Learning to Detect Sepsis with a Multi-output Gaussian Process RNN Classifier (**in the Real World!**)

Joe Futoma
Harvard SEAS
Duke Statistical Science

NeurIPS 2018
All of BNP (Especially the **Useful** Bits)

Outline

- Background
- Patient Story
- MGP-RNNs
- Experiments & Results
- In the Real World

Background

Sepsis

- Life-threatening complication from infection.
- 750,000+ new sepsis cases each year in US; high mortality (**30-50%**).
- Without intervention, progress to septic shock, organ failure, death.
- **Early identification is key:**
  - Earlier treatment associated with improved outcomes.
- **Early identification is hard:**
  - No clear time of onset, no reliable biomarker (yet).

Surviving Sepsis Campaign

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

- **<u>Sepsis Care Bundles</u>**: selected elements of care from evidence-based practice guidelines.

- In first 3 hours:

    1. Measure lactate.

    2. Get blood cultures.

    3. Give antibiotics.

- Other actions at 6 hours.

- **We know what to do, if we know it's there!**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

Christopher W. Seymour, M.D., Foster Gesten, M.D., Hallie C. Prescott, M.D., Marcus E. Friedrich, M.D., Theodore J. Iwashyna, M.D., Ph.D., Gary S. Phillips, M.A.S., Stanley Lemeshow, Ph.D., Tiffany Osborn, M.D., M.P.H., Kathleen M. Terry, Ph.D., and Mitchell M. Levy, M.D.

