

# CSC 2541: Machine Learning for Healthcare

## Lecture 2: Supervised Learning for Classification, Risk Scores and Survival

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Vector Institute



# Course Reminders!

- Submit the weekly reflection questions to MarkUs!
- Start the homework early (e.g., last week)!
- Sign up for a [paper presentation slot!](#)
- Think about your projects!

# Logistics

- Course website:  
<https://cs2541-ml4h2020.github.io>
- Piazza:  
<https://piazza.com/utoronto.ca/winter2020/csc2541>
- Grading:
  - 20% Homework (3 problem sets)
  - 10% Weekly reflections on Markus (5 questions)
  - 10% Paper presentation done in-class (sign-up after the first lecture)
  - 60% course project (an eight-page write up)

# Schedule

Jan 9, 2020, Lecture 1: Why is healthcare unique?

**Jan 16, 2020, Lecture 2: Supervised Learning for Classification, Risk Scores and Survival**

Jan 23, 2020, Lecture 3: Clinical Time Series Modelling

Jan 30, 2020, Lecture 4: Causal inference with Health Data --- Dr. Shalmali Joshi (Vector)

**Problem Set 1 (Jan 31 at 11:59pm)**

Feb 6, 2020, Lecture 5: Fairness, Ethics, and Healthcare

**Project proposals (Feb 6 at 5pm)**

Feb 13, 2020, Lecture 6: Deep Learning in Medical Imaging -- Dr. Joseph Paul Cohen (MILA)

**Problem Set 2 (Feb 14 at 11:59pm)**

Feb 20, 2020, Lecture 7: Clinical NLP and Audio -- Dr. Tristan Naumann (MSR)

Feb 27, 2020, Lecture 8: Clinical Reinforcement Learning

Mar 5, 2020, Lecture 9: Interpretability / Humans-In-The-Loop --- Dr. Rajesh Ranganath (NYU)

**Problem Set 3 (Mar 6 at 11:59pm)**

Mar 12, 2020, Lecture 10: Disease Progression Modelling/Transfer Learning -- Irene Chen (MIT)

Mar 19, 2020, Project Sessions/Lecture

Mar 26, 2020, Course Presentations

April 4, 2020, Course Presentations

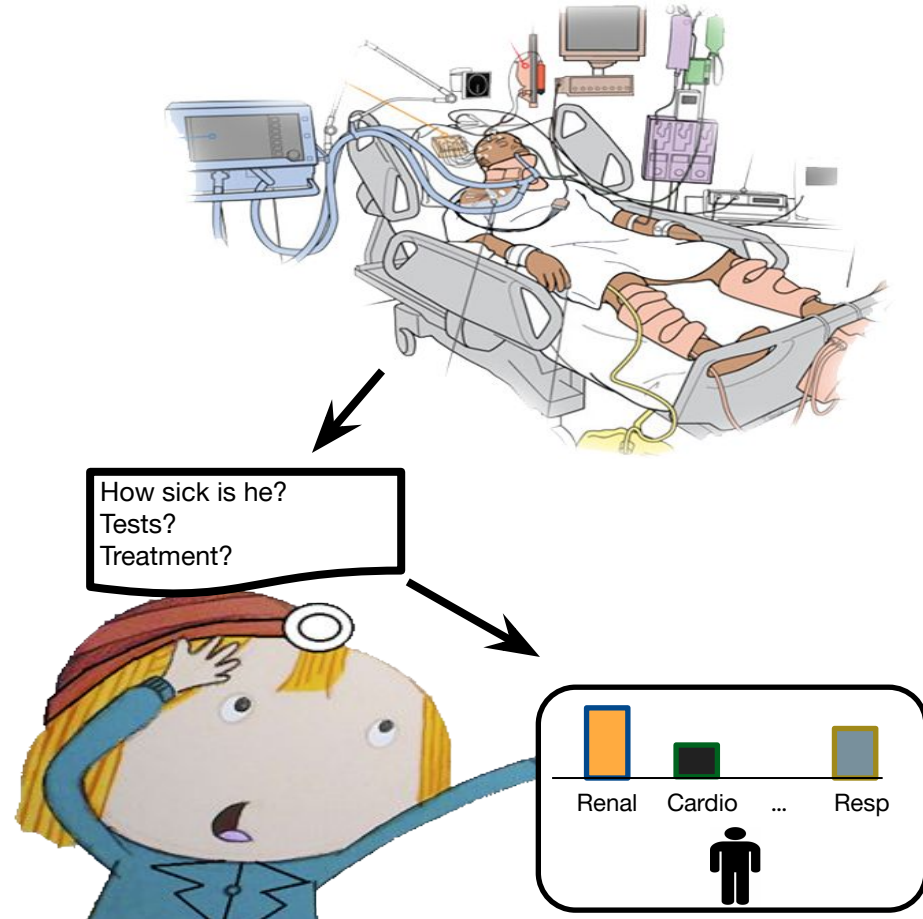
**Project Report (Apr 3 at 11:59pm)**

# Outline

- 1. What can we do with supervised learning?**
2. Case study on intervention predictions:
  - a. Frame the problem
  - b. Evaluation
  - c. Iterate
3. Survival Analysis
4. What else should we be thinking about?

# Clinicians Need to Estimate Patient State and Predict Outcome

- How do I figure out which patient needs my attention now?
- How will the patient's underlying cardiovascular system respond to my plan of care?
- If I discharge this patient, will they be readmitted?
- Are a patient's home behaviors impacting their health?

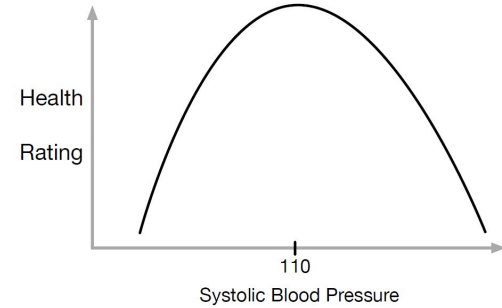


# But Those Challenges...

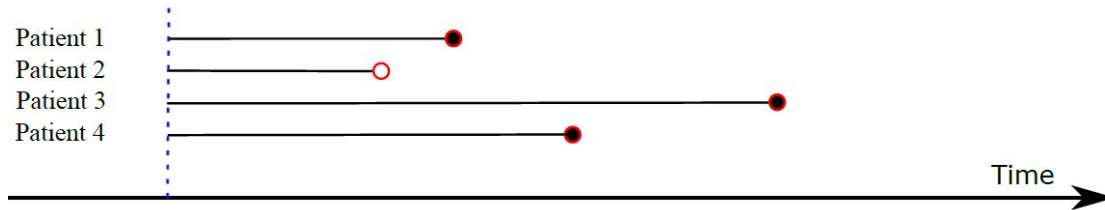
## Incomplete Data

	HCT	CR	BUN	CA
Patient 1	?		?	?
Patient 2			?	?
Patient 3		?	?	

## Non-linear Relationships

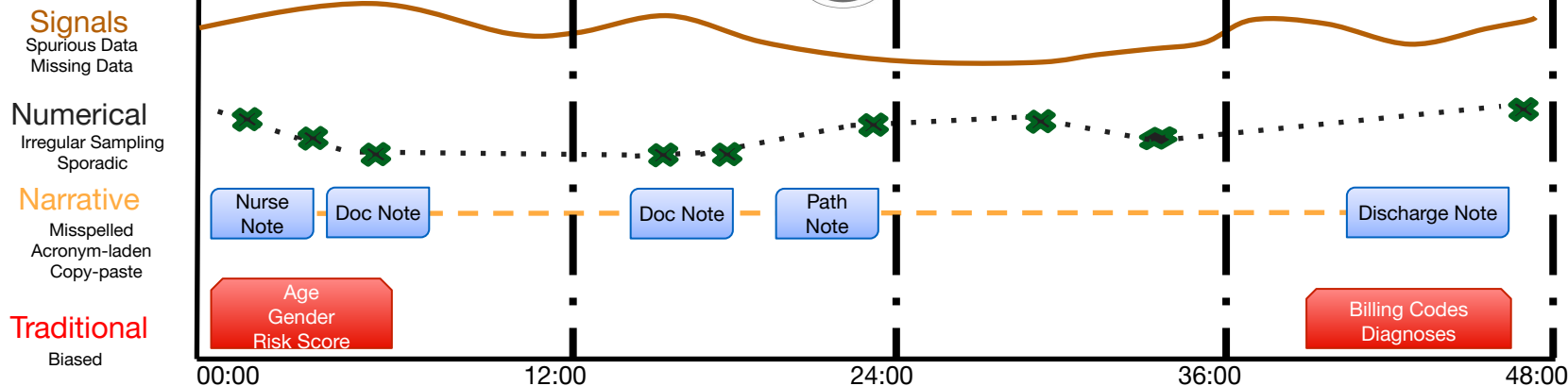
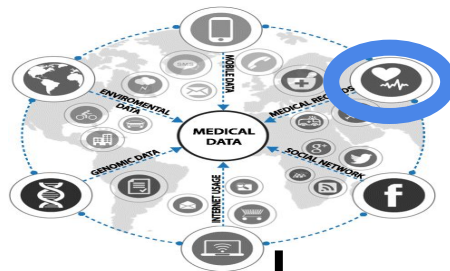
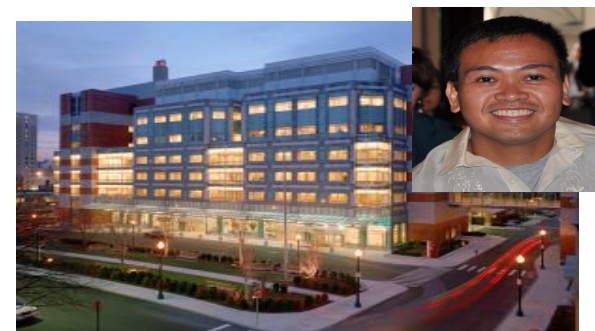


## Censoring



# MIMIC III ICU Data

- Learning with real patient data from the Beth Israel Deaconess Medical Center ICU.<sup>1</sup>

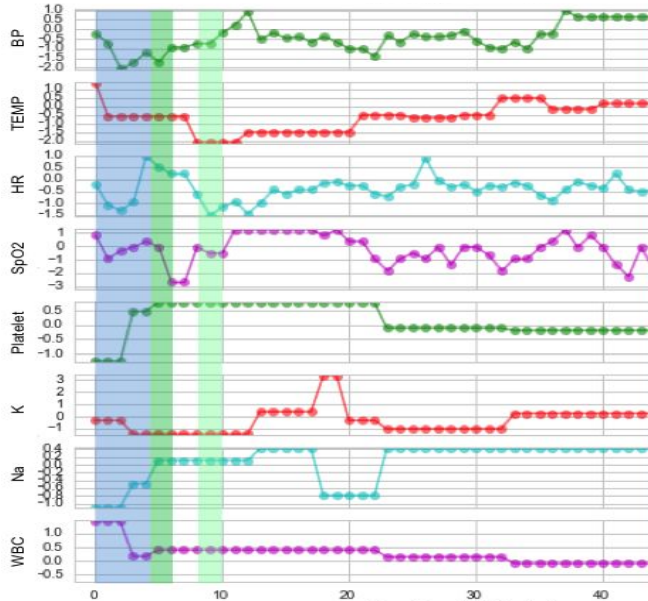


[1] Johnson, Alistair EW, et al. "MIMIC-III, a freely accessible critical care database." Scientific data 3 (2016).



