

# Relative Sparsity Real Data Preliminary Analysis

Anonymized

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## Authors, date

Anonymized

Date:

## [1] "2022-09-29"

## Project summary

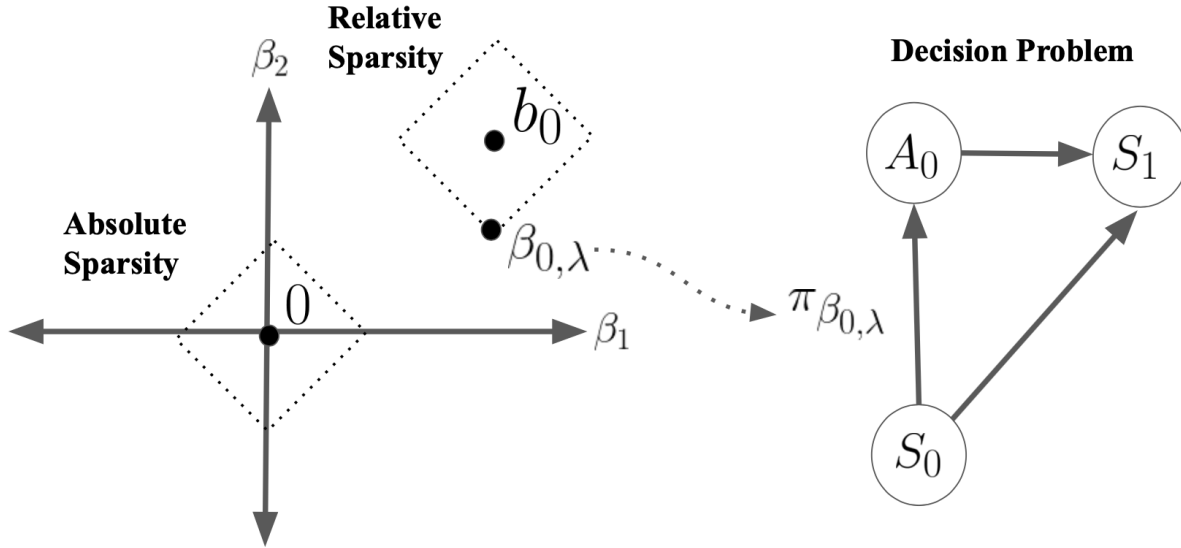


Figure 1: Summary of the methodology that we will be illustrating in this real data analysis.

This is a real data analysis to illustrate our relative sparsity objective function, which allows us to derive a new policy that, like policies derived from existing methods, improves outcomes, but unlike policies derived from existing methods, is easy to explain/justify in the context of the current standard of care.

## File summary

Filename: “mimic.prelim.analysis.Rmd” within the working directory

The file `mimic.prelim.analysis.Rmd` will start with the decision problem (since the covariates we choose are based on this decision problem), first doing a sort of unit test to make sure that all the data processing scripts were correct by looking at a patient in the raw data and then in the final episodes. Then, having confirmed that the decision problem is correct, we will look at state covariates and population level summaries.

## Supporting files

The dataset we analyze here was created by `data_clean.py` and `np_load.py`, which are in this same directory

The file `data_clean.py` is a heavily altered version of the code from Joe Futoma’s Github and the file `np_load.py` I wrote from scratch (it processes the output of `data_clean.py`). The file `data_clean.py` gets covariates, fills in missing covariates, handles outliers, standardizes vasopressors, and creates trajectories. Note that `data_clean.py` reads its input datasets from a folder called `query-data`, which is generated by bash scripts in Joe’s `extract-scripts` directory. These bash scripts process the raw MIMIC data (MIMIC website), and I did not alter them.

I keep `data_clean.py` and `np_load.py` in my base code directory (the directory in which `mimic.prelim.analysis.Rmd` is found), with the rest of my modeling code, so that when I commit git versions to this directory, these files are also committed.

## Unit test: Patient 201098

Because the `data_clean.py` and `np_load.py` files are quite long and based on pre-existing code, we must prove that all the code and changes we made to these files are correct (also, `data_clean.py` originally did not run at all without quite a few changes; ultimately, using this file helped me do something better than what I could have done myself, but I am not sure if in the future I might just write from scratch using Joe's code as a reference, rather than running it directly). To prove this in this document, our strategy will be to show some raw data for a patient from query-data, which is just the output of Joe's bash scripts after processing the raw MIMIC data (I assume Joe's bash scripts, which I didn't change, are correct - they mostly just look things up and reformat), and then to show the same patient here, in the data structure that will be used for modeling. I will just show MAP and vaso, assuming that if MAP is correct so are the other covariates, since covariates are processed similarly, and the major work goes into vaso. This patient is ID 201098.

### Raw data

Some of this patient's raw data is here.

	X	map	end_vaso	start_vaso	vasorate
7	2124-12-23 08:00:00.000	69	0.0000000	0.0000000	0.0000000
8	2124-12-23 08:15:00.000	58	0.0000000	0.0000000	0.0000000
9	2124-12-23 08:30:00.000	48	0.0000000	0.2251835	0.2251835
10	2124-12-23 08:43:59.700	NA	0.2251835	0.0000000	0.2251835
11	2124-12-23 08:44:00.000	NA	0.0000000	0.4507405	0.4507405
12	2124-12-23 08:45:00.000	53	0.0000000	0.0000000	0.0000000
13	2124-12-23 08:56:59.700	NA	0.4507405	0.0000000	0.4507405
14	2124-12-23 08:57:00.000	NA	0.0000000	1.8090946	1.8090946

We see that the patient had a pretty low mean arterial pressure (MAP) of 58 at 8:30 am. They entered the cohort because  $\text{MAP}=58 < 60$  (we condition on hypotension, so our model will only be valid if someone is hypotensive).<sup>1</sup>

I will now describe what happens, but feel free also to refer to the diagram below, which might be quicker to read.

