Clinical Reinforcement Learning

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6.S897 / HST.956 Machine Learning for Healthcare: Recitation 7

Housekeeping

1. Final projects
   - Start early
   - Reach out to professors and TAs if you need help
2. HW5 and HW6
   - Final stretch!
   - HW6 going out Thurs

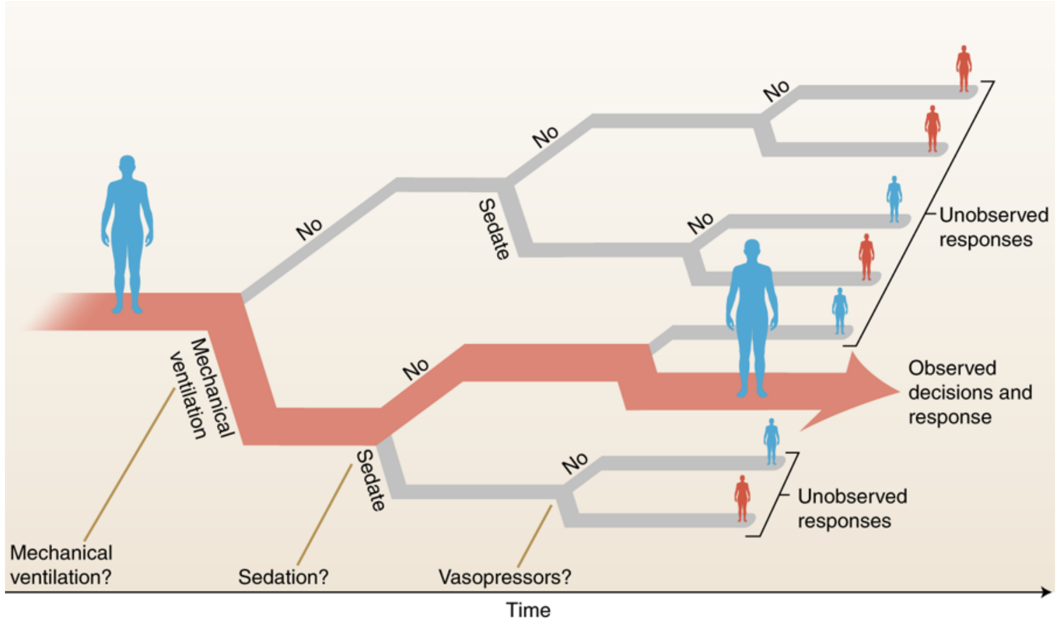
Agenda for today

1. ~~Housekeeping~~
2. Review lecture material [15 mins]
3. Smoking cessation two-stage example [15 mins]
4. Broader discussion [15 mins]

Goal: 1) contextualize RL lectures this week, 2) balance optimism and skepticism about RL in healthcare

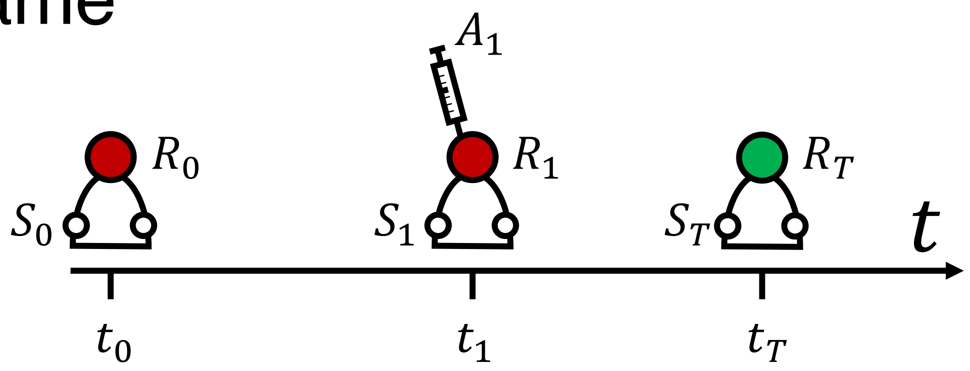
Why clinical reinforcement learning?