# Problem: Hospital decision-making / care planning

## Observe Patient Data

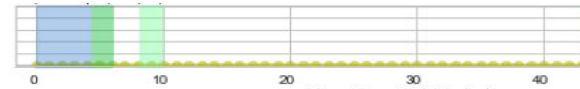


## “Real-time” Prediction

Of {Drug/Mortality/Condition}

By Gap Time

?



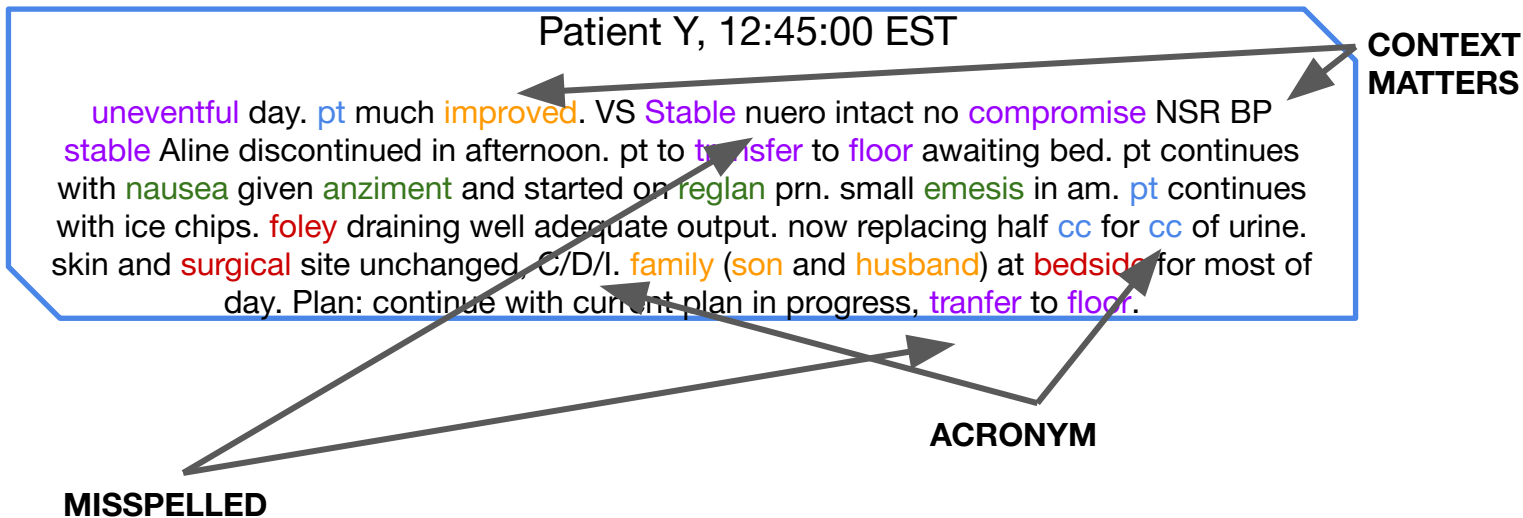
# Part 1: Predict **mortality** with clinical **notes**

- **Acuity** (severity of illness) very important - use **mortality** as a **proxy** for **acuity**.<sup>1</sup>
- Prior state-of-the-art focused on feature engineering in **labs/vitals** for target populations.<sup>2</sup>
- But **clinicians** rely on **notes**.

[1] Siontis, George CM, Ioanna Tzoulaki, and John PA Ioannidis. "Predicting death: an empirical evaluation of predictive tools for mortality." *Archives of internal medicine* 171.19 (2011): 1721-1726.

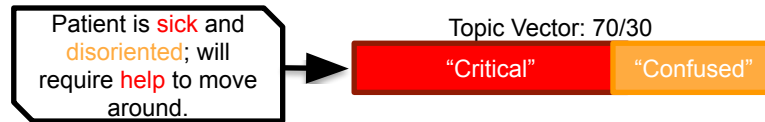
[2] Grady, Deborah, and Seth A. Berkowitz. "Why is a good clinical prediction rule so hard to find?." *Archives of internal medicine* 171.19 (2011): 1701-1702.

# Clinical notes are messy...



# Represent patients as topic vectors

- Model patient stays as an **aggregated set** of notes.
- Model notes as a **distribution** over topics.
- A “topic” is a **distribution** over words, that we learn.



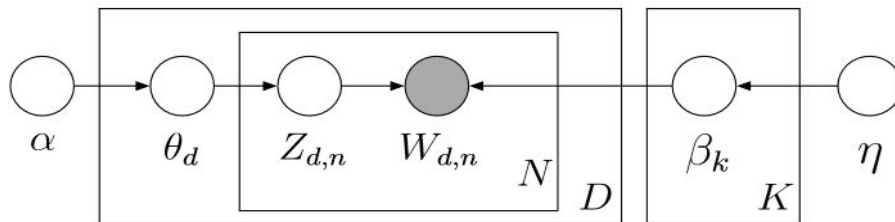
- Use Latent Dirichlet Allocation (LDA)<sup>1</sup> as an **unsupervised** way to **abstract** 473,000 notes from 19,000 patients into “topics”.<sup>2</sup>

[1] Blei, David M., Andrew Y. Ng, and Michael I. Jordan. "Latent dirichlet allocation." *the Journal of machine Learning research* 3 (2003): 993-1022

[2] T. Griffiths and M. Steyvers. Finding scientific topics. In PNAS, volume 101, pages 5228-5235, 2004

# Learning topics

- Observe **words**, infer **Z**:



$$\prod_{i=1}^K p(\beta_i | \eta) \prod_{d=1}^D p(\theta_d | \alpha) \left( \prod_{n=1}^N p(z_{d,n} | \theta_d) p(w_{d,n} | \beta_{1:K}, z_{d,n}) \right)$$

Per-word topic assignment  $Z_{d,n}$

Sparsity  $\alpha$

Per-doc topic proportion  $\theta_d$

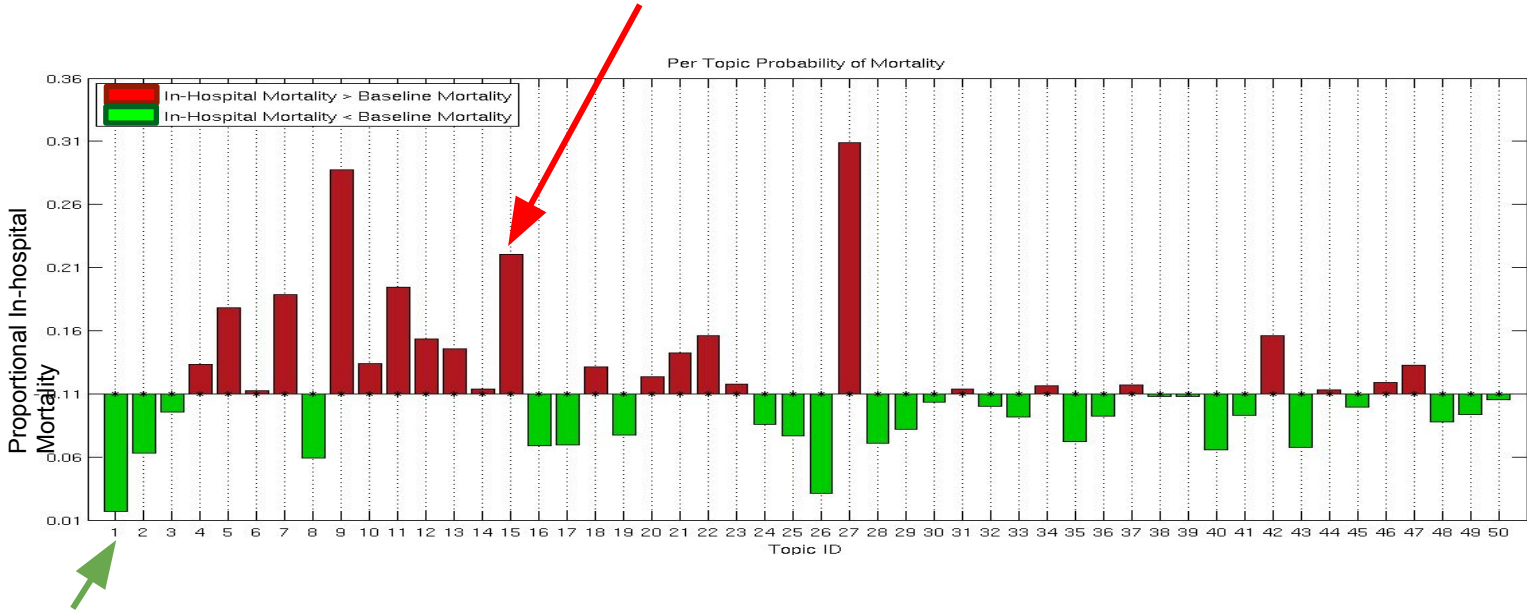
Exclusivity  $\eta$

Corpus topic distribution  $\beta_k$

[1] Blei, David M., Andrew Y. Ng, and Michael I. Jordan. "Latent dirichlet allocation." *the Journal of machine Learning research* 3 (2003): 993-1022  
 [2] T. Griffiths and M. Steyvers. Finding scientific topics. In *PNAS*, volume 101, pages 5228-5235, 2004

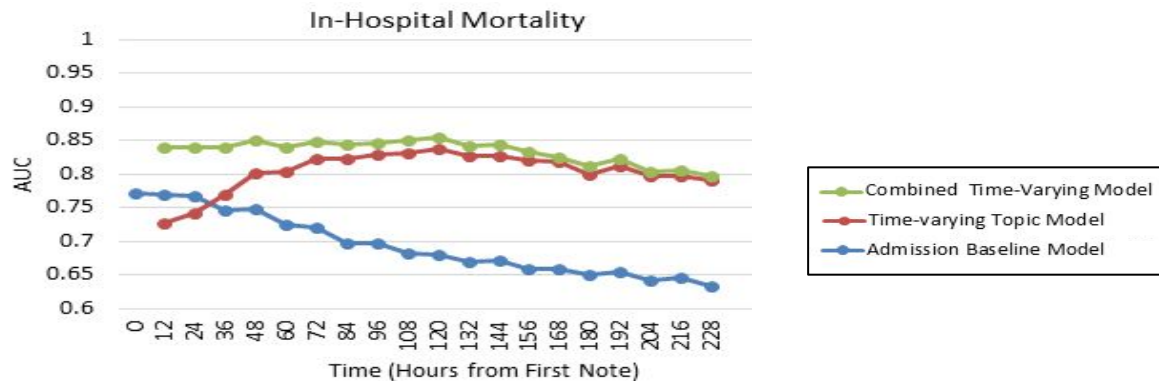
# Correlation between average topic and mortality

Topic #	Top Ten Words	Possible Topic
15	intubated vent ett secretions propofol abg respiratory resp care sedated	Respiratory failure