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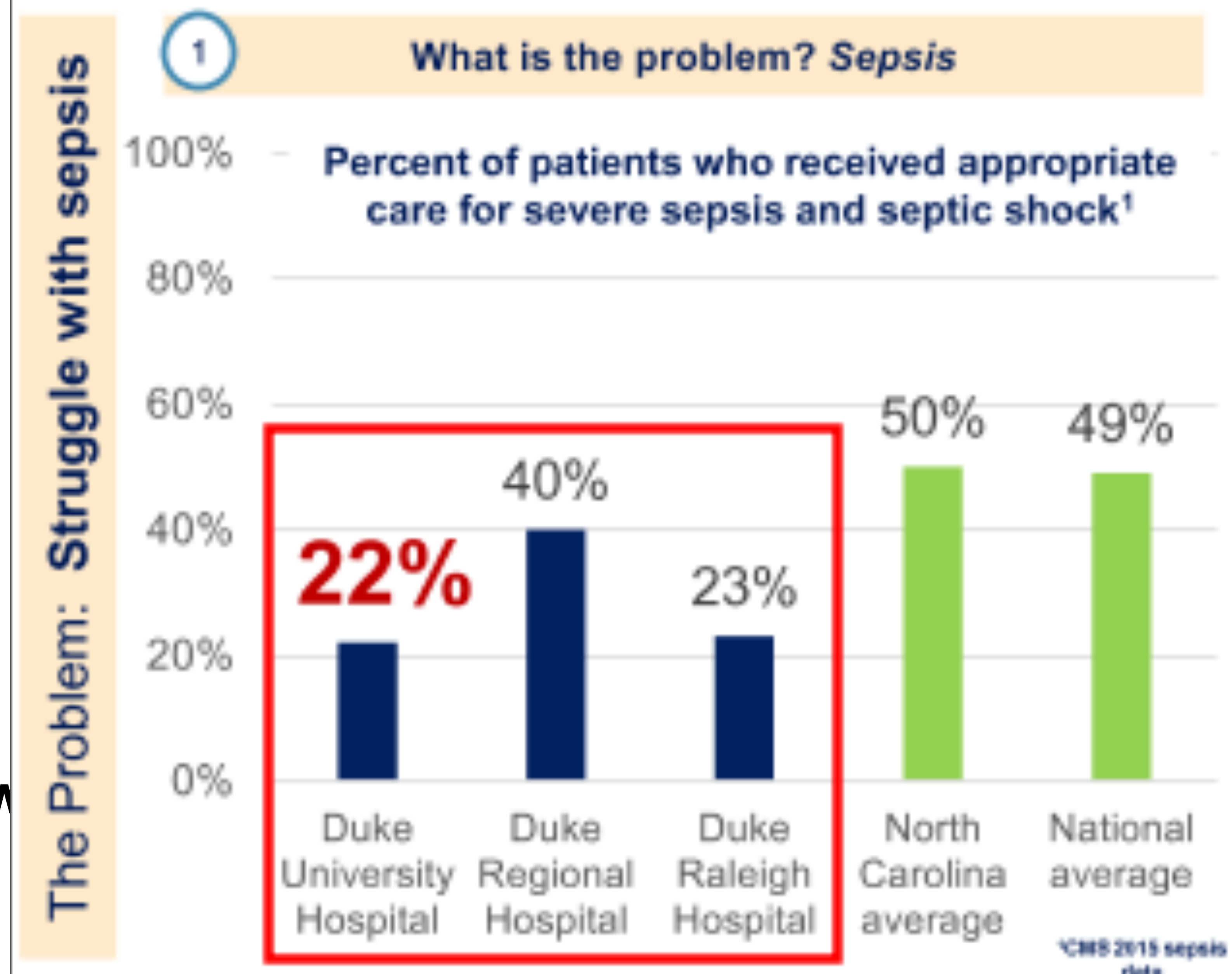
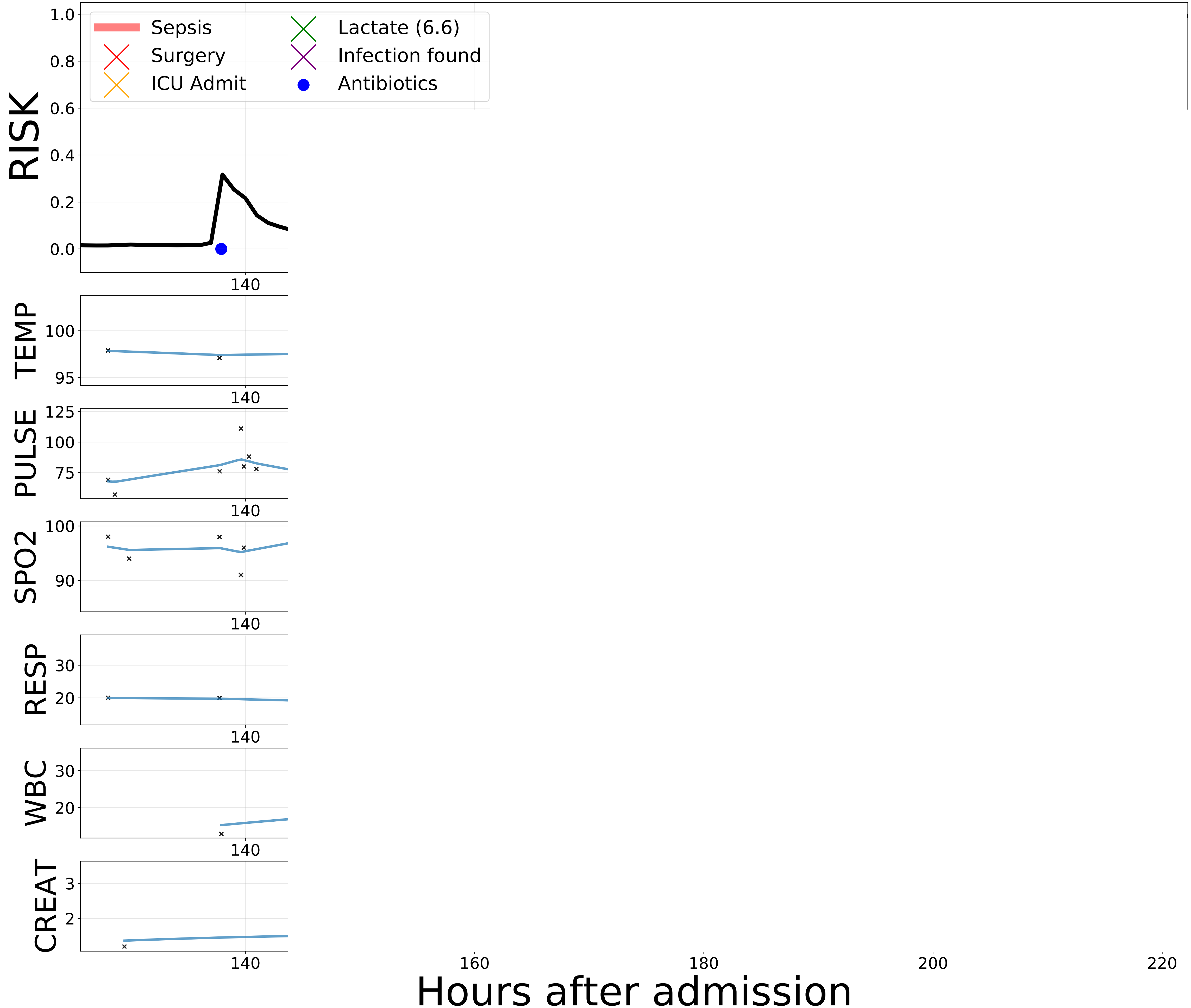