- Recent wins from AlphaGo, AlphaStar, and other video games
- Computational gains and methodological advances mean we can model more complex state and action spaces.
- With tools learned so far, we can only make static decisions.
- How can we make dynamic treatment policies?



Great! Now let's treat patients

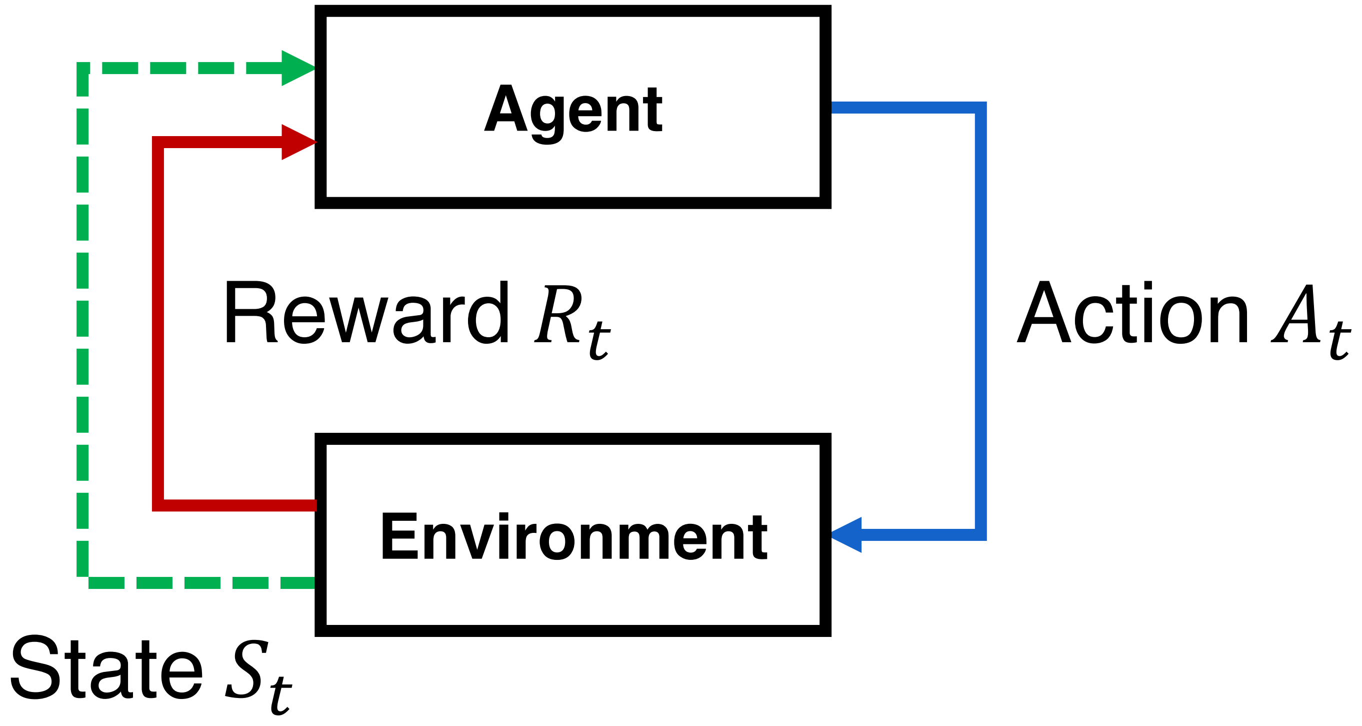
- Patient **state** at time S_t is like the game board
- Medical **treatments** A_t are like the actions
- **Outcomes** R_t are the rewards in the game
- What could **possibly** go wrong?