Over the next 15 minutes, from 8:30 to 8:45, the patient's MAP dropped to 48, and vasos were initiated. Then over the next 15 minutes (8:30-8:45), with vasos being administered, their blood pressure increased to 53. Hence, our single stage decision will use the covariates at the end of the first 15 minutes state as the  $S_0$ , so  $S_0 = 48$ . The action taken will be  $A_0 = 1$ , since vasos were given during the second 15 minutes from 8:30 to 8:45, and the final state will be the MAP we see at 8:45, which will be  $S_1 = 53$ . Since we define  $R(S_0, A_0, S_1) = S_1$ , we will have a reward therefore of 53. So, in this case, it looks like the vasos helped increase this patient's mean arterial pressure, although the effect is not too big.

Note that the states are point measurements at the end of each 15 minute period, but the actions correspond whether vasos were given or not over a 15 minute period. Note again that actions are dichotomized; Joe originally gets continuous actions, then he categorizes, then I further dichotomize.<sup>2</sup>

We do vasos during a 15 minute period just because they are given as a continuous infusion, they act very quickly, and they wear off quickly.<sup>3</sup> Finally, this is not shown in the figure, but the reward is the MAP at the next time step.

---

<sup>1</sup>We begin the trajectory 0.4 minutes after this low MAP (there are a lot of measurements before 8:30, and Joe's code adds all of those earlier ones before the trajectory, so I added a buffer of 0.4 to "catch" those, and thus we start "approximately" at the onset of hypotension).

<sup>2</sup>We are also discretizing time. It could be an interesting future direction to have continuous actions and continuous time.

<sup>3</sup>So, it is better to sort of look over a time span than to try to exactly capture the peak effect - it is possible there is a subproblem with states that are very short in duration that has even more signal than what we look at.

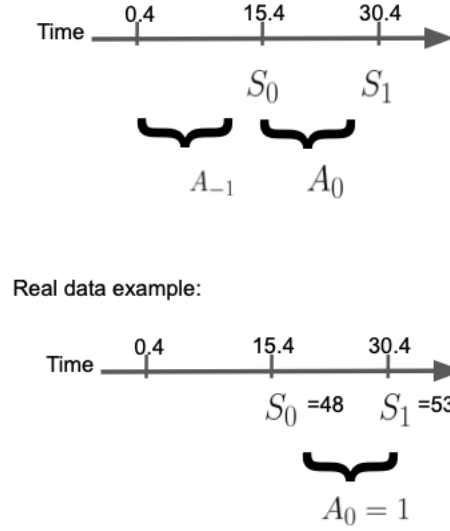


Figure 2: Arbitrary and real trajectory (patient 201098).

Now, between the raw data I showed above and the data we use to perform the real data analysis for the paper, there is `data_clean.py`, `np_load.py`, and some parts of the `mimic.R` file, which has been converted into this preliminary analysis file. I want to just show that the real data above is processed into an “episode” here in this script - a tuple  $(S_0, A_0, S_1)$  that aligns with the real data we saw above for patient 201098.

### Expected trajectory after all the processing

Here is what we we will want to see. This corresponds to the raw data above. Note that I have set things up so that the decision problem we want starts at index 3 and gives us the decision for time 15 to 30. Recall that we define reward  $R(S_0, A_0, S_1) = S_1$ , so it’s the blood pressure at the next step.

Index	1	2	3	4	
T(min)	.4	15.4	30.4	45.4	(it's time of action, reward)
Act	1	1	a_0=1	1	
S	58	58	s_0=48	53	(states are one step behind)
map	58	48	s_1=53	67	
R	58	48	53	67	(One ahead of S. Time corresponds to Time above)

### Trajectory we see after all the processing

I will now build the table above directly from the data we have available here, which passed through `data_clean.py`, `np_load.py`, and the first part of this file.

time(min)	0.4	15.4	30.4	45.4
states	58	58	48	53
actions	1	1	1	1
rewards	58	48	53	67

It looks like this matches expectations.

## Population level statistics

Now that we have strengthened our confidence in the pre-processing, let's look at some population level statistics. `## Percentage vaso per time` Let's look at percentage vaso per stage. We are interested in the action that ends at 30, which will be the third column.

```
##           X0           X1           X2           X3
## times      0.4000000 15.4000000 30.4000000 45.4000000
## percentVaso 0.1270414 0.1415535 0.1503823 0.1566752
```

## Vaso trajectories from time 0-15 and 15-30.

Let's look at how vasos were prescribed over time, ie, the vasos in intervals 0-15 and 15-30:

```
##           0 0           0 1           0 NA           1 0           1 1
## "3990 (84.62%)"      "52 (1.1%)"      "3 (0.06%)"      "10 (0.21%)"      "656 (13.91%)"
##           1 NA           NA NA
##      "1 (0.02%)"      "3 (0.06%)"
```

It's interesting that so many people start on vasos trajectory (1,1) in the first 15. I guess if they have a blood pressure measurement of 60, they're in high suspicion to be on vasos quickly.

## Dropout

We see that some of the people have no second action, it's NA, ostensibly because they leave. We check that no patients have no first action, and we write the number we exclude based on dropout below.

```
## [1] "% without first (why would these occur)"
## [1] 0
## [1] "excluding n = 7"
## [1] "subsetting by first map zero"
```

It is a small number who dropout in the first 30 minutes. Possibly if they have already survived long enough to have a hypotensive episode, they are robust.

## Initial state covariates, $S_0$ (confounders, on which we will base our decision of how to draw $A_0$ )

Recall that  $A_0|s_0 \sim \text{Bern}(\text{expit}(\beta^T s_0))$ . We will show the 9 covariates in  $s_0$ , which we chose because they were the covariates in Futoma 2020, and Futoma 2020 mentioned that they had consult from a critical care doctor and had Leo Celi, MD, in the acknowledgements.