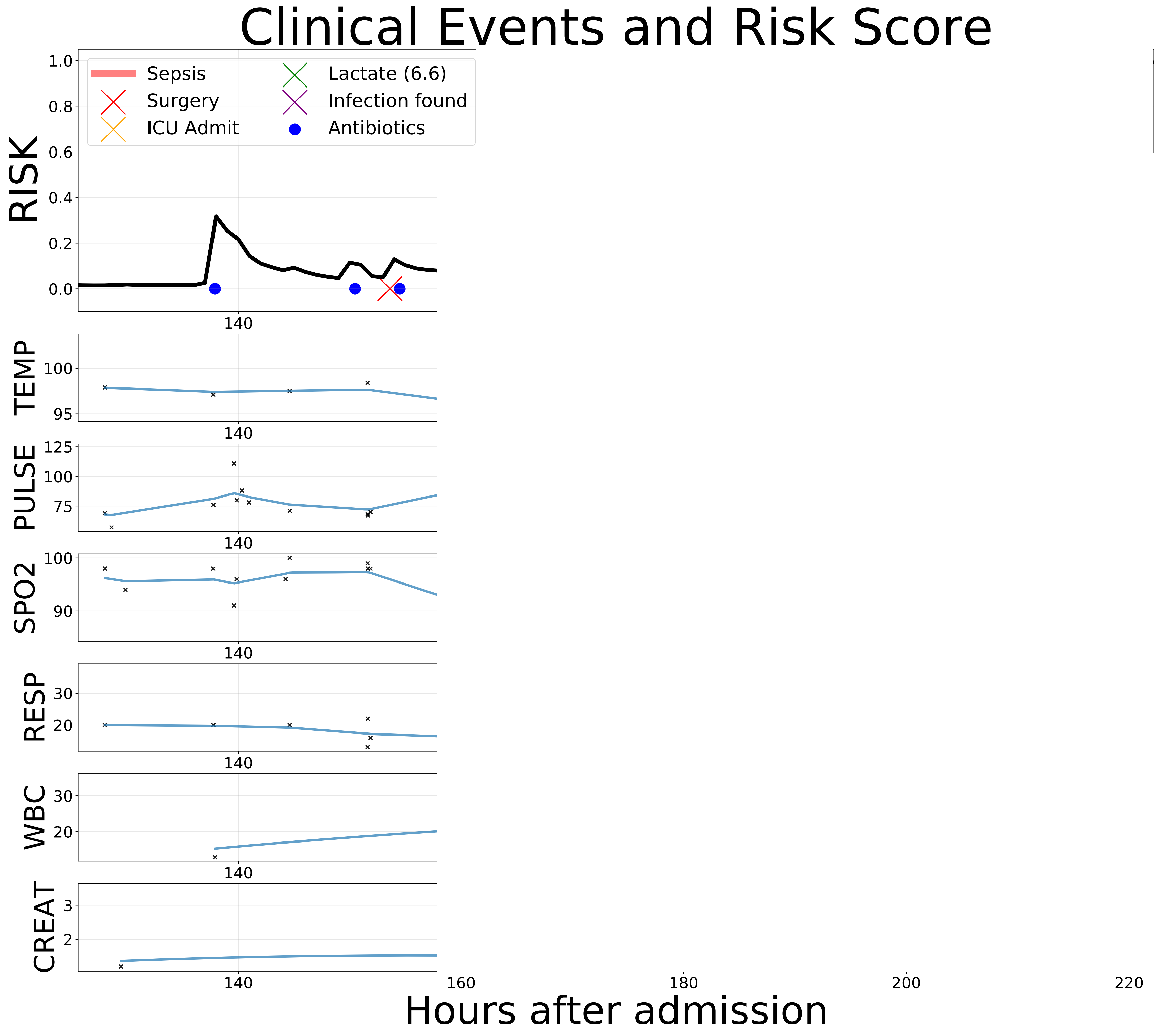
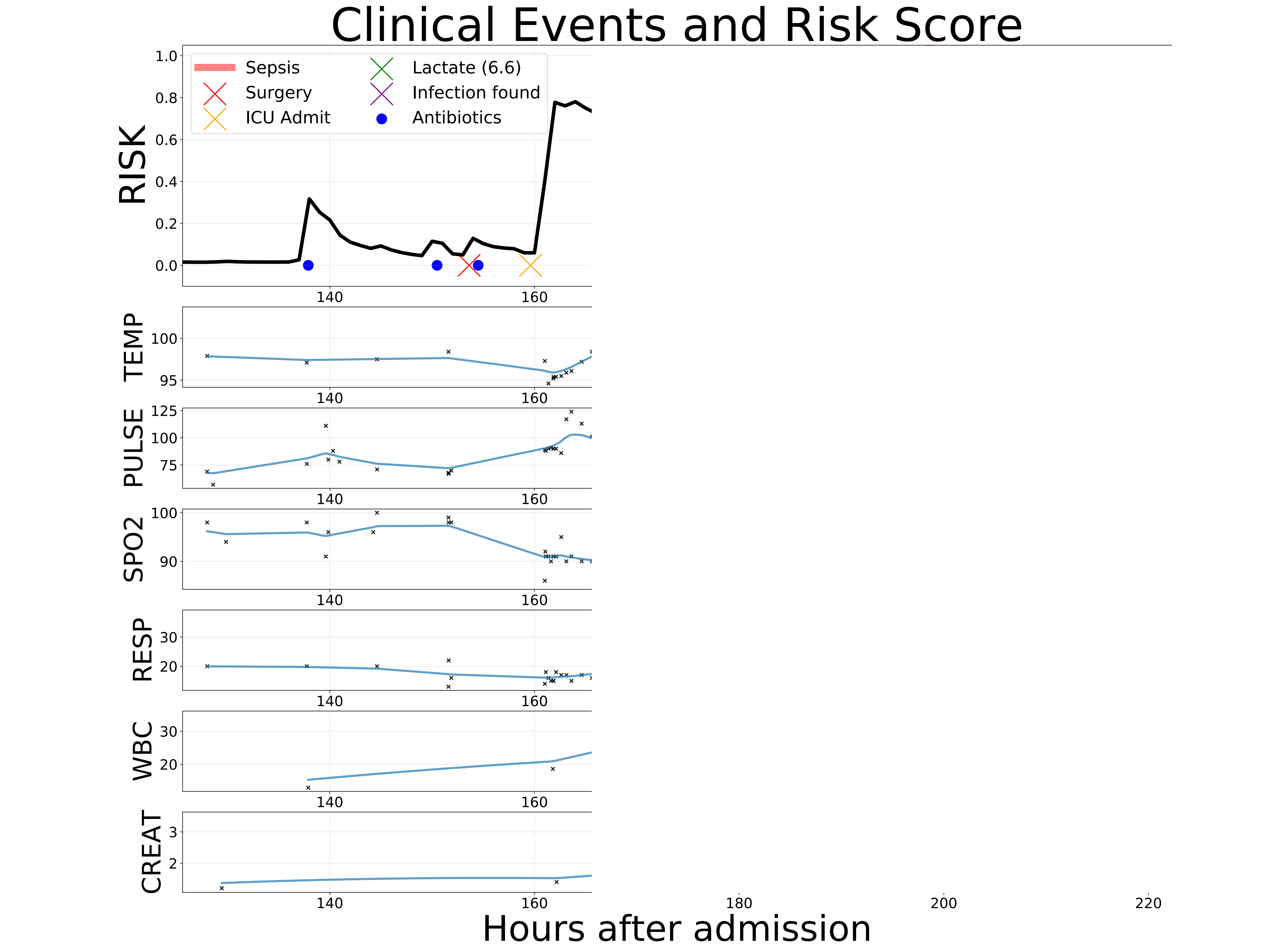