[Slide 14 of Lecture 16]

Decision processes

- An **agent** repeatedly, at times t takes **actions** A_t to receive **rewards** R_t from an **environment**, the **state** S_t of which is (partially) observed



[Slide 16 of Lecture 16]

	Model-based RL	**Value-based RL**	**Policy-based RL**
Want to learn			
Tools			
Useful for observational data?			
Relevant Lectures			

	Model-based RL	**Value-based RL**	**Policy-based RL**
Want to learn	Transitions $p(S_t \mid S_{t-1}, A_{t-1})$	Value/return $p(G_t \mid S_t, A_t)$	Policy $p(A_t \mid S_t)$
Tools			
Useful for observational data?			
Relevant Lectures			

	Model-based RL	**Value-based RL**	**Policy-based RL**
Want to learn	Transitions $p(S_t \mid S_{t-1}, A_{t-1})$	Value/return $p(G_t \mid S_t, A_t)$	Policy $p(A_t \mid S_t)$
Tools		Q-learning, G-estimation	
Useful for observational data?		Yes	
Relevant Lectures		Fredrik Johansson (L16)	

	Model-based RL	**Value-based RL**	**Policy-based RL**
Want to learn	Transitions $p(S_t \mid S_{t-1}, A_{t-1})$	Value/return $p(G_t \mid S_t, A_t)$	Policy $p(A_t \mid S_t)$
Tools	G-computation, MDP estimation	Q-learning, G-estimation	
Useful for observational data?	Yes	Yes	
Relevant Lectures	Barbra Dickerman (L17)	Fredrik Johansson (L16)	

	Model-based RL	**Value-based RL**	**Policy-based RL**
Want to learn	Transitions $p(S_t \mid S_{t-1}, A_{t-1})$	Value/return $p(G_t \mid S_t, A_t)$	Policy $p(A_t \mid S_t)$
Tools	G-computation, MDP estimation	Q-learning, G-estimation	REINFORCE, marginal structural models
Useful for observational data?	Yes	Yes	No
Relevant Lectures	Barbra Dickerman (L17)	Fredrik Johansson (L16)	AlphaGo on Netflix

Recap: Fredrik Johansson (Lecture 16)

- "Assign value to a state-action pair and maximize over time"
- Similar to covariate adjustment (from causal inference) with regression as a moving target
- Solve Bellman equations with dynamic programming

Recap: Barbra Dickerman (Lecture 17)

- “Simulate a weighted average of risks and then analyze”
- G-formula assesses a given policy based on observational data
- MC sampling to estimate risk over 10k population, bootstrap to get confidence intervals
- Sensitivity analysis for the confounder of serious medical condition

FAQs: Clinical Reinforcement Learning

- **Where does the deep learning come in?**
  - Anywhere we have a probability function, we can estimate the probability density
- **When should we use model-based vs value-based learning?**
  - Model-based when you can build simulator; value-based otherwise
- **Why can we beat the world's best player in Go but not solve a problem of when to use vassopressors for sepsis?**
  - Review lectures 16 and 17.
- **All of these papers and approaches have big limitations.**
  - Yes, yes they do. We make assumptions and then sensitivity analyses.

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Smoking Cessation: Two steps