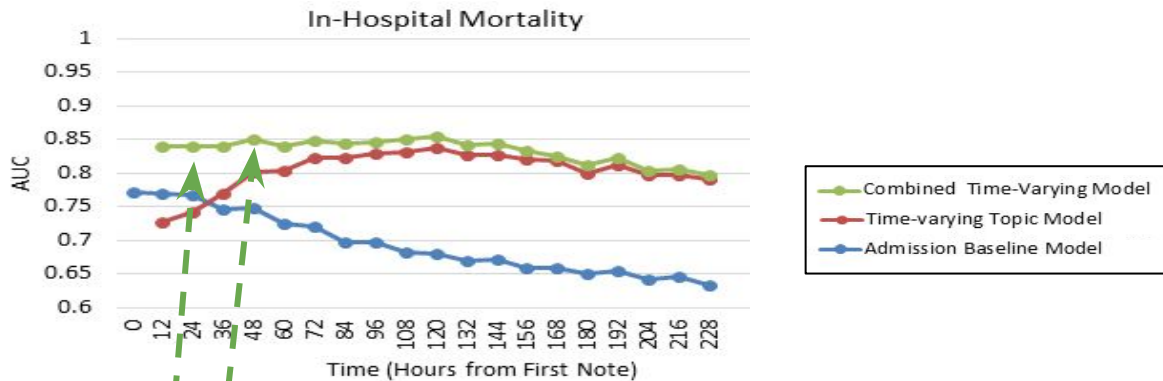
Topic #	Top Ten Words	Possible Topic
1	cabg, pain, ct, artery, coronary, valve, post, wires, chest, sp	Cardiovascular surgery

# Topics improve in-hospital mortality prediction



- **First** to do **forward-facing ICU mortality** prediction with notes.
- **Latent** representations **add** predictive power.
- Topics enable accurately **assess risk** from **notes**.

# More complex models are not always better



**More  
Complex ≠  
Better**

Author	AUC	Method	Episodes	Hours	Variables
Ghassemi, 2014	0.84/0.85	LDA	19,308	24/48	53 - notes
Caballero, 2015	0.86	Text processing + medication	15,000	24	? - notes/meds
Che, 2015	0.8-0.82	Deep Learning (LSTM)	3,940	48	30 - vitals
Che, 2016	0.7/0.85	Deep Learning (GRU)	19,714	12/48	99 - vitals/meds
Che, 2018	<b>0.85</b>	Deep Learning (GRU-D)	19,714	48	99 - vitals/meds

Caballero Barajas, Karla L., and Ram Akella. "Dynamically Modeling Patient's Health State from Electronic Medical Records: A Time Series Approach." *Proceedings of the 21th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*. ACM, 2015.

Che, Zhengping, et al. "Deep computational phenotyping." *Proceedings of the 21th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*. ACM, 2015.

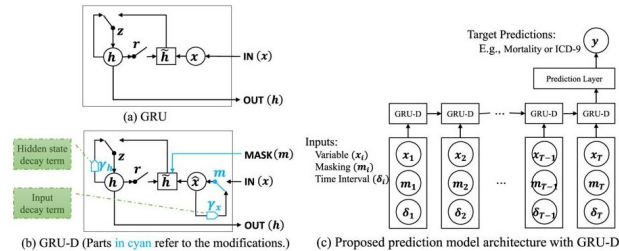
Che, Zhengping, et al. "Recurrent Neural Networks for Multivariate Time Series with Missing Values." arXiv preprint arXiv:1606.01865 (2016).

Che Z, Purushotham S, Cho K, Sontag D, Liu Y. Recurrent neural networks for multivariate time series with missing values. *Scientific reports*. 2018 Apr 17;8(1):6085.



# Even when complex and clever!

- Explicitly capture and use missing patterns in RNNs via systematically modified architectures.



- Performance bump is small, is MIMIC mortality our MNIST?

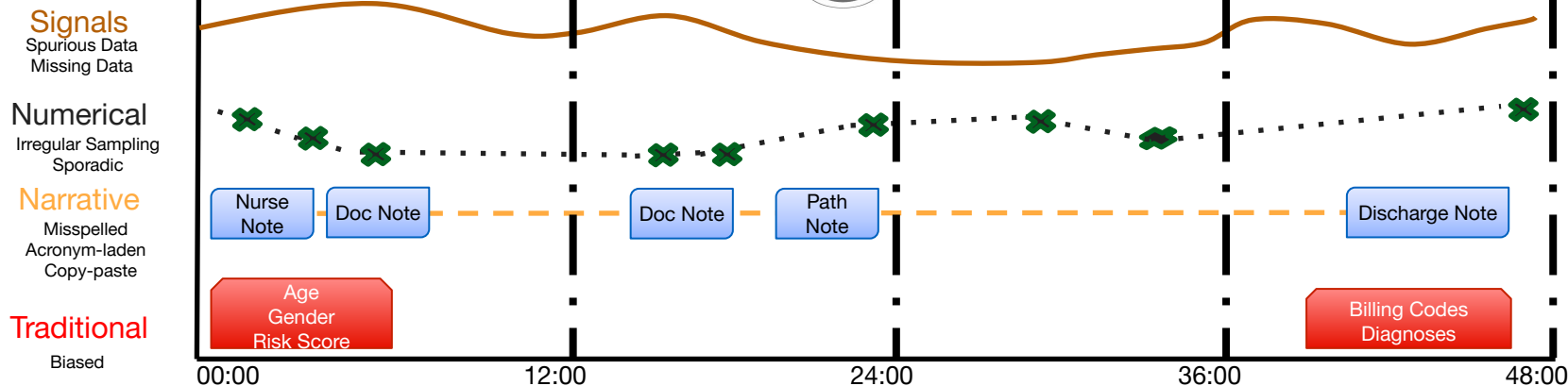
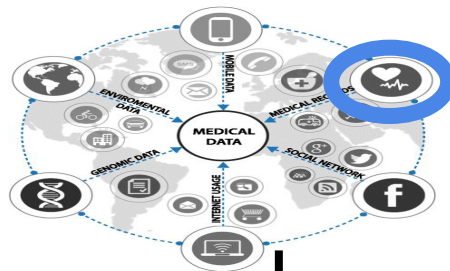
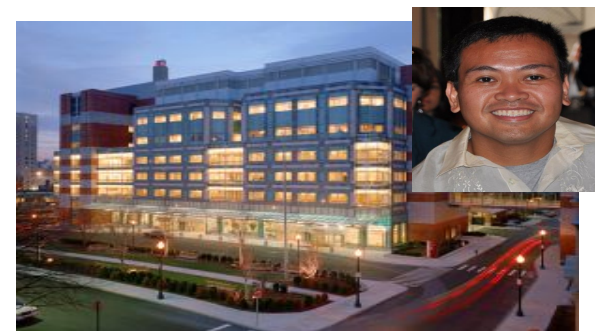
Non-RNN Models					RNN Models		
Mortality Prediction On MIMIC-III Dataset					LSTM-Mean	0.8142 ± 0.014	
LR-Mean	0.7589 ± 0.015	SVM-Mean	0.7908 ± 0.006	RF-Mean	0.8293 ± 0.004	GRU-Mean	0.8252 ± 0.011
LR-Forward	0.7792 ± 0.018	SVM-Forward	0.8010 ± 0.004	RF-Forward	0.8303 ± 0.003	GRU-Forward	0.8192 ± 0.013
LR-Simple	0.7715 ± 0.015	SVM-Simple	0.8146 ± 0.008	RF-Simple	0.8294 ± 0.007	GRU-Simple w/o $\mathcal{O}^{22}$	0.8367 ± 0.009
LR-SoftImpute	0.7598 ± 0.017	SVM-SoftImpute	0.7540 ± 0.012	RF-SoftImpute	0.7855 ± 0.011	GRU-Simple w/o $m^{23,24}$	0.8266 ± 0.009
LR-KNN	0.6877 ± 0.011	SVM-KNN	0.7200 ± 0.004	RF-KNN	0.7135 ± 0.015	GRU-Simple	0.8380 ± 0.008
LR-CubicSpline	0.7270 ± 0.005	SVM-CubicSpline	0.6376 ± 0.018	RF-CubicSpline	0.8339 ± 0.007	GRU-CubicSpline	0.8180 ± 0.011
LR-MICE	0.6965 ± 0.019	SVM-MICE	0.7169 ± 0.012	RF-MICE	0.7159 ± 0.005	GRU-MICE	0.7527 ± 0.015
LR-MF	0.7158 ± 0.018	SVM-MF	0.7266 ± 0.017	RF-MF	0.7234 ± 0.011	GRU-MF	0.7843 ± 0.012
LR-PCA	0.7246 ± 0.014	SVM-PCA	0.7235 ± 0.012	RF-PCA	0.7747 ± 0.009	GRU-PCA	0.8236 ± 0.007
LR-MissForest	0.7279 ± 0.016	SVM-MissForest	0.7482 ± 0.016	RF-MissForest	0.7858 ± 0.010	GRU-MissForest	0.8239 ± 0.006
						<b>Proposed GRU-D</b>	<b>0.8527 ± 0.003</b>

# Outline

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2. **Case study on intervention predictions:**
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# MIMIC III ICU Data

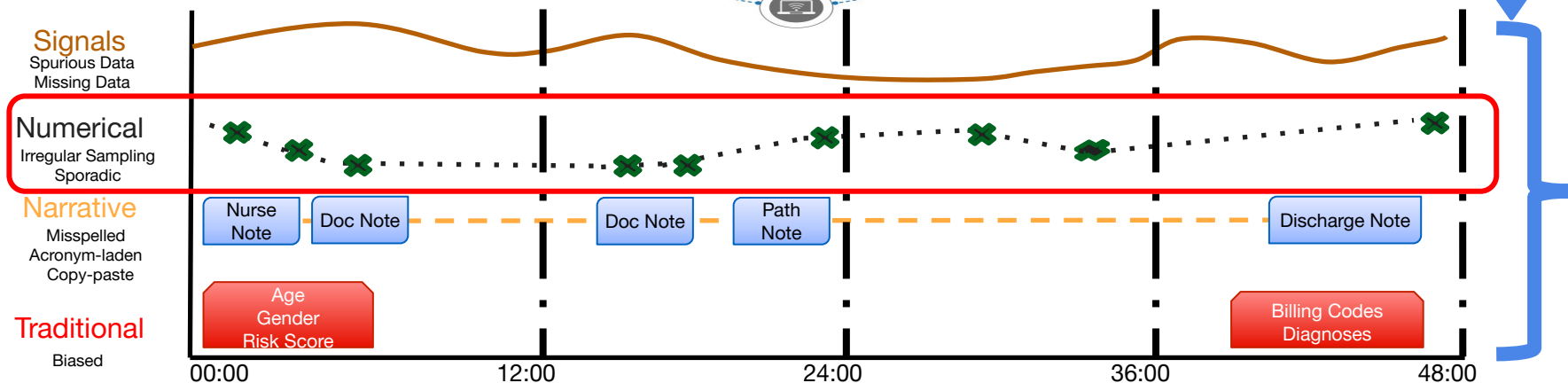
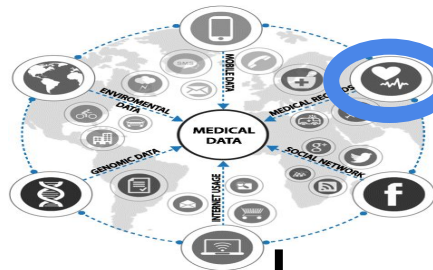
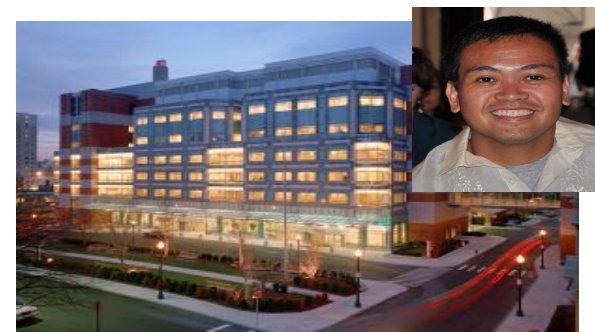
- Learning with real patient data from the Beth Israel Deaconess Medical Center ICU.<sup>1</sup>



[1] Johnson, Alistair EW, et al. "MIMIC-III, a freely accessible critical care database." Scientific data 3 (2016).