Patient Story

Clinical Events and Risk Score




Clinical Events and Risk Score
Sepsis
Surgery
ICU Admit
Lactate (6.6)
Infection found
Antibiotics
RISK
TEMP
PULSE
SPO2
RESP
WBC
CREAT
Hours after admission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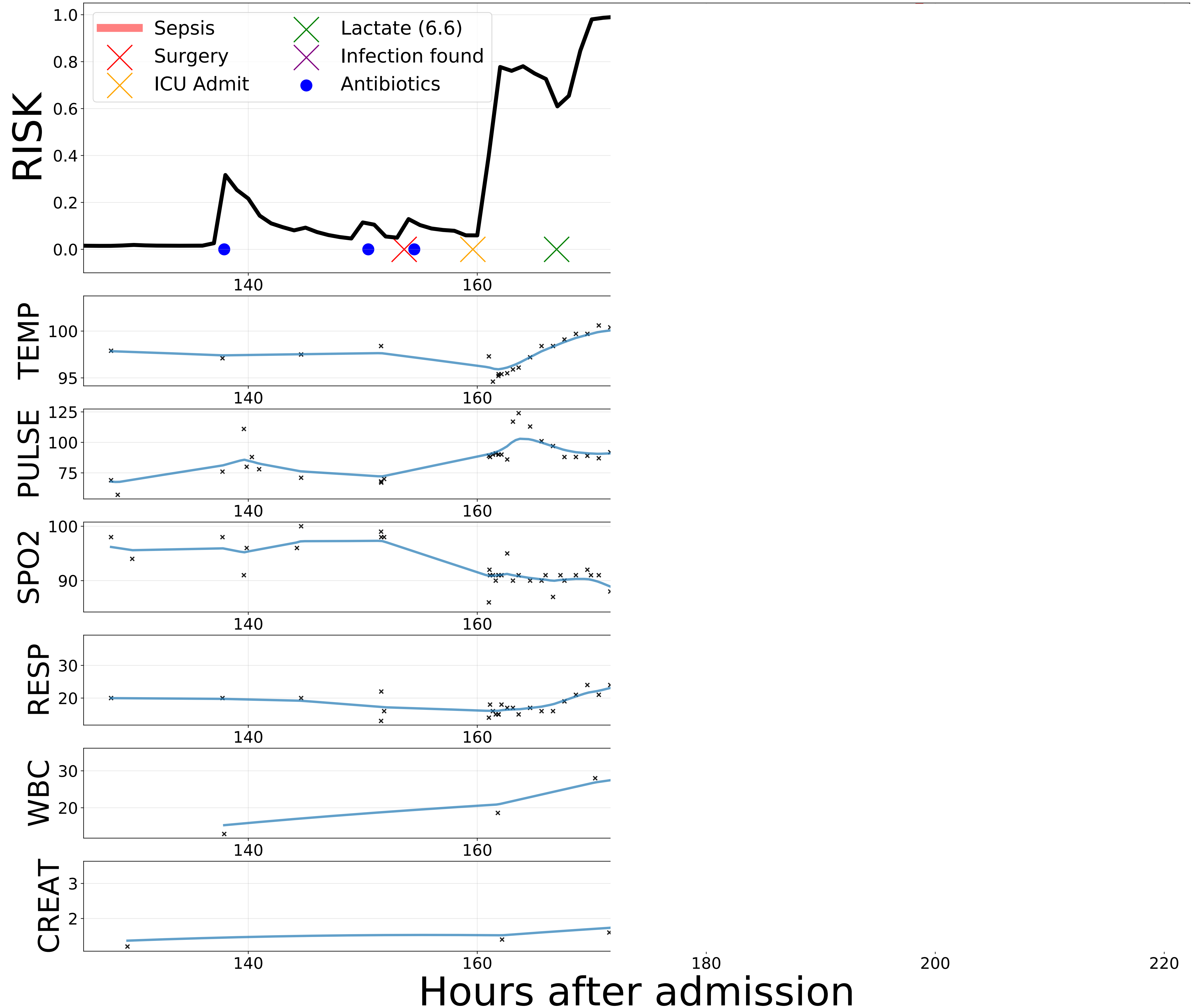