Source

Story

FFarm

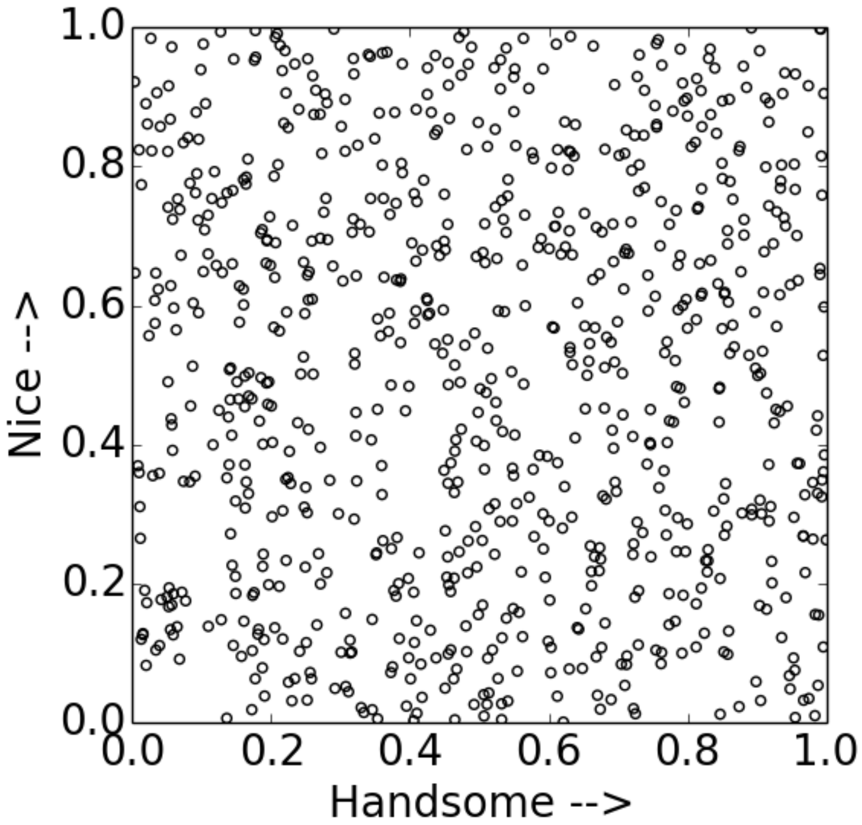
t1

t2

Motivation
Self efficacy
Education

[3.4.3 from Statistical Methods for Dynamic Treatment Regimes]

Interlude: Berkson's paradox

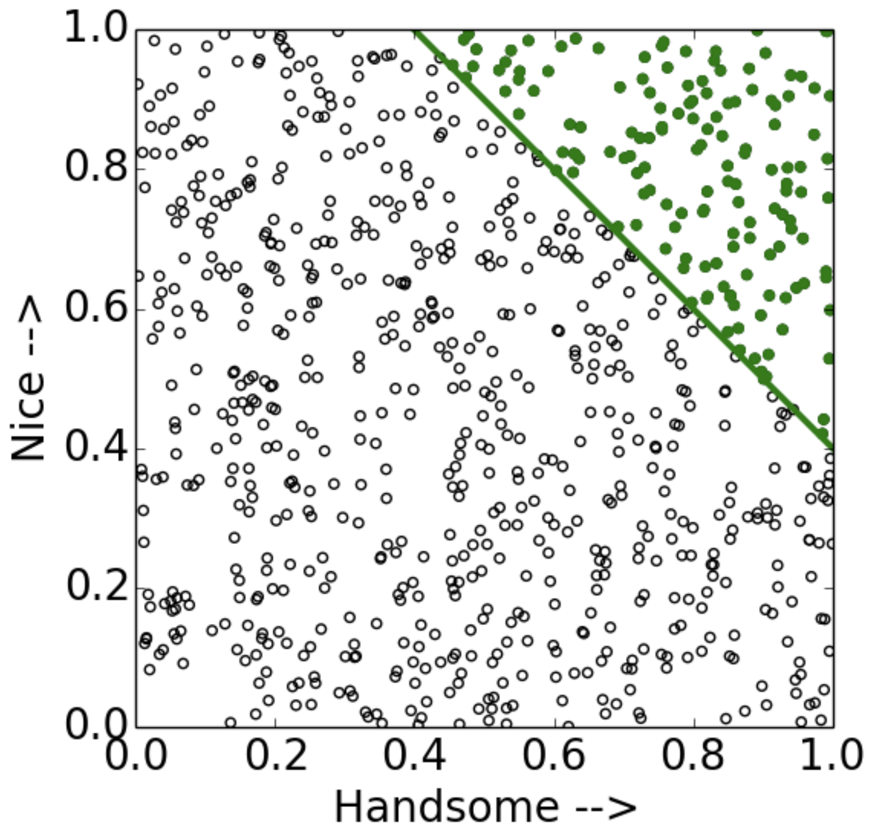


$P(A|B) = A$
$P(B|A) = B$

Q: Are handsome guys really jerks?