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# Example: Early prediction of vasopressor interventions

- Vasopressors are a **common** drug to raise blood pressure.
- All drugs can be **harmful**, we'd like to avoid when possible.<sup>1,2</sup>
- Assume that real **clinical** actions are good learning **data**.
- Predict **upcoming interventions** based on evidence.<sup>3,4</sup>

[1] Müllner, Marcus, Bernhard Urbaneck, Christof Havel, Heidrun Losert, Gunnar Gamper, and Harald Herkner. "Vasopressors for shock." *The Cochrane Library* (2004).

[2] D'Aragon, Frederick, Emilie P. Belley-Cote, Maureen O. Meade, François Lauzier, Neill KJ Adhikari, Matthias Briel, Manoj Lalu et al. "Blood Pressure Targets For Vasopressor Therapy: A Systematic Review." *Shock* 43, no. 6 (2015): 530-539.

[3] Vincent, Jean-Louis, and Mervyn Singer. "Critical care: advances and future perspectives." *The Lancet* 376.9749 (2010): 1354-1361.

[4] Ospina-Tascón, Gustavo A., Gustavo Luiz Büchele, and Jean-Louis Vincent. "Multicenter, randomized, controlled trials evaluating mortality in intensive care: Doomed to fail?." *Critical care medicine* 36.4 (2008): 1311-1322.

# Define clinically actionable prediction tasks:

## Tasks:

1. Short Term (5-10 hr) Need:  
Predicts before a clinician would have given.
2. Imminent ( $< 4$  hr) Need:  
Predict when a clinician would have given.
3. Weaning ( $< 4$  hr):  
Predict when a doctor would have stopped.

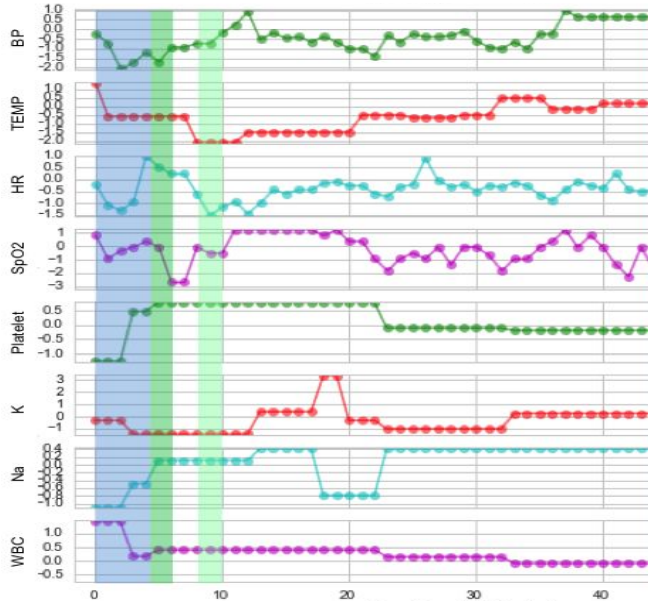
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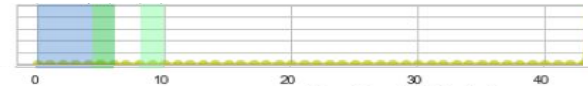
# Define predictive task

## Observe Physiological Signals



?

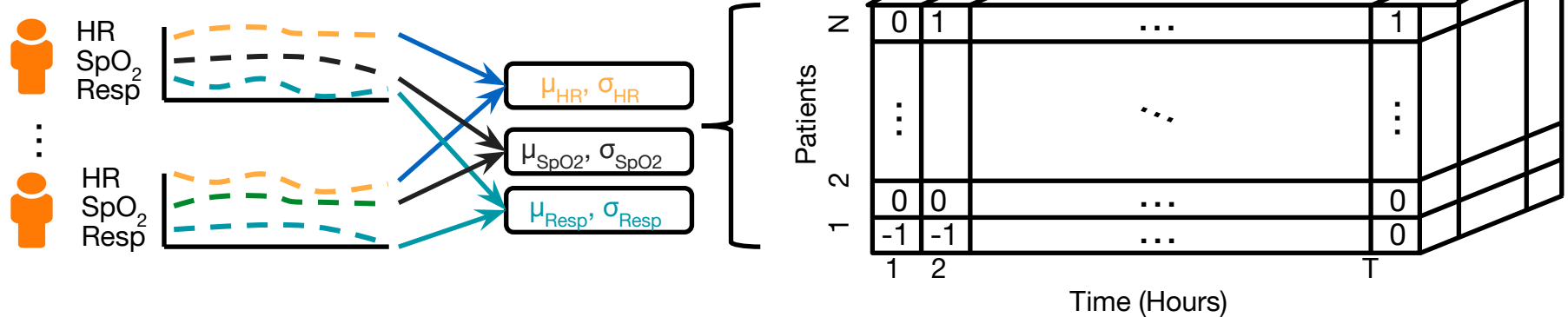
Every Hour  
**Predict Onset of Drug**  
Before the Doctor





# Domain knowledge: Shared underlying physiological state

- **Z-score** (standardize) and **quantize** time series data.

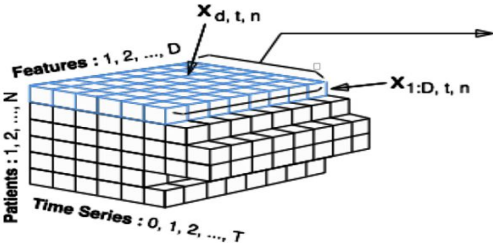


- Every  $x_{n,t,d}$  is one of ten possible **characters**,  $-4:0:4$  or  $NaN$ .
- Every  $x_{n,t}$  is one of  $10^D$  possible **words**.

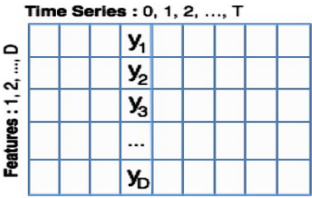
# Switching State Autoregressive Model Representation

- A patient  $n$  is a **sequence** of latent physiological **states**  $y$ .

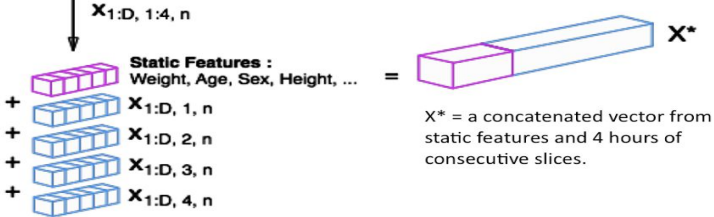
**1** Demographic features, vital signs, lab results, and derived features.



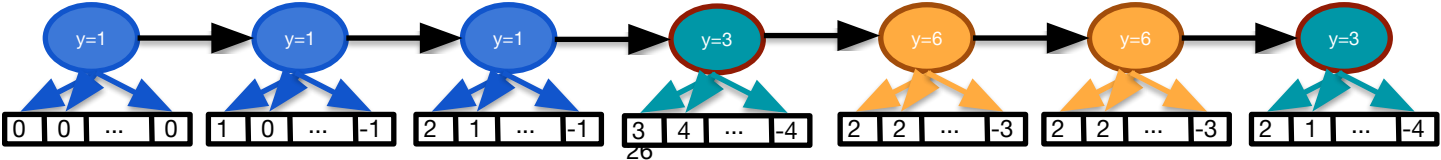
Time-series of features for one patient. Each blue square contains 1 character.



**2** Data is grouped into 4 hour segments and flattened.



- A physiological state  $y$  is a **distribution** over physiological words  $x$ .



# Extracting latent belief states from SSAM

- HMM sequence  $y_t^n$  on the signals  $x_t^n$

$$y_t^n \sim T_y(\cdot | y_{t-1}^n)$$

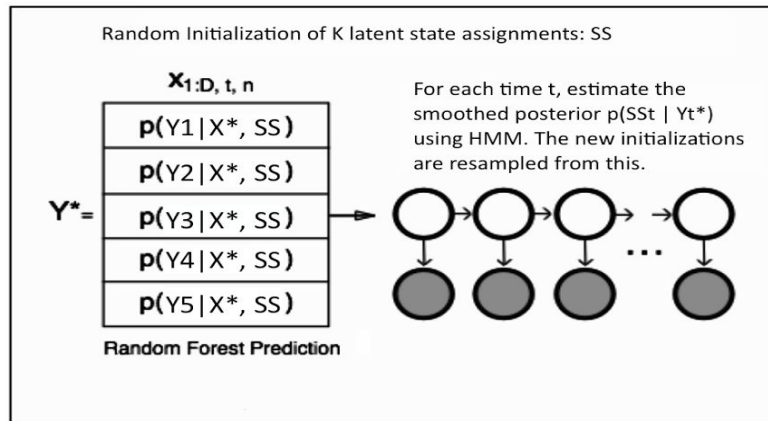
$$x_t^n(p) \sim T_x(x_t^n(p) | x_{t-1}^n, \theta_{p, y_{t-1}^n})$$

- $x_t^n$  modeled by  $T_x(x_t^n(p) | x, \theta)$ ;  $\theta$  are governed by  $y_t^n$
- Each state  $1 \dots k$  has distinct set of parameters  $\{\theta_{d,k}\}$ , via  $K$  sets of tuples and  $D$  classifiers.
- Train  $\theta_{d;k}$  to predict  $x_t^n(d) | x_{t-4:t-1}^n$ .
- Update state sequences  $y_t^n$  given  $\{\theta_{d,k}\}$ .

3

A switching-state autoregressive model is applied to the data.