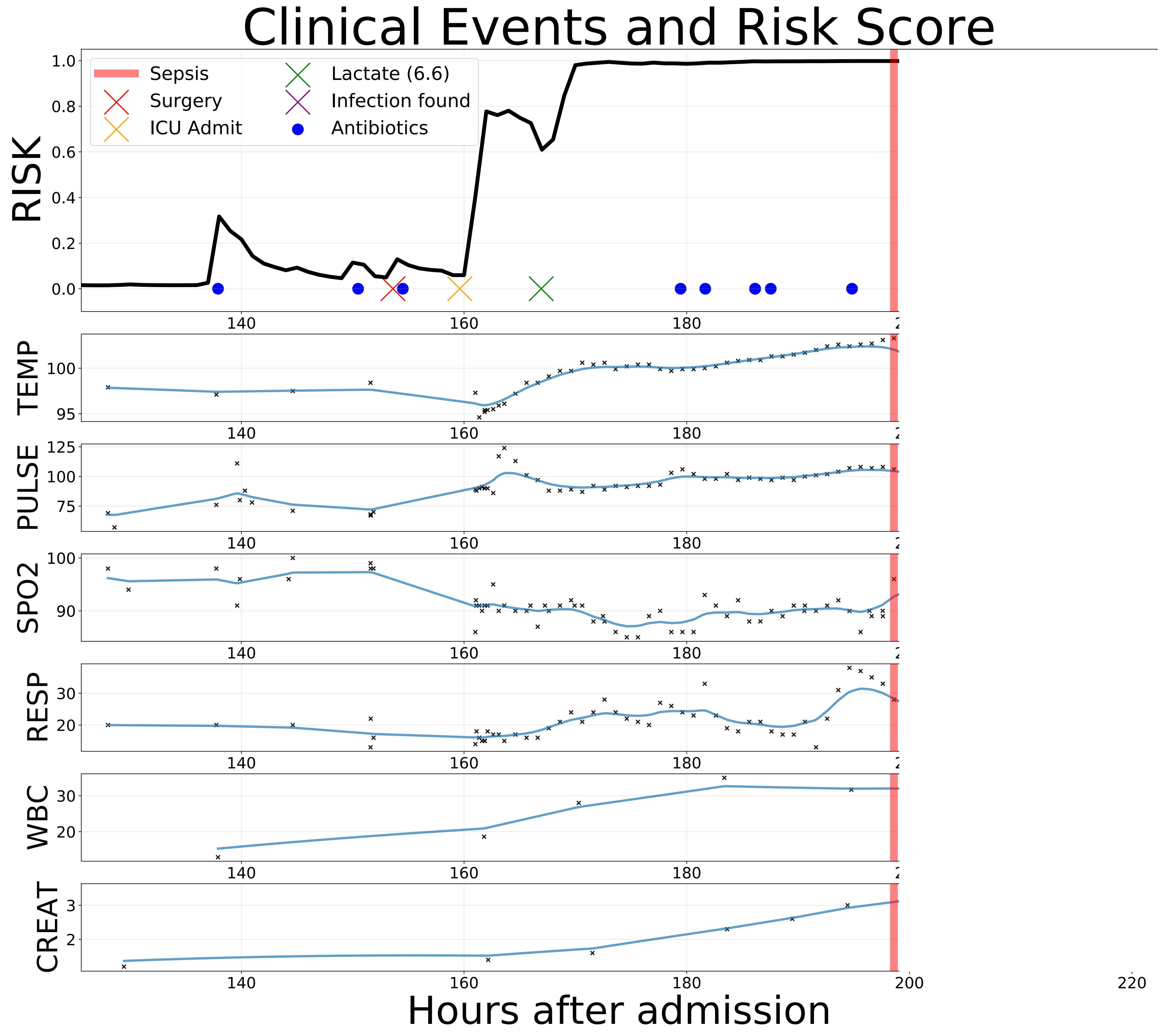

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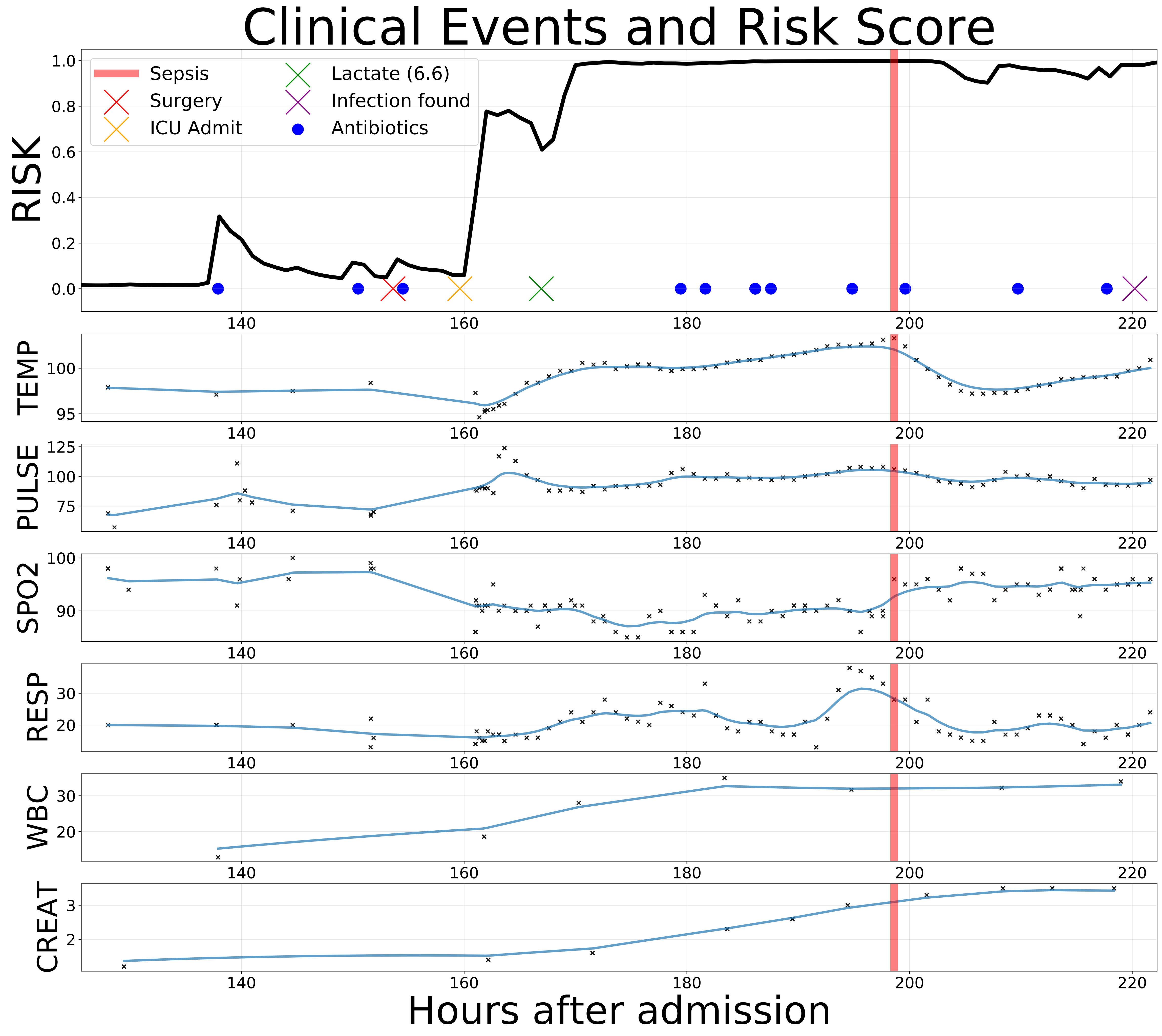