[corysimon.github.io]

Interlude: Berkson's paradox

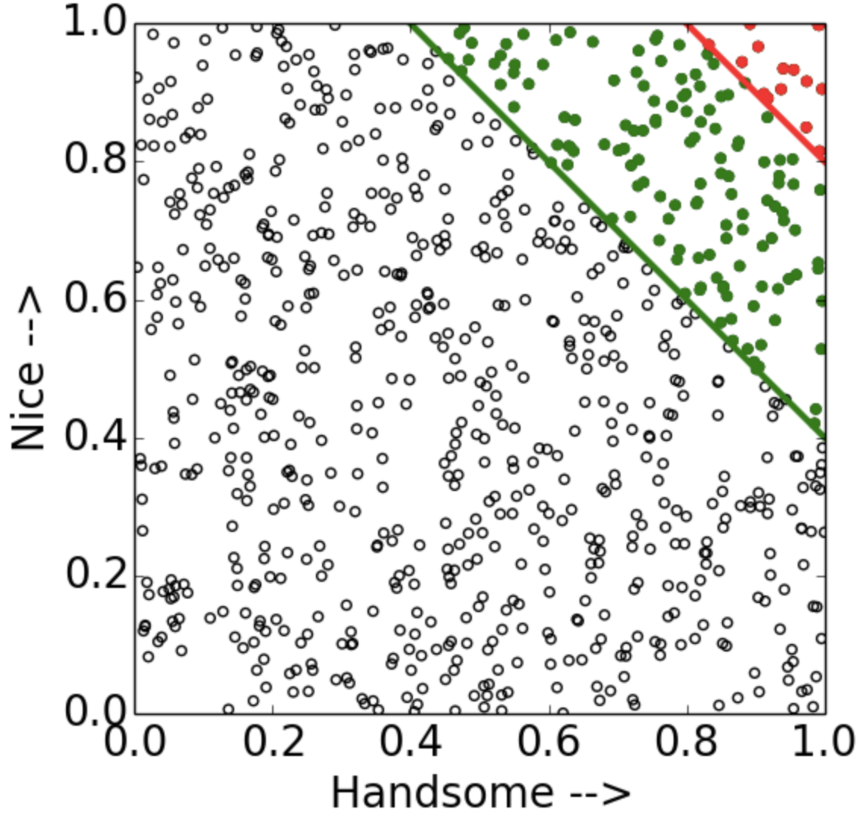


P(A|B, A or B) <
P(A|A or B)

Dating criterion is subset of field.

[corysimon.github.io]

Interlude: Berkson’s paradox



P(A|B, A or B) <
P(A|A or B)

Therefore, negative correlation in variables in subset despite uncorrelated overall.

[corysimon.github.io]

Back to Smoking Cessation

- Clearly naïve estimation at the end is wrong.
- How can we estimate the impact of the first stage of treatment?
- Assuming linear (with some interaction terms) models, how can set up a two-stage analysis?

Smoking Cessation: Two steps

- Actions:
  - A1: Source x Story
  - A2: FFarm
- Observed:
  - O1: motivation, self efficacy, education at t0
  - O2: quit status, reduction in avg cigarettes smoked, num months not smoked at t1
  - O3: same variables as O2 but at t2
- Outcome:
  - Y: quit status at the end of the study
  - PQ6Quitstatus: quit at stage 1
  - PQ6Quitstatus: quit at stage 2

[3.4.3 from Statistical Methods for Dynamic Treatment Regimes]

1. Fit stage 2 regression ($n = 281$) of `FF6Quitstatus` using the model:

$$\begin{aligned}\texttt{FF6Quitstatus} = \beta_{20} &+ \beta_{21} \times \texttt{motivation} + \beta_{22} \times \texttt{source} \\ &+ \beta_{23} \times \texttt{selfefficacy} + \beta_{24} \times \texttt{story} \\ &+ \beta_{25} \times \texttt{education} + \beta_{26} \times \texttt{PQ6Quitstatus} \\ &+ \beta_{27} \times \texttt{source} \times \texttt{selfefficacy} \\ &+ \beta_{28} \times \texttt{story} \times \texttt{education} \\ &+ \boxed{\left(\psi_{20} + \psi_{21} \times \texttt{PQ6Quitstatus}\right)} \times \texttt{FFarm} + \text{error}.\end{aligned}$$