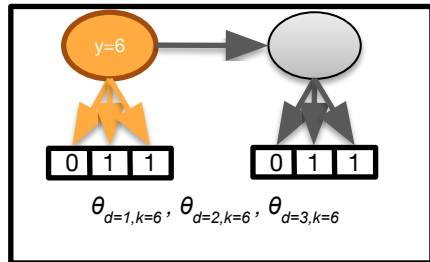
## SSAM Clustering : Repeat Q iterations



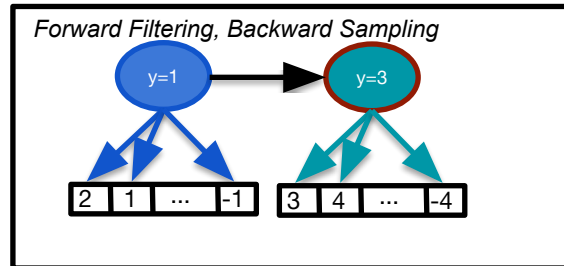
# Discrete state space and per-variable missingness

- Use discrete state space.
- Model *NaN* (missing) as a valid emission.
- Cluster similar underlying states.
- For  $D$  variables and  $K$  latent states, perform inference iteratively:

1. Optimize parameters  $\theta_{d,k}$

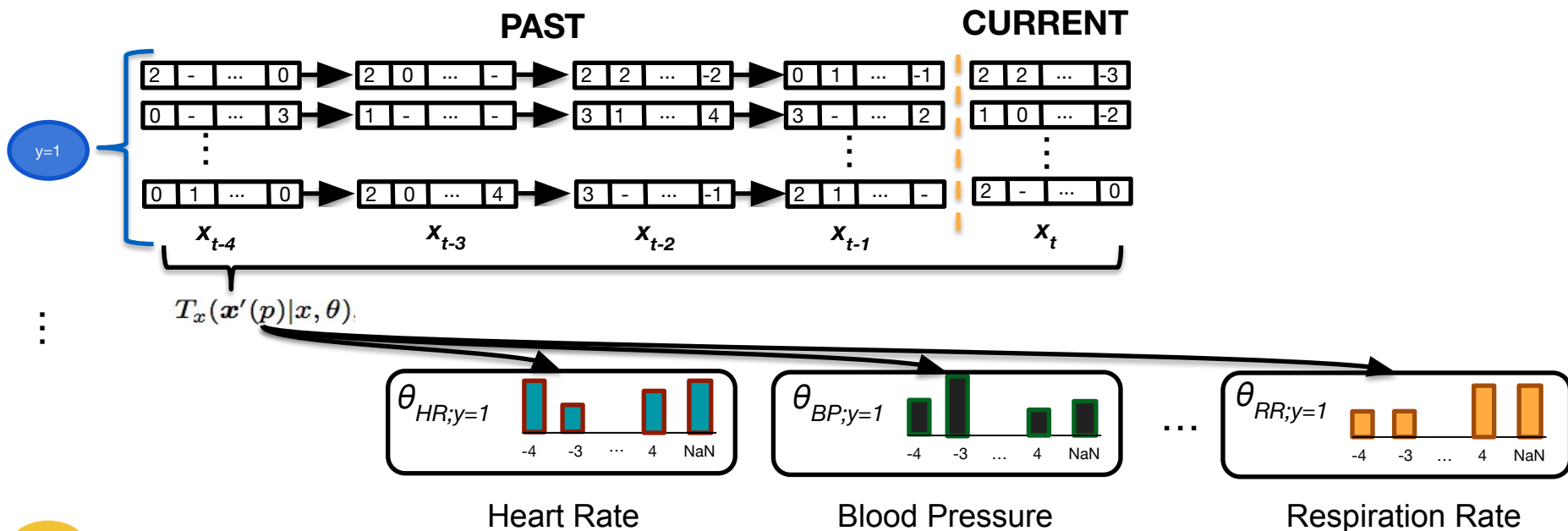


2. Sample states  $y_t^n$



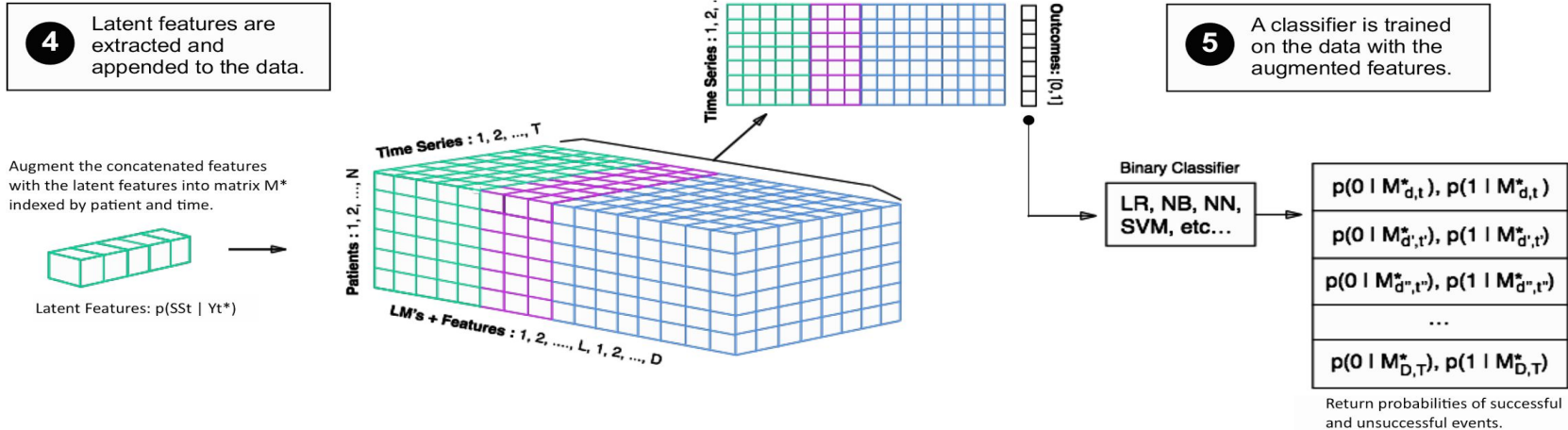
# Distribution of values per-variable and latent

- Train parameters  $\theta_{d;k}$  to predict  $x_t^n(d)$  given  $x_{t-4:t-1}^n$



# Using SSAM for structured prediction

- SSAM states are **learned** in an **unsupervised** setting.
- **Evaluate** them in a **supervised** setting, on clinical tasks.



# Outline

1. What can we do with supervised learning?
2. **Case study on intervention predictions:**
  - a. Frame the problem
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# Previous work - use strong baselines

- **Baseline 1:** Prior work<sup>1</sup> predicted vasopressor onset in ICU patients with pre-treatment (fluids).
  - 2 hour gap
  - 3 demographics and 22 signals
  - AUC of 0.79

[1] Fialho, A. S., et al. "Disease-based modeling to predict fluid response in intensive care units." *Methods Inf Med* 52.6 (2013): 494-502.

\* 2 hour gap, 22 derived/3 static features.



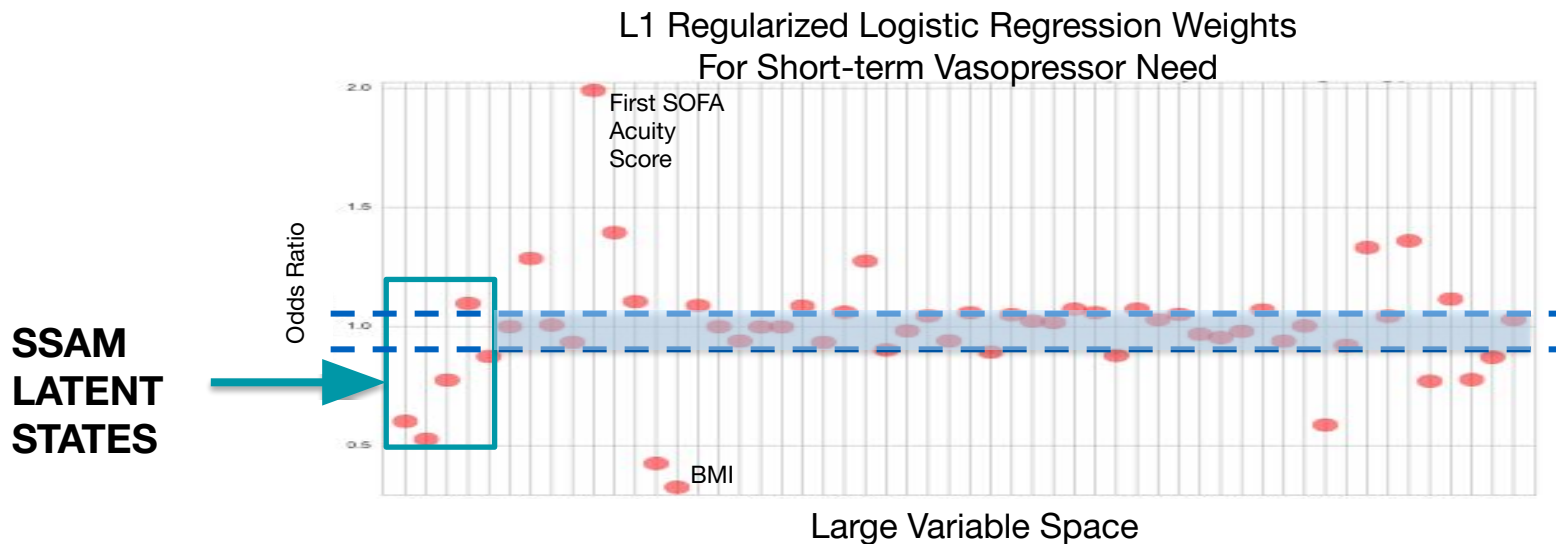
# Vasopressor onset prediction beats SOTA results

	<b>AUC</b>
Baseline 1 – Prior Work	0.79
Baseline 2 – Raw Data	0.83
SSAM Representations	0.83
<b>Raw Data + SSAM Rep.</b>	<b>0.88</b>

- **Latent** representations **add** predictive power.
- New state-of-the art prediction, 0.88 = thousands of **people treated early!**

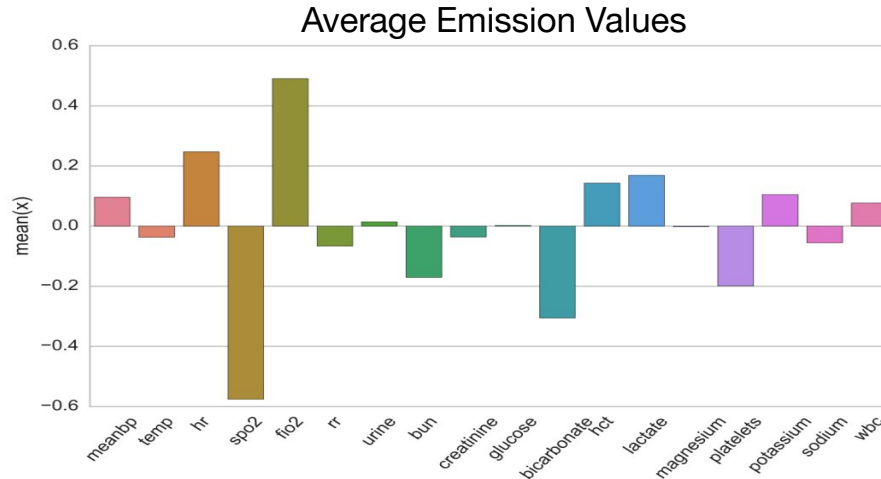
# Regularized prediction emphasizes latent states

- **Latent states** are consistently **significant** across a large **variable space**.