Here is a diagram from (<https://www.cvphysiology.com/Blood%20Pressure/BP030>), which is not an official source, but I think it is a good overview.

Here are the covariates and descriptions.

```
##      renamed.cov.of.int descr
## [1,] "MAP"                "Mean Arterial Pressure (1/3 systolic+ 2/3 systolic)"
## [2,] "HR"                 "Heart rate (beats per minute)"
## [3,] "urine"              "Urine output (unit?)"
## [4,] "lactate"            "Lactate (increases if hypotensive)"
## [5,] "GCS"               "Glasgow Coma Score (3 worst, 15 best)"
```

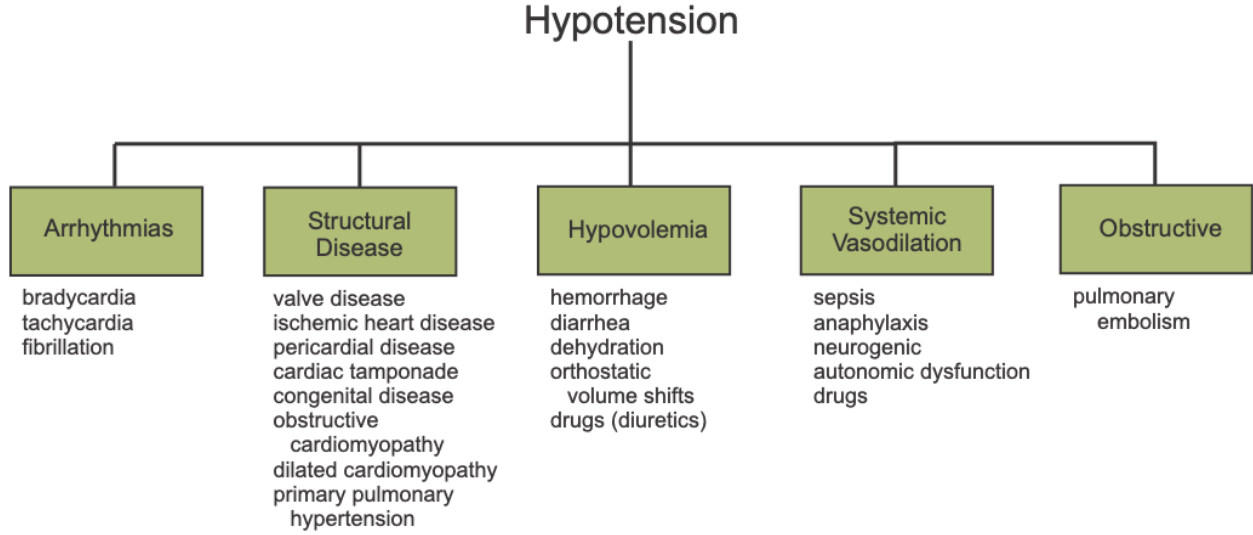


Figure 3: Hypotension etiology.

```

## [6,] "creatinine"      "Creatinine (increases if kidney damage)"
## [7,] "Fio2"           "Fraction inspired oxygen (decreases if hypo?)"
## [8,] "bilirubin"      "Bilirubin (liver)"
## [9,] "platelets"      "platelets (clotting)"

```

## Adjusting for past vasopressors

Note that past vasos are not included in this list. One could argue that there is an arrow from past to future vasopressors.

Note that if we define the action taken before  $A_0$  to be  $A_{-1}$ , then we do not adjust for  $A_{-1}$  in the behavioral policy as a confounder, because, by the standard MDP assumptions, the transition probability  $S_1|A_0, S_0$  depends only on  $A_0, S_0$ . In other words, the standard MDP assumptions consider  $S_0$  a sufficient summary of  $A_{-1}$ . We think this assumption is reasonable because the duration of action of norepinephrine is so short, which we discuss in the manuscript.

## Proportion vaso vs average reward

Marginal summary of proportion patients given vasos vs average reward (this not so relevant for single stage). Recall that we define reward  $R(S_0, A_0, S_1) = S_1$ , so it's the blood pressure at the next step.

Blue=conditioned. If we need to condition on it, we need to include it in the behavioral policy