Actions

Outcomes

[3.4.3 from Statistical Methods for Dynamic Treatment Regimes]

2. Construct the pseudo-outcome ($\hat{Y}_1$) for the stage 1 regression by plugging in the stage 2 estimates:

$$\hat{Y}_1 = \texttt{PQ6Quitstatus} + \hat{\beta}_{20} + \hat{\beta}_{21} \times \texttt{motivation} + \hat{\beta}_{22} \times \texttt{source} \\ + \hat{\beta}_{23} \times \texttt{selfefficacy} + \hat{\beta}_{24} \times \texttt{story} \\ + \hat{\beta}_{25} \times \texttt{education} + \hat{\beta}_{26} \times \texttt{PQ6Quitstatus} \\ + \hat{\beta}_{27} \times \texttt{source} \times \texttt{selfefficacy} + \hat{\beta}_{28} \times \texttt{story} \times \texttt{education} \\ + \boxed{\left|\hat{\psi}_{20} + \hat{\psi}_{21} \times \texttt{PQ6Quitstatus}\right|}.$$

[3.4.3 from Statistical Methods for Dynamic Treatment Regimes]

do so.

3. Fit stage 1 regression ($n = 1{,}401$) of the pseudo-outcome using a model of the form:

$$\begin{aligned}\hat{Y}_1 = \beta_{10} + \beta_{11} \times \texttt{motivation} + \beta_{12} \times \texttt{selfefficacy} + \beta_{13} \times \texttt{education} \\ + \left(\psi_{10}^{(1)} + \psi_{11}^{(1)} \times \texttt{selfefficacy}\right) \times \texttt{source} \\ + \left(\psi_{10}^{(2)} + \psi_{11}^{(2)} \times \texttt{education}\right) \times \texttt{story} + \texttt{error}.\end{aligned}$$

[3.4.3 from Statistical Methods for Dynamic Treatment Regimes]

Table 3.1 Regression coefficients and 95 % bootstrap confidence intervals at stage 1 (significant effects are in bold)

Variable	Coefficient	95 % CI
motivation	0.04	(–0.00, 0.08)
selfefficacy	**0.03**	(0.00, 0.06)
education	–0.01	(–0.07, 0.06)
source	–0.15	(–0.35, 0.06)
source × selfefficacy	**0.03**	(0.00, 0.06)
story	0.05	(–0.01, 0.11)
story × education	**–0.07**	(–0.13, –0.01)

[3.4.3 from Statistical Methods for Dynamic Treatment Regimes]

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Evaluating Reinforcement Learning Algorithms in Observational Health Settings

Omer Gottesman[1], Fredrik Johansson[2], Joshua Meier[1], Jack Dent[1], Donghun Lee[1], Srivatsan Srinivasan[1], Linying Zhang[3], Yi Ding[3], David Wihl[1], Xuefeng Peng[1], Jiayu Yao[1], Isaac Lage[1], Christopher Mosch[4], Li-wei H. Lehman[2], Matthieu Komorowski[5,6], Aldo Faisal[7], Leo Anthony Celi[5,8,9], David Sontag[2], and Finale Doshi-Velez[1]

[1]Paulson School of Engineering and Applied Sciences, Harvard University
[2]Institute for Medical Engineering and Science, MIT
[3]T.H. Chan School of Public Health, Harvard University
[4]Department of Statistics, Harvard University
[5]Laboratory for Computational Physiology, Harvard-MIT Health Sciences & Technology, MIT
[6]Department of Surgery and Cancer, Faculty of Medicine, Imperial College London
[7]Department of Bioengineering, Imperial College London
[8]Division of Pulmonary, Critical Care and Sleep Medicine, Beth Israel Deaconess Medical Center
[9]MIT Critical Data