# Post-hoc justification

- Investigate state associated with vasopressor onset?



- Low average values of blood oxygenation and bicarbonate.
- Highest lactate levels of any state.

# Similar trends in other predictive tasks

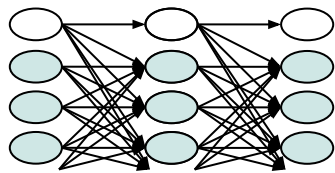
	<b>Short-Term Need (Gapped AUC)</b>	<b>Imminent Need (Ungapped AUC)</b>	<b>Weaning</b>
Baseline 1 – Prior Work	0.79	-	-
Baseline 2 – Raw Data	0.83	0.89	0.67
SSAM Representations	0.83	0.87	0.63
<b>Raw Data + SSAM Rep.</b>	<b>0.88</b>	<b>0.92</b>	<b>0.71</b>

- Our representations are **useful abstractions** for **multiple tasks**.

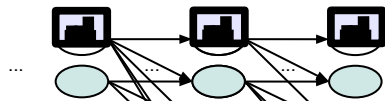
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3. Survival Analysis
4. What else should we be thinking about?

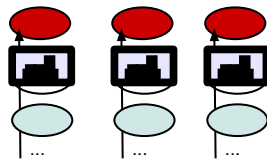
# More outcomes and improved dynamics



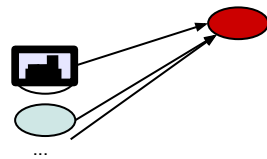
Learn model parameters over patients with variational EM.



Infer hourly distribution over hidden states with HMM DP (fwd alg.).



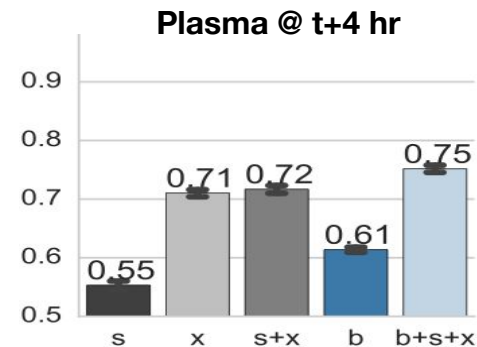
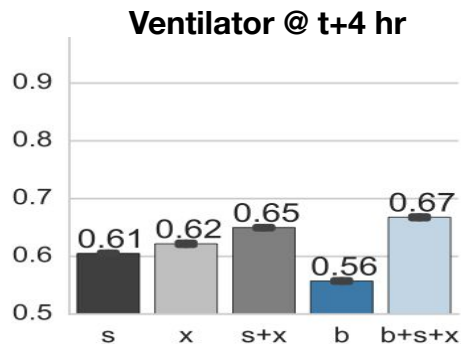
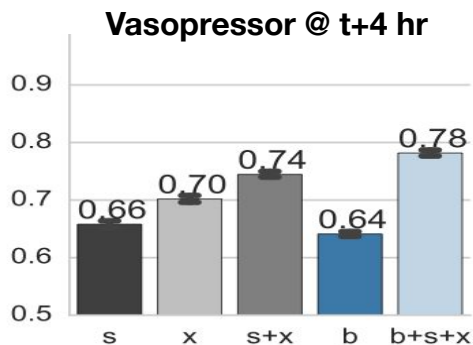
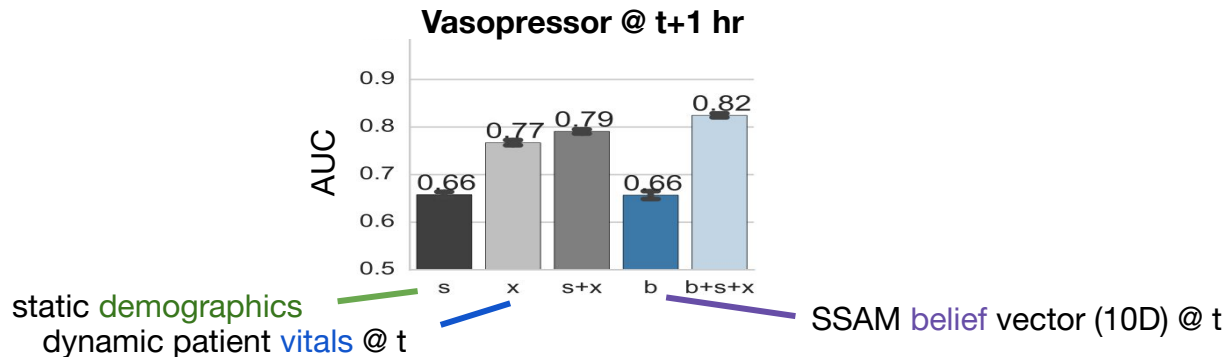
Logistic regression (with label-balanced cost function)



Predict onset in advance

- More Interventions: fresh-frozen-plasma transfusion (ffp), platelet transfusion, red-blood-cell (rbc) transfusion, vasopressor administration, and ventilator intubation.
- Gaussian Emission Model for Dynamics:
  - Static observations  $s$  (10 dimensions using one-hot encoding),
  - Dynamic time-series observations  $x$  (18 dimensions)
  - Belief state vectors  $b$  ( $K=10$  dimensions) from the switching state model forward belief state

# State space beliefs improve prediction



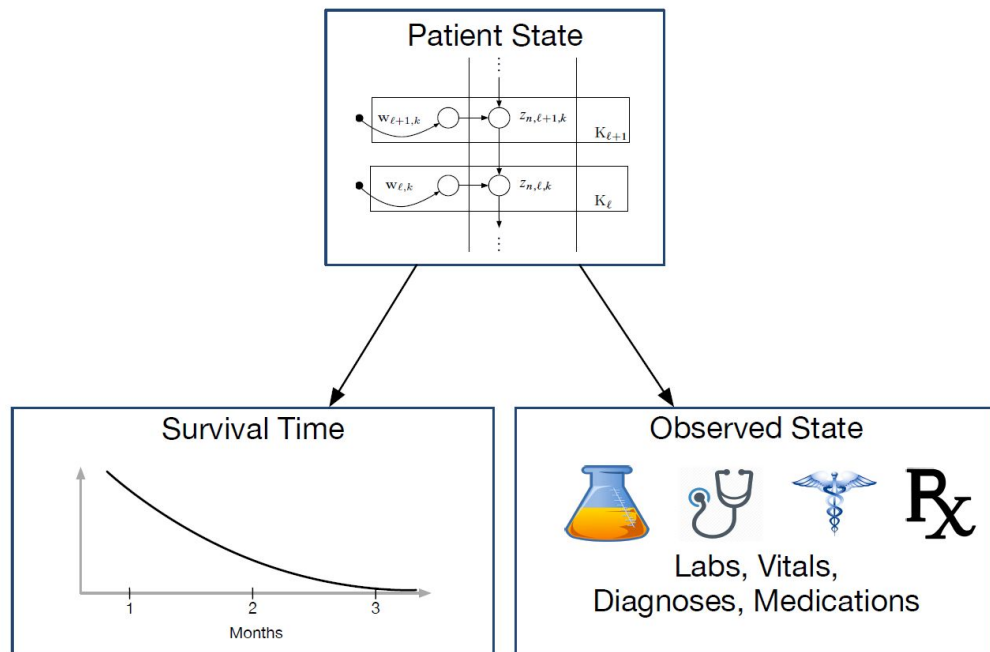
# Outline

1. What can we do with supervised learning?
2. Case study on intervention predictions:
  - a. Frame the problem
  - b. Evaluation
  - c. Iterate
3. **Survival Analysis**
4. What else should we be thinking about?



# Survival Analysis

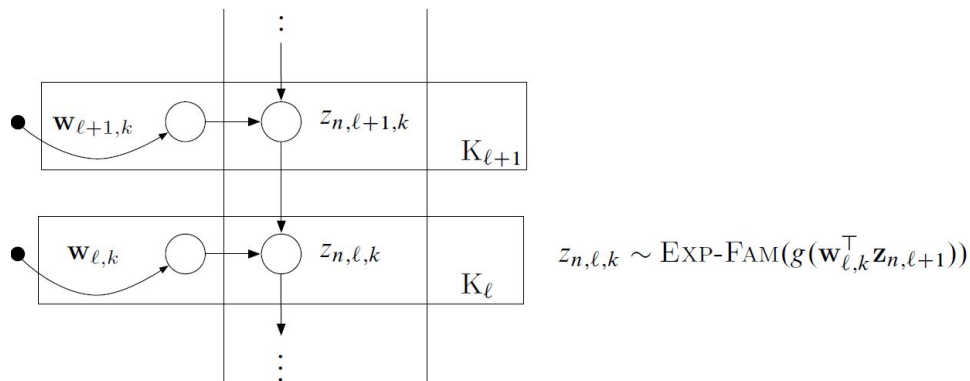
- Survival Analysis studies the time to an event.
- Commonly used in EHR for “time to” discharge/death/etc.
- We need **flexible hidden structures** to describe patient state.



# Deep Exponential Families

- $\mathbf{x}$ , the set of covariates
- $\boldsymbol{\beta}$ , the parameters for the data with some prior  $p(\boldsymbol{\beta})$
- $k$ , a fixed scalar
- $n$ , the index to an observation
- $\mathbf{z}$ , the latent variable
- $L$ , the number of layers of latent variables each observation has

# Deep Exponential Families



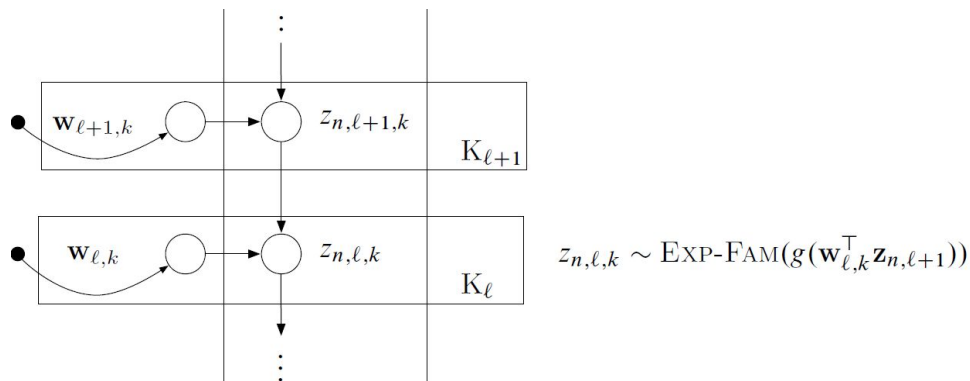
- Use a DEF to represent state.
- All distributions are canonical in exponential family form

$$p(z_{n, \ell, k} | \mathbf{z}_{n, \ell+1}, \mathbf{w}_{\ell, k}) = \exp\{\eta(\cdot)^\top t(z_{n, \ell, k}) - a(\eta(\cdot))\}$$

$$\eta(\cdot) = g(\mathbf{z}_{n, \ell+1}^\top \mathbf{w}_{\ell, k})$$

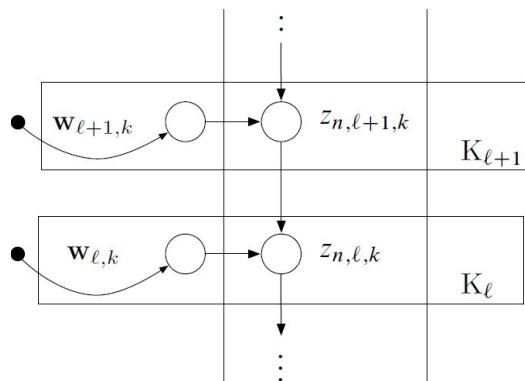
- More general functions can also be used.