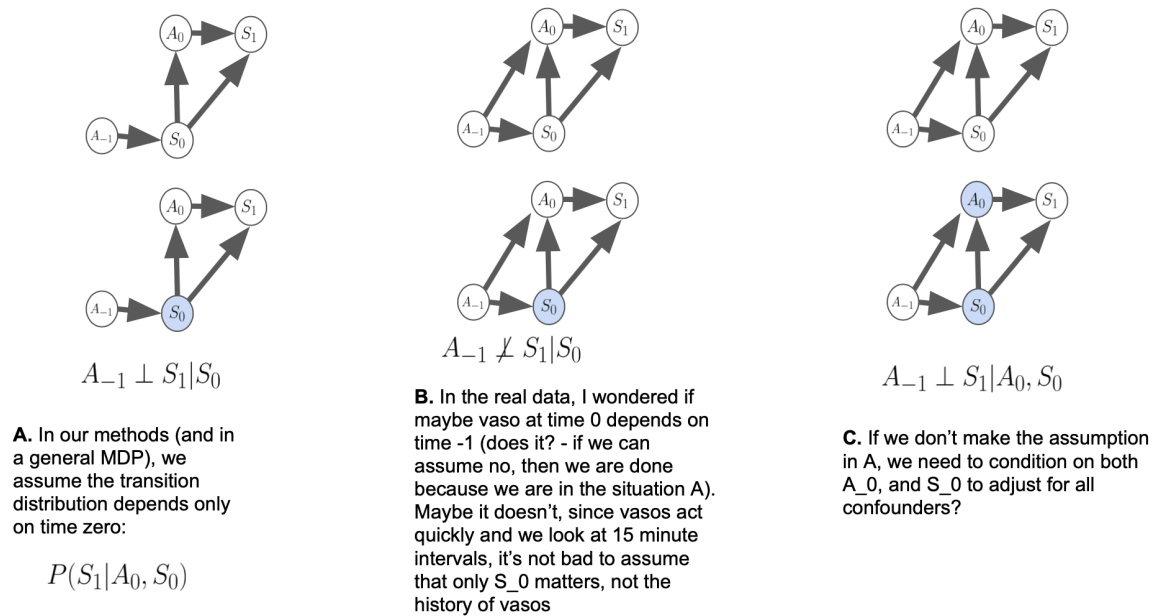
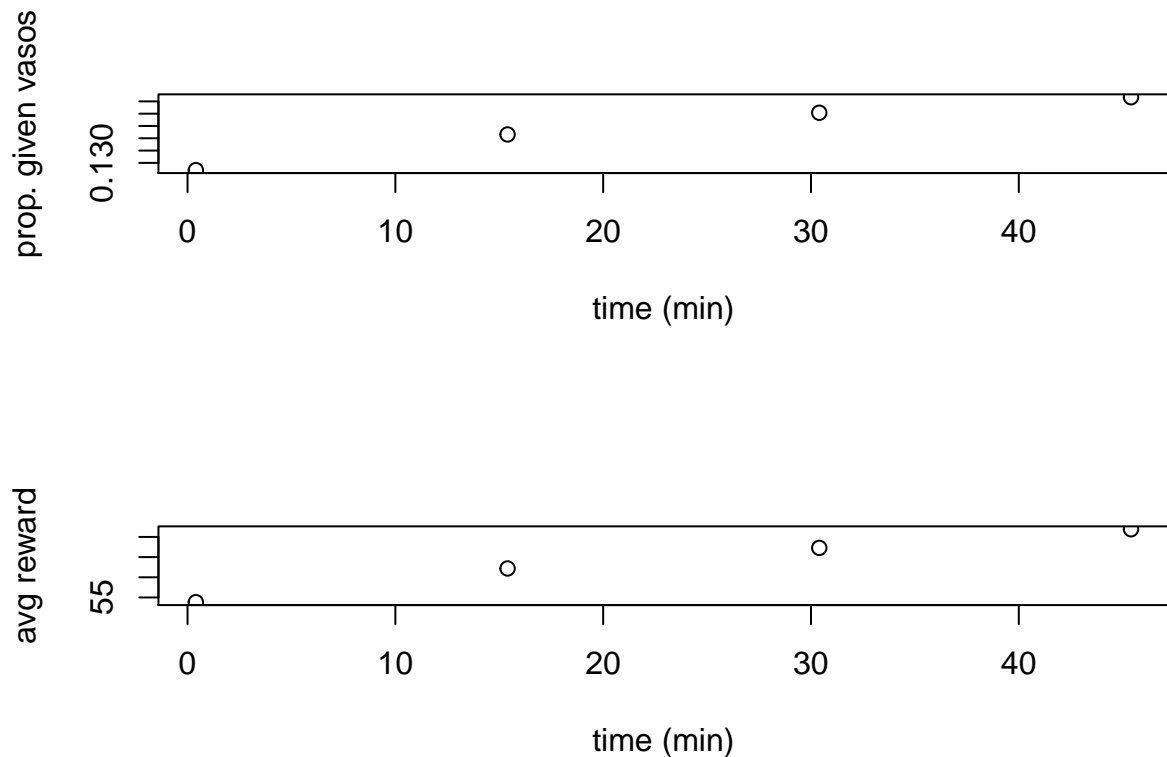


Figure 4: On past vasopressors



see that reward increases with increasing vasos.

We

## State covariates

Look at some  $S_0$  data

##	map	hr	urine	lactate	GCS	creatinine	fio2	bilirubin_total	platelets
## [1,]	49	82	80	1.0	15	1.0	21	0.9	208
## [2,]	59	106	35	1.4	10	0.8	70	0.7	152
## [3,]	52	109	80	1.0	9	0.8	100	1.1	196
## [4,]	59	60	150	1.3	15	1.5	21	0.9	174
## [5,]	59	72	75	1.3	10	0.7	50	0.9	184
## [6,]	58	100	40	0.8	15	0.7	100	0.4	339