https://arxiv.org/pdf/1805.12298.pdf

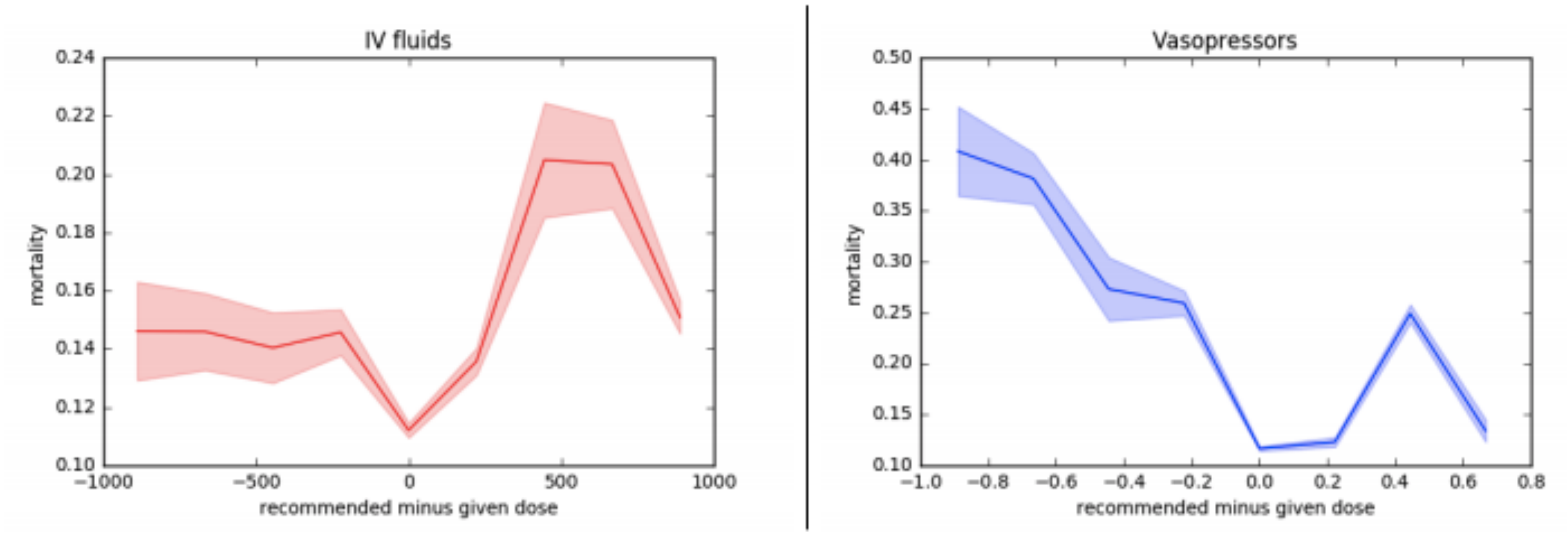
What is the correct representation?

- We want to include all confounders in patient history
- Large feature spaces may make reinforcement learning intractable, so how do we learn a succinct but comprehensive representation?
- Mini experiment:
  - K-means cluster into 100 or 200 “patient types”
  - Find optimal sepsis treatment based on patient type as covariate
  - Repeat 5 times with different clustering initializations
- When 100 types, agreement on optimal treatment was 26%; when 200 types, agreement was 14%

[Gottesman et al, 2018 Nature Medicine]

