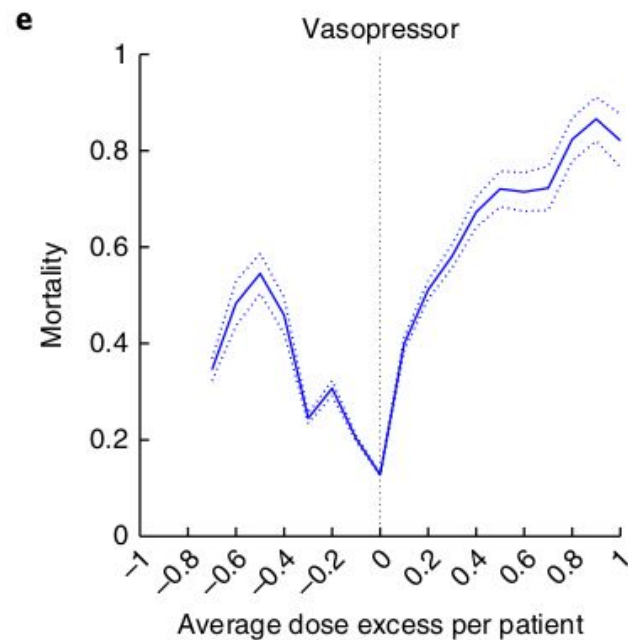
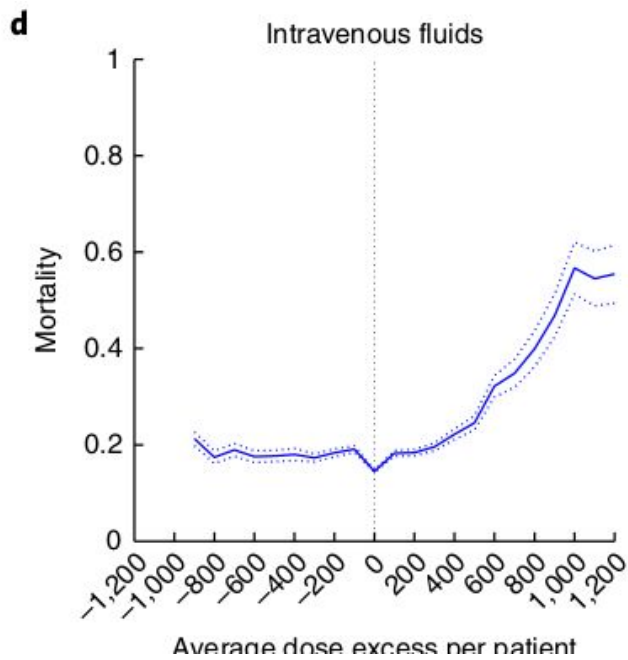




AI suggests low amount IV and high amount vasopressors



AI policy leads to low mortality rate



AI policy enabled personalized treatment for sepsis

Personalized model for treatment of sepsis.

Evaluation of AI and clinician policy.

Justification and interpretation of AI policy based on knowledge in medical science.