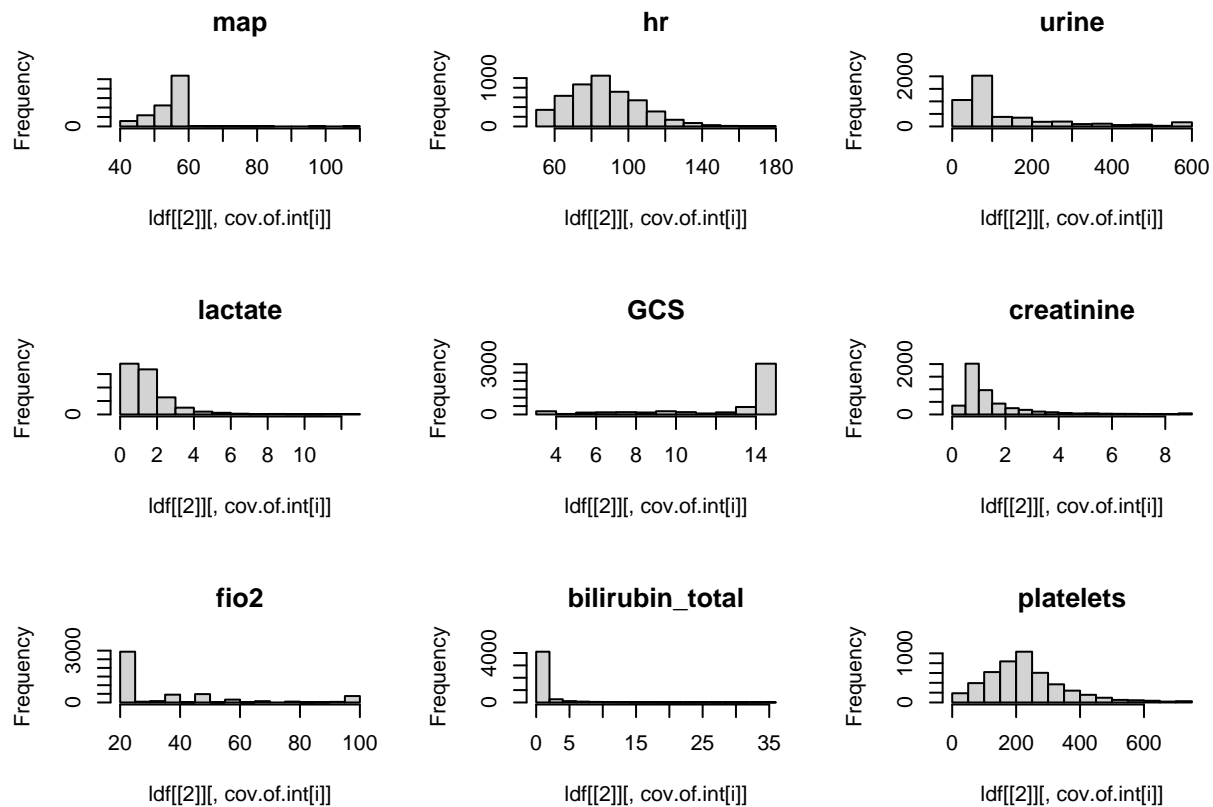
## Univariate

Summary table

These data look relatively good because Joe preprocessed them. His rules are very complex and tailored to each variable, likely done in consult with critical care experts.

Histograms

We can look at some of the raw, unscaled data.



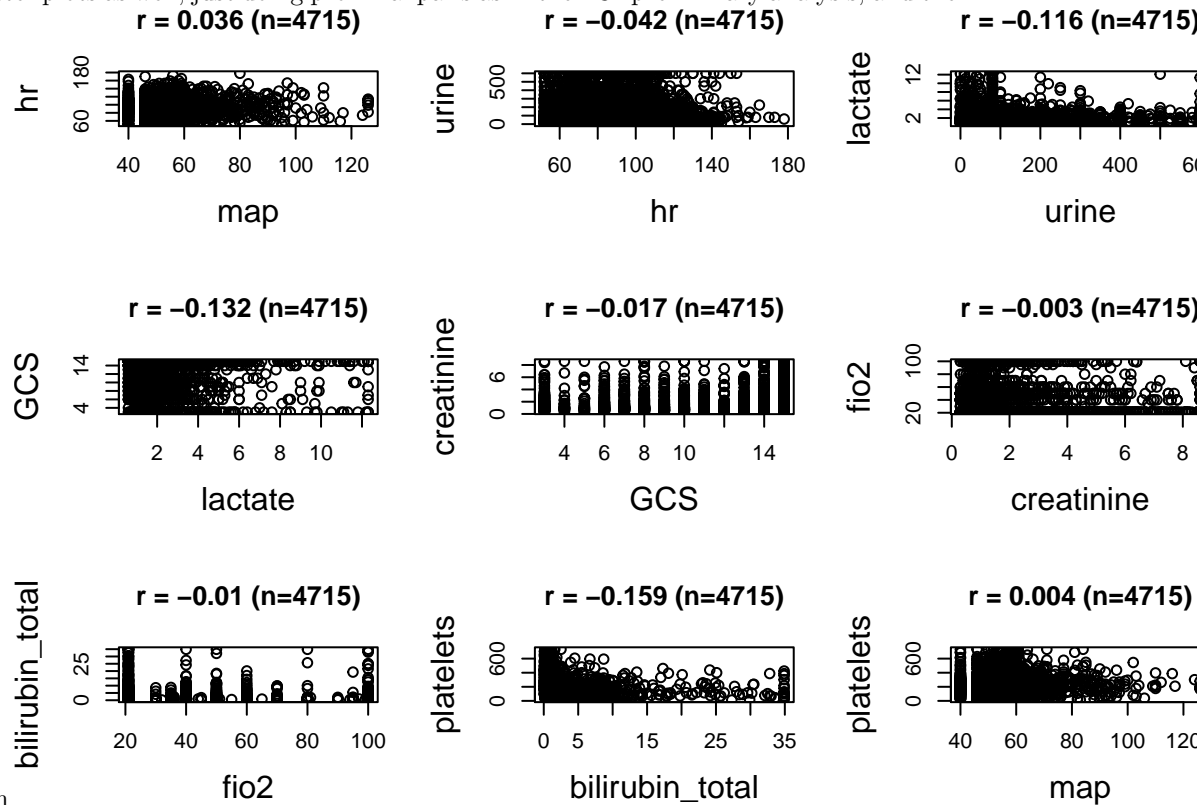
Things are often skewed.