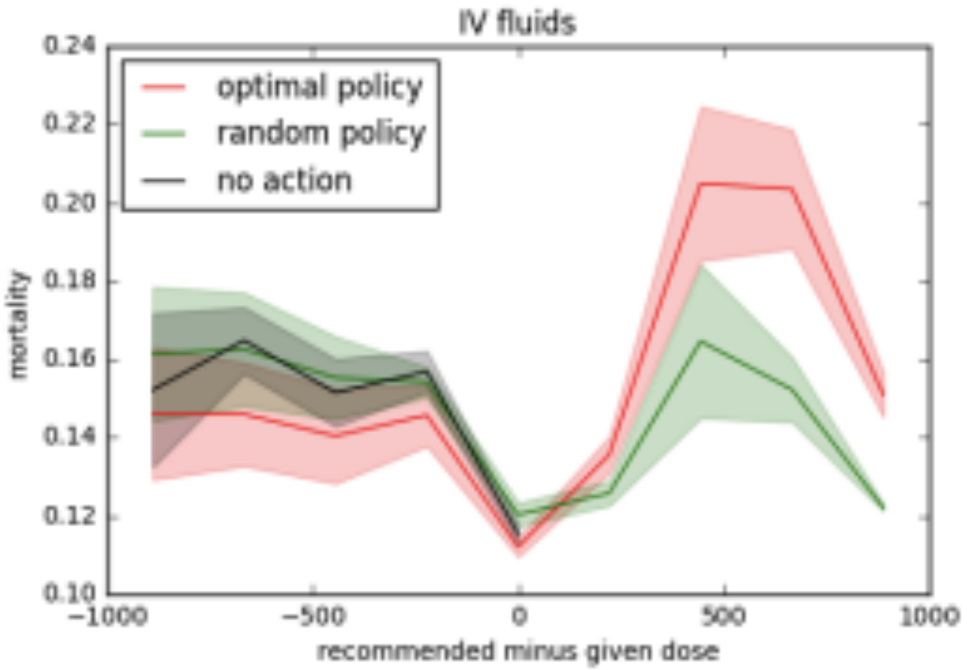
What about ad-hoc evaluation methods?

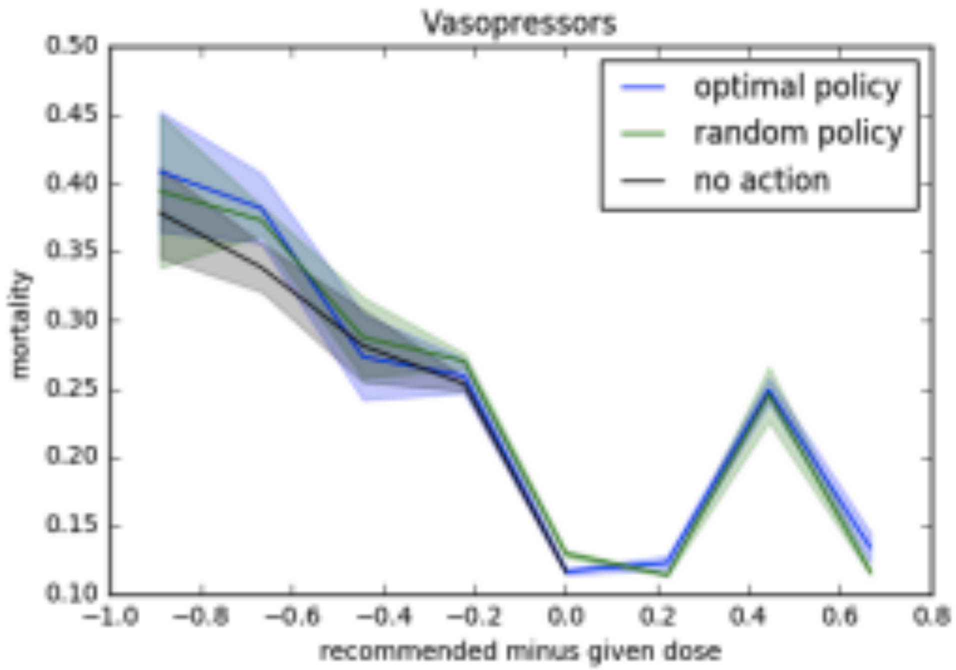
- U-curve evaluation: Difference between clinician policy and evaluation policy should be correlated with outcome like mortality



[Gottesman et al, 2018 Nature Medicine]

What about ad-hoc evaluation methods?





[Gottesman et al, 2018
Nature Medicine]

Other considerations and recommendations

- Design data collection and representations to make causal conclusions
- Limit yourself to actions and policies similar to physicians
- Be cognizant of effective sample size
- Clearly explain limitations

[Gottesman et al, 2018 Nature Medicine]

Takeaways: Clinical RL

- In theory, RL fits well into existing clinical workflow
- Model-based and value-based learning work well on observational healthcare data – with well defined actions and states
- Current bleeding edge research works through very few steps
- Design analysis to mimic clinician perspective and test sensitivity and robustness

Have a great weekend!