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RISK
Sepsis
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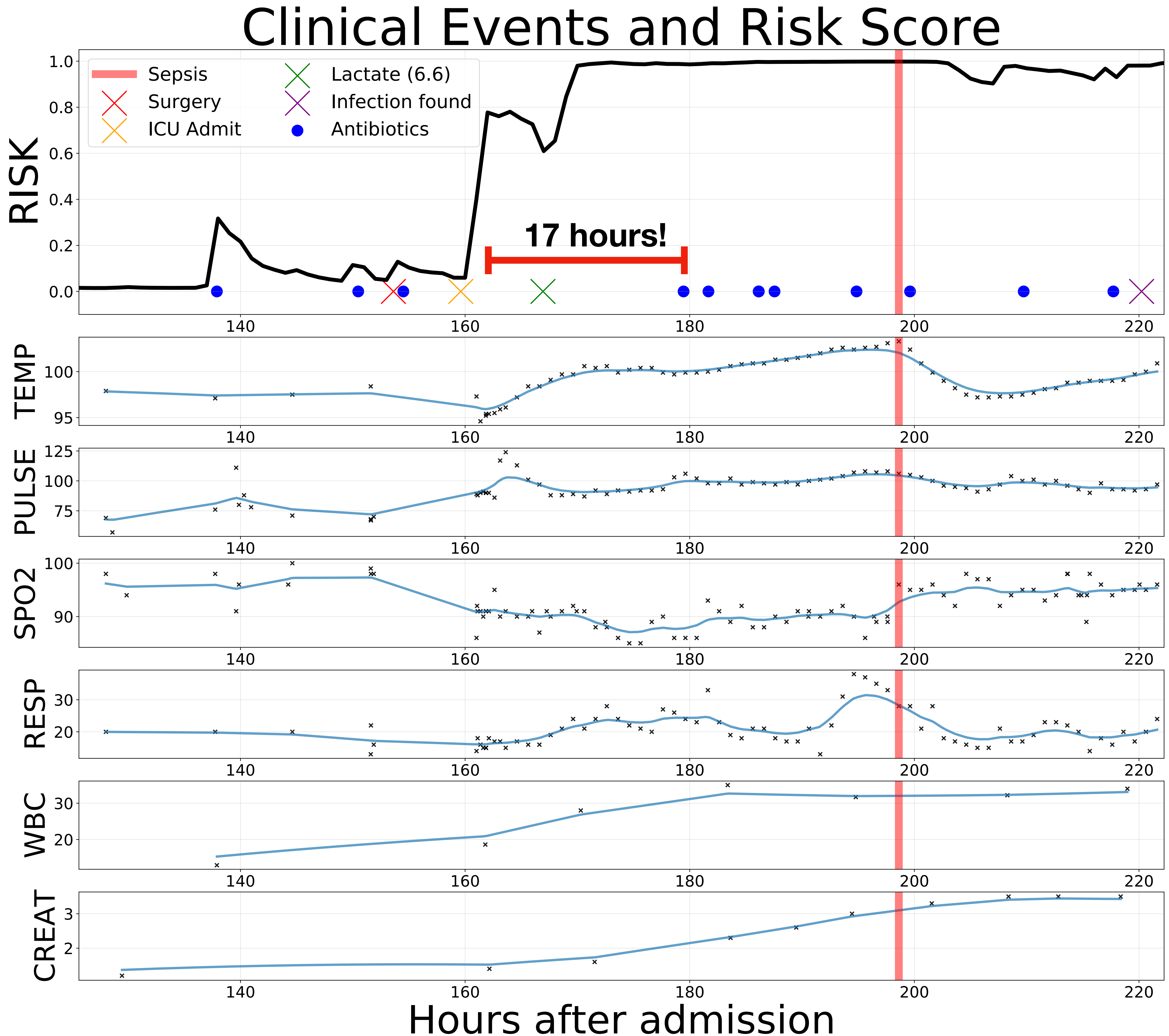
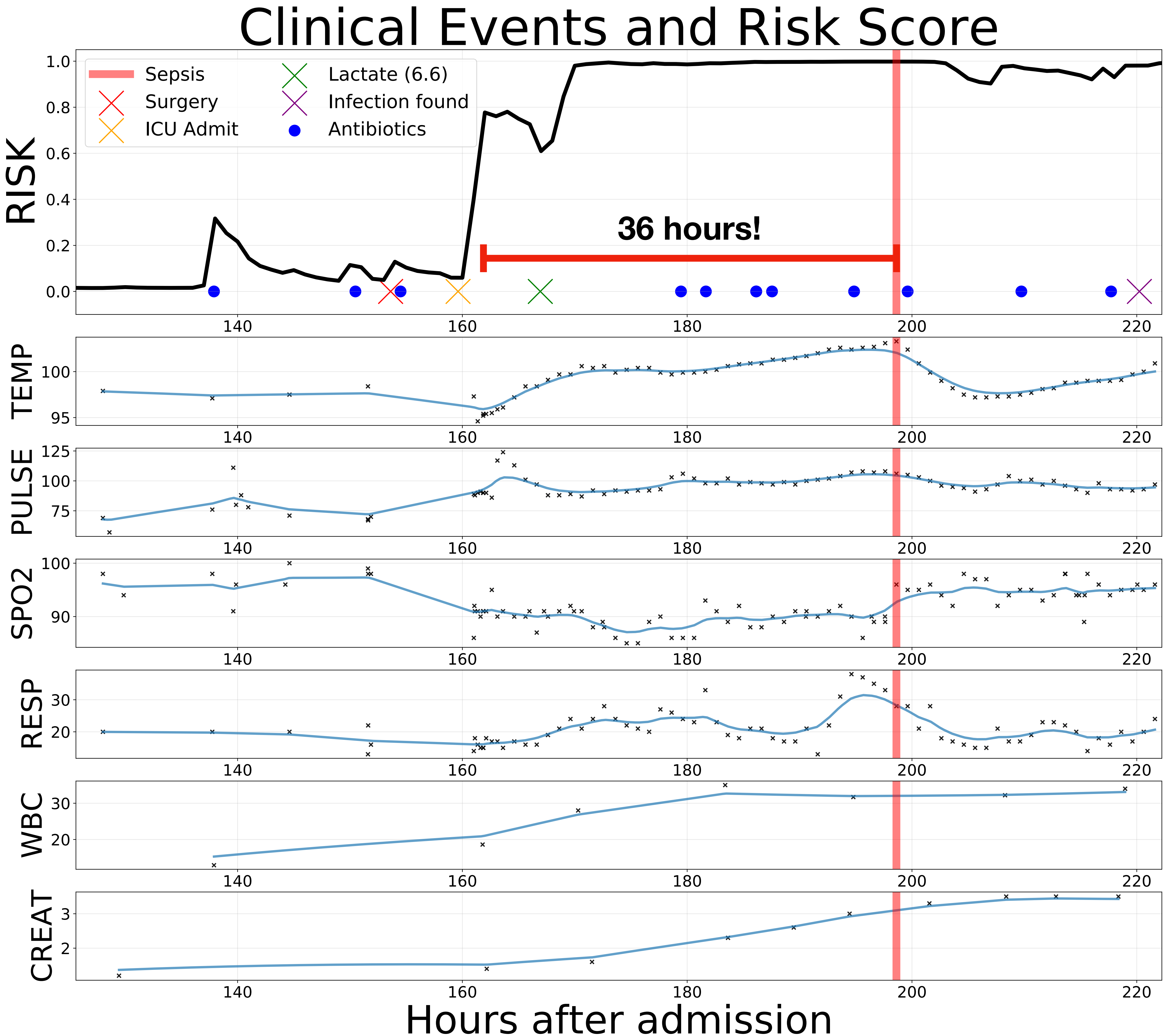