## Bivariate

Scatter



We can plot some scatter plots as well, just doing proximal pairs as in the T32 preliminary analysis, and then in-

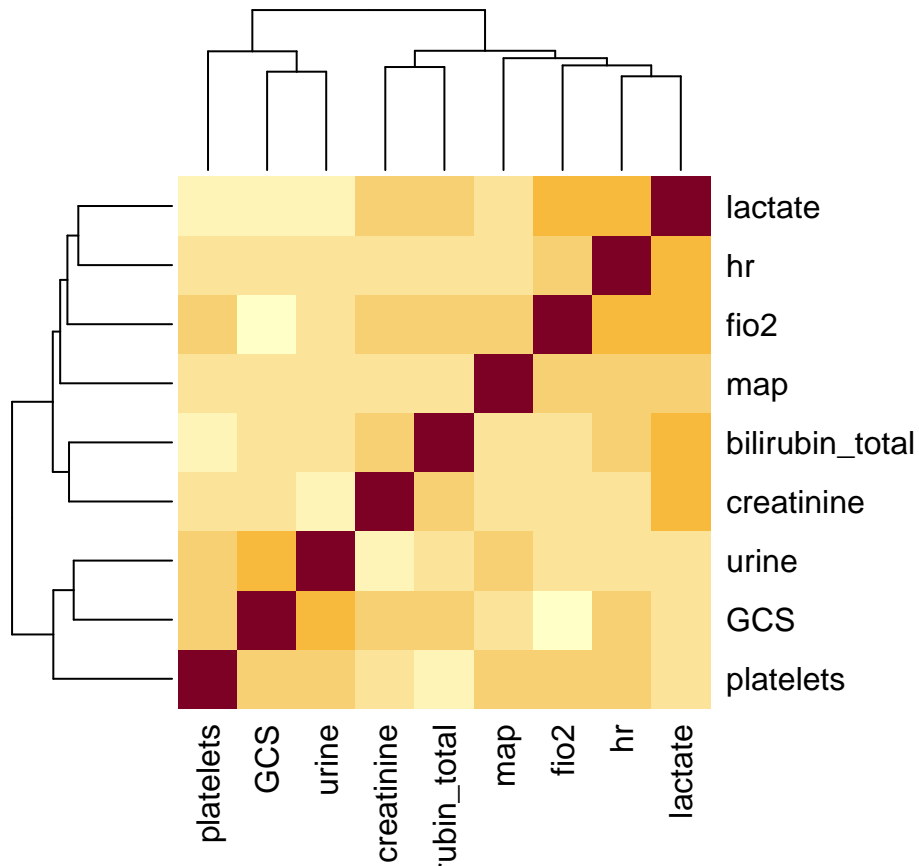


cluding the correlation

Joe deals with outliers in his scripts (I did not change any of those parts), so we see that the data spread is pretty good. There are substantial data quality issues with EHR data. However ICU data, and in particular the lab values, are usually the best data.

We can show correlations. The heatmap is easier to see maybe, but I include numbers also

Correlation

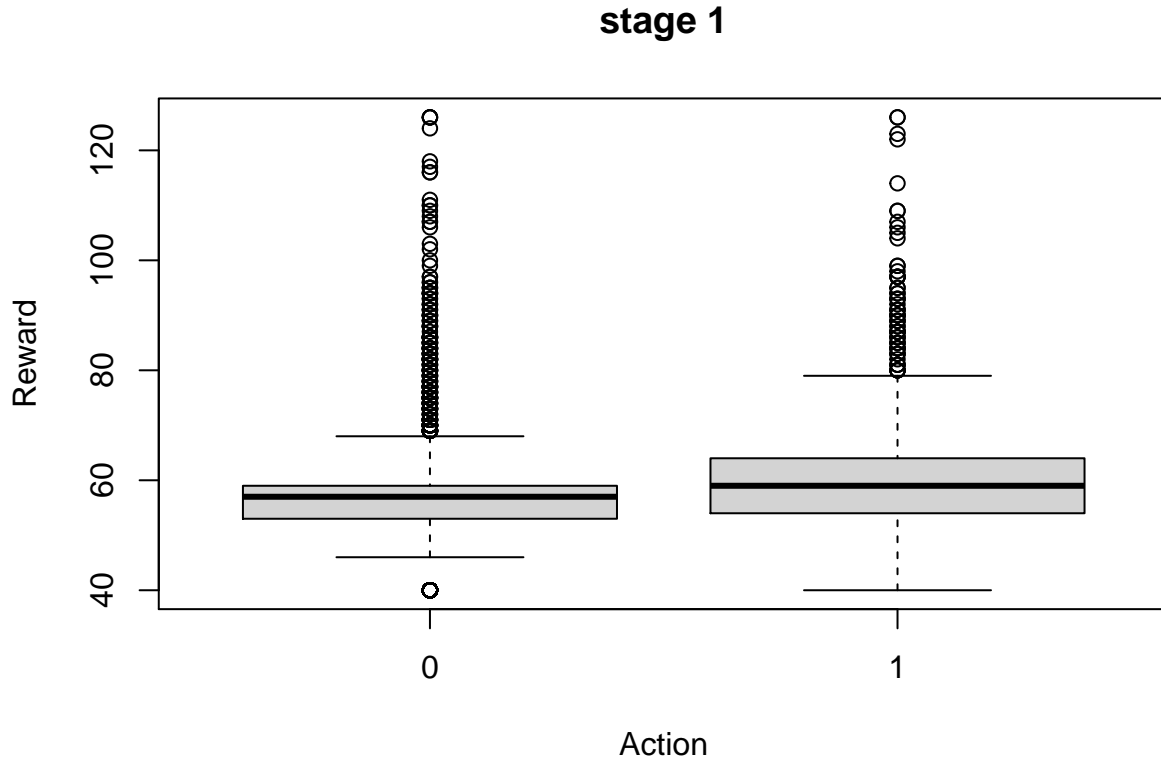


	map	hr	urine	lactate	GCS	creatinine	fio2	bilirubin_total	platelets
map	1.00	0.04	-0.01	0.03	-0.07	-0.01	0.08	0.01	0.00
hr	0.04	1.00	-0.04	0.19	-0.02	-0.03	0.11	0.04	0.02
urine	-0.01	-0.04	1.00	-0.12	0.16	-0.17	-0.11	-0.06	0.01
lactate	0.03	0.19	-0.12	1.00	-0.13	0.14	0.17	0.15	-0.09
GCS	-0.07	-0.02	0.16	-0.13	1.00	-0.02	-0.38	0.00	0.00
creatinine	-0.01	-0.03	-0.17	0.14	-0.02	1.00	0.00	0.09	-0.08
fio2	0.08	0.11	-0.11	0.17	-0.38	0.00	1.00	-0.01	0.02
bilirubin_total	0.01	0.04	-0.06	0.15	0.00	0.09	-0.01	1.00	-0.16
platelets	0.00	0.02	0.01	-0.09	0.00	-0.08	0.02	-0.16	1.00