# Deep Exponential Families



- Possibilities for the hidden layers
  - Binary: Bernoulli
  - Count: Poisson
  - Non-negative (and sparse): Gamma
  - Real-valued: Gaussian

# Deep Exponential Families



$$z_{n,\ell,k} \sim \text{EXP-FAM}(g(\mathbf{w}_{\ell,k}^T \mathbf{z}_{n,\ell+1}))$$

- Many existing models are DEFs
  - Mixture models
  - Factorial mixture models [Ghahramani+ 1995]
  - Poisson factorization [Canny+ 2004]
  - Exponential family factor analysis [Mohamed+ 2008]
  - Correlated topic models [Blei+ 2007]

# Deep Survival Analysis

$$b \sim \text{Normal}(0, \sigma_b)$$

$$a \sim \text{Normal}(0, \sigma_W)$$

$$z_n \sim \text{DEF}(\mathbf{W})$$

$$\mathbf{x}_n \sim p(\cdot | \boldsymbol{\beta}, z_n)$$

$$t_n \sim \text{Weibull}(\log(1 + \exp(z_n^\top a + b)), k)$$

- Use the Weibull distribution to model failure times as its cdf and pdf are both analytically tractable.

# Deep Survival Analysis

$$b \sim \text{Normal}(0, \sigma_b)$$

$$a \sim \text{Normal}(0, \sigma_W)$$

$$z_n \sim \text{DEF}(\mathbf{W})$$

$$\mathbf{x}_n \sim p(\cdot | \boldsymbol{\beta}, z_n)$$

$$t_n \sim \text{Weibull}(\log(1 + \exp(z_n^\top a + b)), k)$$

- $\mathbf{x}_n$  can be missing ✓
- Relationships flexible through latent space ✓
- Censoring through tractable CDF ✓
- Make predictions via posterior inference
  - Works empirically! ✓

# Predicting CHD from EHR

- 300K individuals from a large metropolitan hospital
- Adults with at least 5 interactions with the hospital's network
- Covariates:
  - 9 vital signs
  - 80 laboratory test measurements
  - 5K medication orders
  - 13K diagnosis
- Data aggregated at a month level
- CHD events were defined by the occurrence of
  - 413 (angina pectoris)
  - 410 (myocardial infarction)
  - 411 (coronary insufficiency)



# Results

Model	Concordance (%)
<b>Baseline Framingham Risk Score</b>	<b>65.57</b>
Deep Survival Analysis; K=10	69.35
Deep Survival Analysis; K=5	70.45
Deep Survival Analysis; K=25	71.20
Deep Survival Analysis; K=75	71.65
Deep Survival Analysis; K=100	72.71
<b>Deep Survival Analysis; K=50</b>	<b>73.11</b>

**Table 1:** Concordance on a held-out set of 25,000 patients for different values of K and for the baseline risk score. All deep survival analysis dimensionalities outperform the baseline.

- It works, but remember!
  - Survival analysis is conditional distribution modeling
  - Imputation not useful for pure predictions
  - Reduces to deep-multiclass regression with missingness indicators

# Outline

1. What can we do with supervised learning?
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3. Survival Analysis
4. **What else should we be thinking about?**

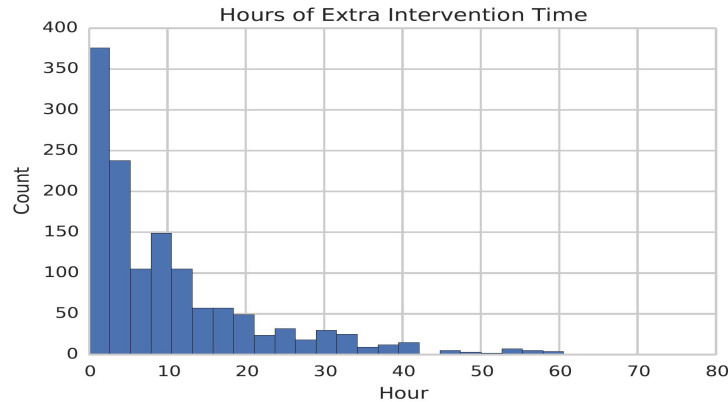
# Similar trends in other tasks, except!

	<b>Short-Term Need (Gapped AUC)</b>	<b>Imminent Need (Ungapped AUC)</b>	<b>Weaning</b>
Baseline 1 – Prior Work	0.79	-	-
Baseline 2 – Raw Data	0.83	0.89	0.67
SSAM Representations	0.83	0.87	0.63
<b>Raw Data + SSAM Rep.</b>	<b>0.88</b>	<b>0.92</b>	<b>0.71</b>

- For the patients with vasopressors, we often predicted an early wean.

# What exactly are we learning?

- Patients can be left on interventions longer than necessary.

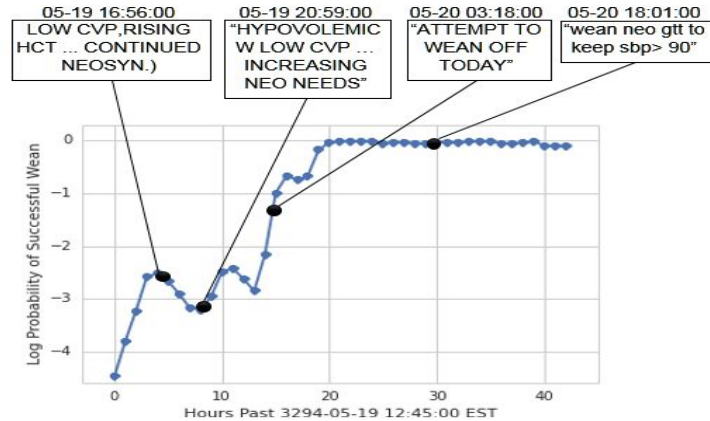


- Extended interventions can be costly and detrimental to patient health.<sup>1,2</sup>

[1] Müllner, Marcus, Bernhard Urbanek, Christof Havel, Heidrun Losert, Gunnar Gamper, and Harald Herkner. "Vasopressors for shock." *The Cochrane Library* (2004).

[2] D'Aragon, Frederick, Emilie P. Belley-Cote, Maureen O. Meade, François Lauzier, Neill KJ Adhikari, Matthias Briel, Manoj Lalu et al. "Blood Pressure Targets For Vasopressor Therapy: A Systematic Review." *Shock* 43, no. 6 (2015): 530-539.

# Finding where we “could” wean early?



- One example of a 62-year-old male patient with a cardiac catheterization.
- More complexity/higher misclassification penalty don't solve this!

# Missingness and representation

- How do we represent missing data?
- If we remove patients via a threshold, what groups are impacted?

## Biases in electronic health record data due to processes within the healthcare system: retrospective observational study

Denis Agniel,<sup>1</sup> Isaac S Kohane,<sup>1,2</sup> Griffin M Weber<sup>1,3</sup>

### ABSTRACT

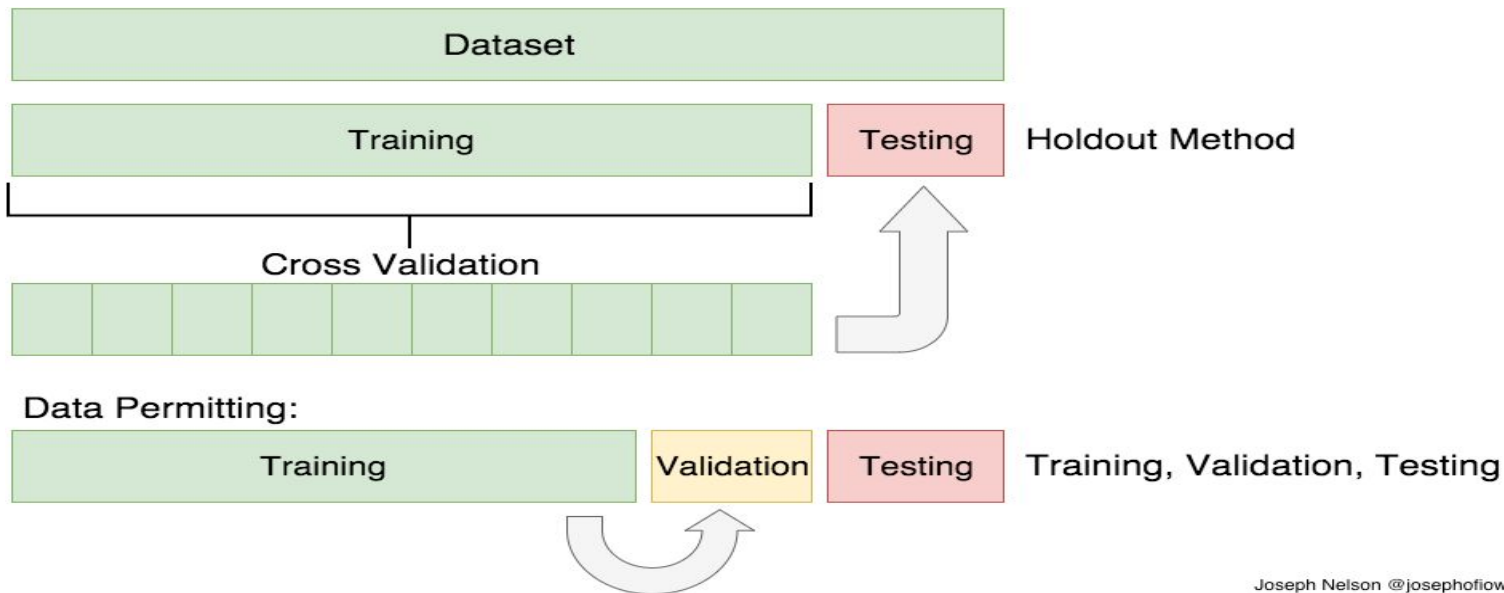
#### OBJECTIVE

To evaluate on a large scale, across 272 common types of laboratory tests, the impact of healthcare processes on the predictive value of electronic health record (EHR) data.

the routine delivery of healthcare.<sup>1-3</sup> This, in turn, is transforming biomedical research as investigators now have access to information on millions of patients through informatics tools that can query and analyze EHRs,<sup>4-7</sup> link to genomic and other types of biomedical data,<sup>8-9</sup> and scale to a national level and beyond.<sup>10-14</sup>

“Doctors typically do not **order a white blood cell** count test for a **patient on the weekend** or for a patient who **just had a white blood cell count** less than one day earlier, unless **they believe the patient is sick.**”

# Details in training can be impactful



Joseph Nelson @josephfiowa

- Split by patient... generalize to new subjects?
- Split by hospital site... generalize to new doctors?
- Split by year... generalize to new policies?