## Average reward vs vaso

We can look at a boxplot of the average reward given vaso or not.

```
## [1] "subsetting by first map zero"
```



## Revisiting Patient 201098 in the episode data structure for a single stage decision

Here is just the single stage data not in the episode data structure, but after all `data_clean.py`, etc

	x
reward (s_1)	53.00
action (a_0)	1.00
time	0.51
state (s_0).map	48.00

Here is the data in the episode data structure

Behind the scenes here, we create a multistage data object taht can be read directly by the optimization routines, etc. We will show the single stage data in this format. Note that MAP is the first covariate.

```
## $Ss
##      [,1]
## [1,] 48.0
## [2,] 69.0
## [3,] 600.0
## [4,]  1.0
## [5,] 15.0
## [6,]  1.7
## [7,] 100.0
## [8,]  0.7
## [9,] 206.0
##
## $As
```

```
## [1] 1
##
## $Rs
## [1] 53
```

## Behavioral policy (overlap, positivity)

Technically, we are “modeling” when we do the behavioral policy fitting, but it is sort of a preliminary step to the modeling we do later, so I include it here.

Recall that our estimator for  $V_n$  is

$$V_n(\beta, b_n) = \frac{1}{n} \sum_{i=1}^n \frac{\pi_\beta(A_{i,0} = a_{i,0} | S_{i,0} = s_{i,0})}{\pi_{b_n}(A_{i,0} = a_{i,0} | S_{i,0} = s_{i,0})} R(S_{i,0}, A_{i,0}, S_{i,1}). \quad (1)$$

We therefore need to estimate  $\pi_{b_n}(A_0 = 1 | S_0 = s_0)$ , which we do with logistic regression. It is important that  $\pi_{b_n}(A_{i,0} = a_{i,0} | S_{i,0} = s_{i,0})$  not equal zero for any  $i$ , since it is in the denominator, so we check this.

Note that often when we estimate for example the “effect” of treatment  $A_0$ , we are considering the relationship between the action  $A_0$  and the outcome, blood pressure, adjusting for confounders in  $S_0$ , and a linear model might be

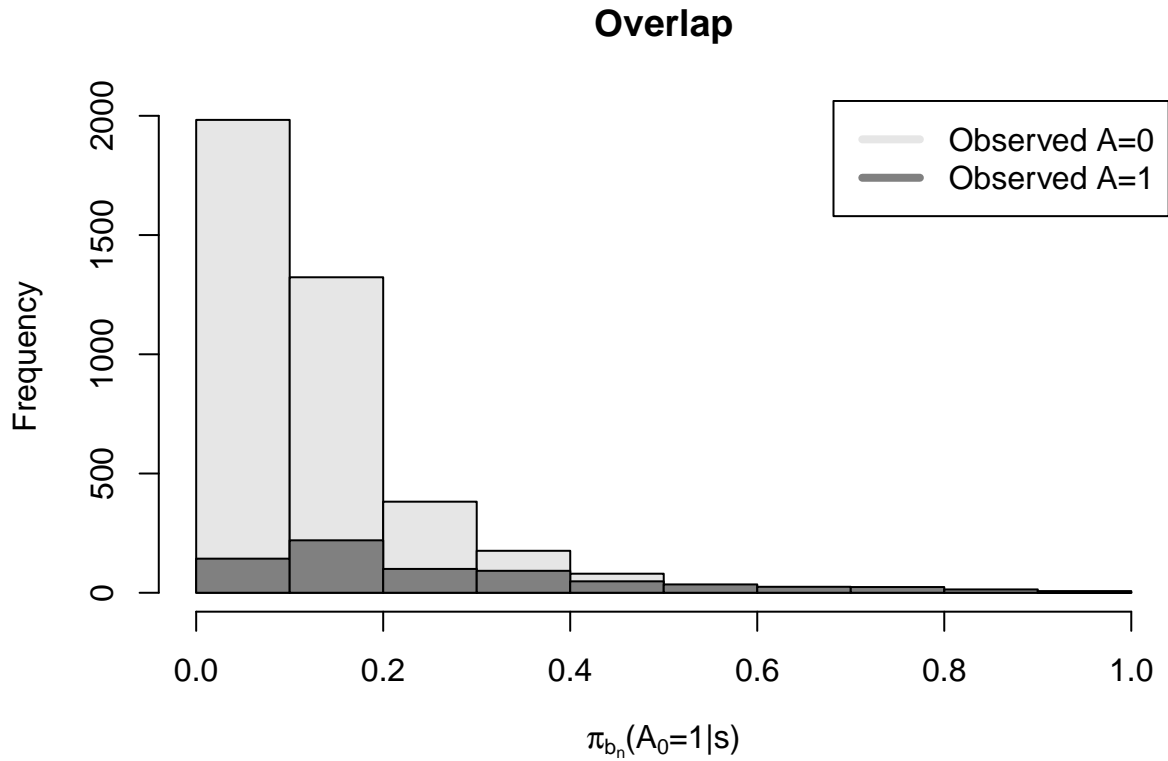
$$(S_{i,1})_2 = \tau A_{i,0} + \beta S_{i,0} + \epsilon_i, \quad (2)$$

where  $\tau$  is a treatment effect and  $\beta$  is the confounder main effect. Here, as in the literature on statistical decision analysis, we will instead be interested in obtaining a policy  $\pi(A_0 | S_0)$ , which will tell us how to draw a treatment given the initial state. This is the problem the provider and patient must solve at the point of care. The linear model in Equation (2) will actually be considered a part of the “environment,” which is encoded in the transition probability. In the case of  $R(S_0, A_0, S_1) = (S_1)_2$ , it turns out that what we traditionally consider to be the “outcome” and the reward are the same, but this need not be the case; the reward can be any function of  $S_0$ ,  $A_0$ , and  $S_1$ .

Note that the inverse probability (IPTW) estimator for the effect is

$$IPTW = E(R(1)) - E(R(0)) \approx \frac{1}{n} \sum_{i=1}^n \frac{R_i A_i}{\pi_{b_n}(A_i | S_i)} - \frac{1}{n} \sum_{i=1}^n \frac{R_i (1 - A_i)}{\pi_{b_n}(A_i | S_i)}$$

## Treatment effect, overlap, summary statistics



	tb
n	4708
Prop. R<0	0
Prop A=1	0.15
min $\pi_b$	0.016
mean $\pi_b$	0.5
max $\pi_b$	0.984
IPTW treat. eff.	3.155
Par. treat. eff (p-val)	1.953 (0)

In summary, we have a sample size of 4708, a single stage decision ( $T=1$ ), an action proportion of 0.15 - not bad exploration, adequate overlap, a minimum  $\pi_b(a_{i,0}|s_{i,0})$  that is above 0 (note that this is taken over all  $a_{i,0}$  and  $s_{i,0}$ ) a strong positive treatment effect (vasos increase blood pressure) both with a IPTW (nonparametric) and parametric outcome model.

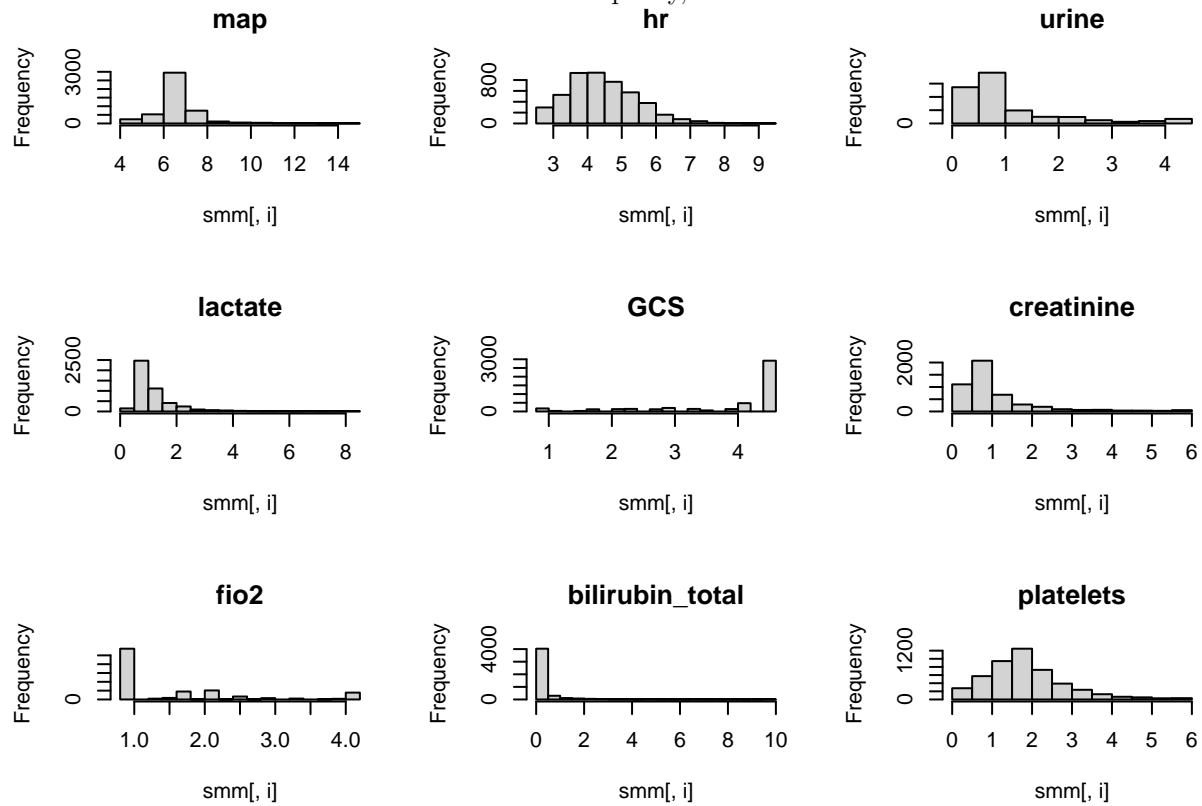
## Behavioral policy coefficients

We conclude with the coefficients of the behavioral policy. I was not sure how to best check linearity for a GLM, and I am afraid to do so, because I think it is unlikely it holds (although it may hold well enough).

	Estimate	Std. Error	z value	Pr(> z )
smmmap	-0.0751431	0.0297774	-2.5234936	0.0116195
smmhr	0.0191173	0.0396304	0.4823899	0.6295290
smmurine	-0.3566294	0.0604768	-5.8969607	0.0000000
smmlactate	0.3784541	0.0384234	9.8495846	0.0000000
smmGCS	-0.4865298	0.0353917	-13.7470036	0.0000000
smmcreatinine	0.1586937	0.0385681	4.1146390	0.0000388
smmfio2	0.1806741	0.0415440	4.3489849	0.0000137
smmbilirubin_total	-0.0168750	0.0411583	-0.4100036	0.6818033
smmplatelets	-0.0964085	0.0440263	-2.1897924	0.0285393

## Scaled covariates

We will also plot histograms of the scaled covariates, just to show that scaled covariates are large, so the coefficients are small in the behavioral policy, but this is because the covariates are large



```
## [1] 10
```