# Careful evaluation is extremely important

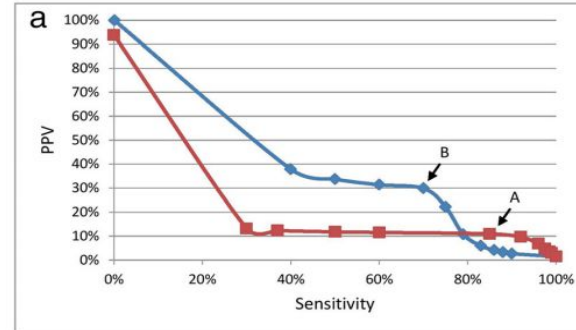
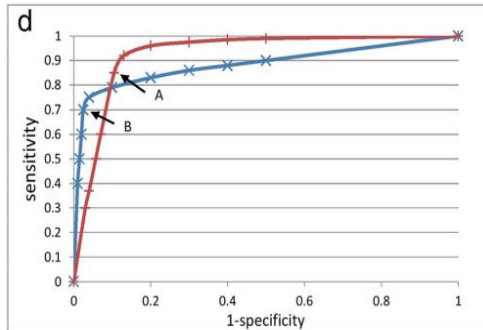
- Spend as much time designing evaluation as with model prototyping.
- Make diagnostic plots, not just tables, and think about actual utility.

## Why the C-statistic is not informative to evaluate early warning scores and what metrics to use



Santiago Romero-Brufau<sup>1,2\*</sup>, Jeanne M. Huddleston<sup>1,2,3</sup>, Gabriel J. Escobar<sup>4</sup> and Mark Liebow<sup>5</sup>

By AUC...  
red is  
better



But blue is  
much better  
for alarm  
fatigue

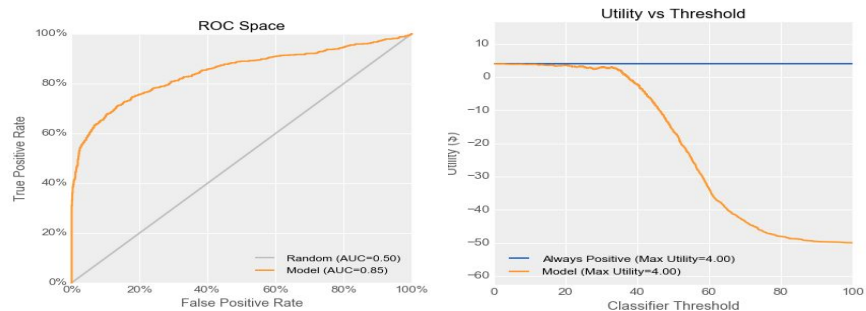


# Calibration matters in practice

- What is the cost of an incorrect decision?

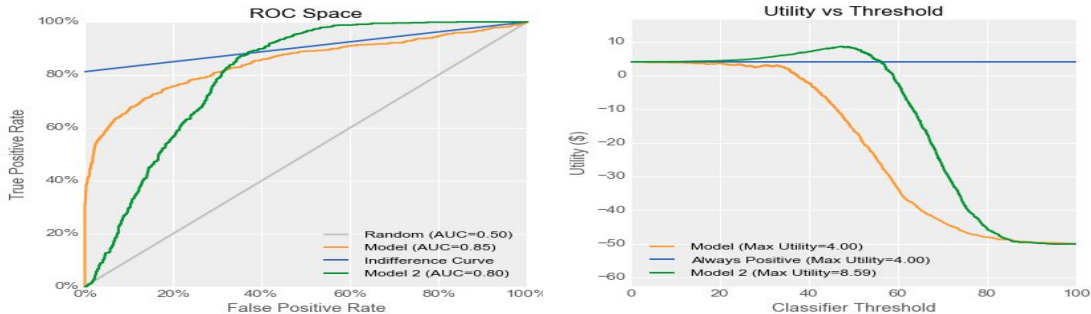
	Good	Bad
Positive	True Positive utility = +\$20 $rate(t) = TPR(t) \cdot 95\%$	False Positive utility = -\$300 $rate(t) = FPR(t) \cdot 5\%$
Negative	False Negative utility = -\$50 $rate(t) = (1 - TPR(t)) \cdot 95\%$	True Negative utility = -\$50 $rate(t) = (1 - FPR(t)) \cdot 5\%$

VS.



- Domain specific evaluation requires a goal.

Model 2  
(green) has  
lower AUC

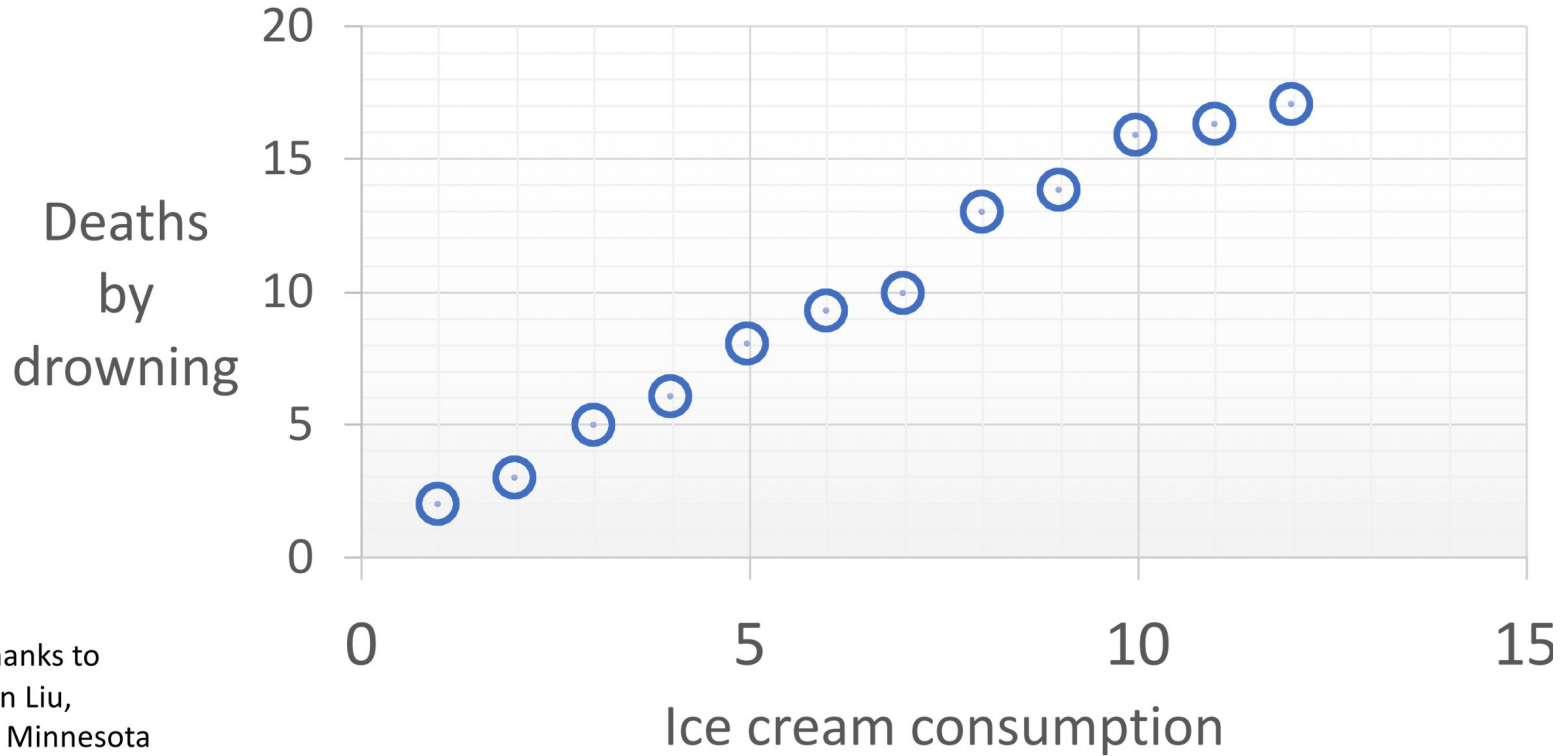


... but has  
operating points  
with much higher  
utility!

# Causality is looming in healthcare

- Question: Who will be diabetic in 1 year?
- We build predictive model:  
features  $X = [\text{lab\_tests}, \text{diagnoses}, \text{medications}]$   
label  $y = [\text{diabetic}]$
- We can predict  $y$  from  $X$  with AUC 0.8
- What **action** do we take with this knowledge?

# Can you spot the confounding?

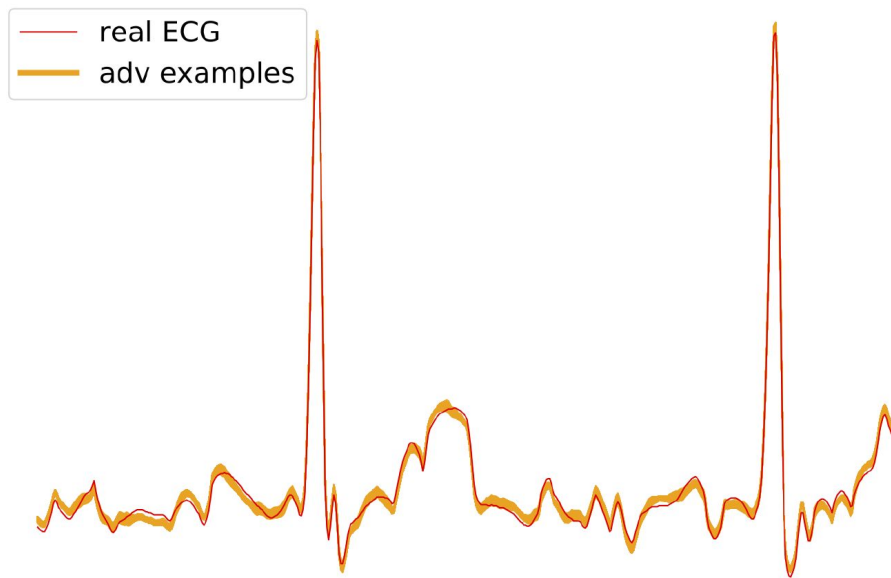


Thanks to  
Lan Liu,  
U. Minnesota

# Remember Adversarial Examples?

- How hard is it to adversarially fool networks?
- Remember that bad loss means misclassification, and:
  1. Start with trained model
  2. Compute gradient with respect to loss function with respect to input
  3. Follow gradient to increase the loss
  4. Limit the movement to a norm
- Popular technique: Projected Gradient Descent [Madry+ 2017]

# Adversarial Examples Are Not Rare



- Smooth adversarial perturbations that fool networks exist for over 85% of ECG tracings in the 2017 PhysioNet Challenge.