Clinical Events and Risk Score
RISK
Sepsis
Surgery
ICU Admit
Lactate (6.6)
Infection found
Antibiotics
17 hours!
TEMP
PULSE
SPO2
RESP
WBC
CREAT
Hours after admission



Clinical Events and Risk Score
Sepsis
Surgery
ICU Admit
Lactate (6.6)
Infection found
Antibiotics
36 hours!
RISK
TEMP
PULSE
SPO2
RESP
WBC
CREAT
Hours after admission

MGP-RNNs

Related Works

- Clinical Early Warning Scores, e.g. NEWS, SIRS, MEWS, Apache II.
  - NEWS at Duke: 63.4% of triggered alerts cancelled by nurse; avg. of 447 alerts/day on only 42 patients!
  - Broad, not targeted for particular conditions.
  - Low precision, leading to **high alarm fatigue**.
- (Henry et al, Science Translational Medicine 2015): TREWS score: Cox regression to predict time to septic shock, using 54 potential features.
- (Ghassemi et al, AAAI 2015): Use MGPs for modeling multivariate physiological time series data from the ICU.
- (Cheng-Xian & Marlin, NIPS 2016): “GP-adapter” for classifying univariate irregularly spaced time series, of the same fixed length.
- More recent papers as well:
  - (Chung et al 2018): Mixed Effect Composite RNN-GP: A Personalized and Reliable Prediction Model for Healthcare
  - (Heo et al 2018): Uncertainty-Aware Attention for Reliable Interpretation and Prediction

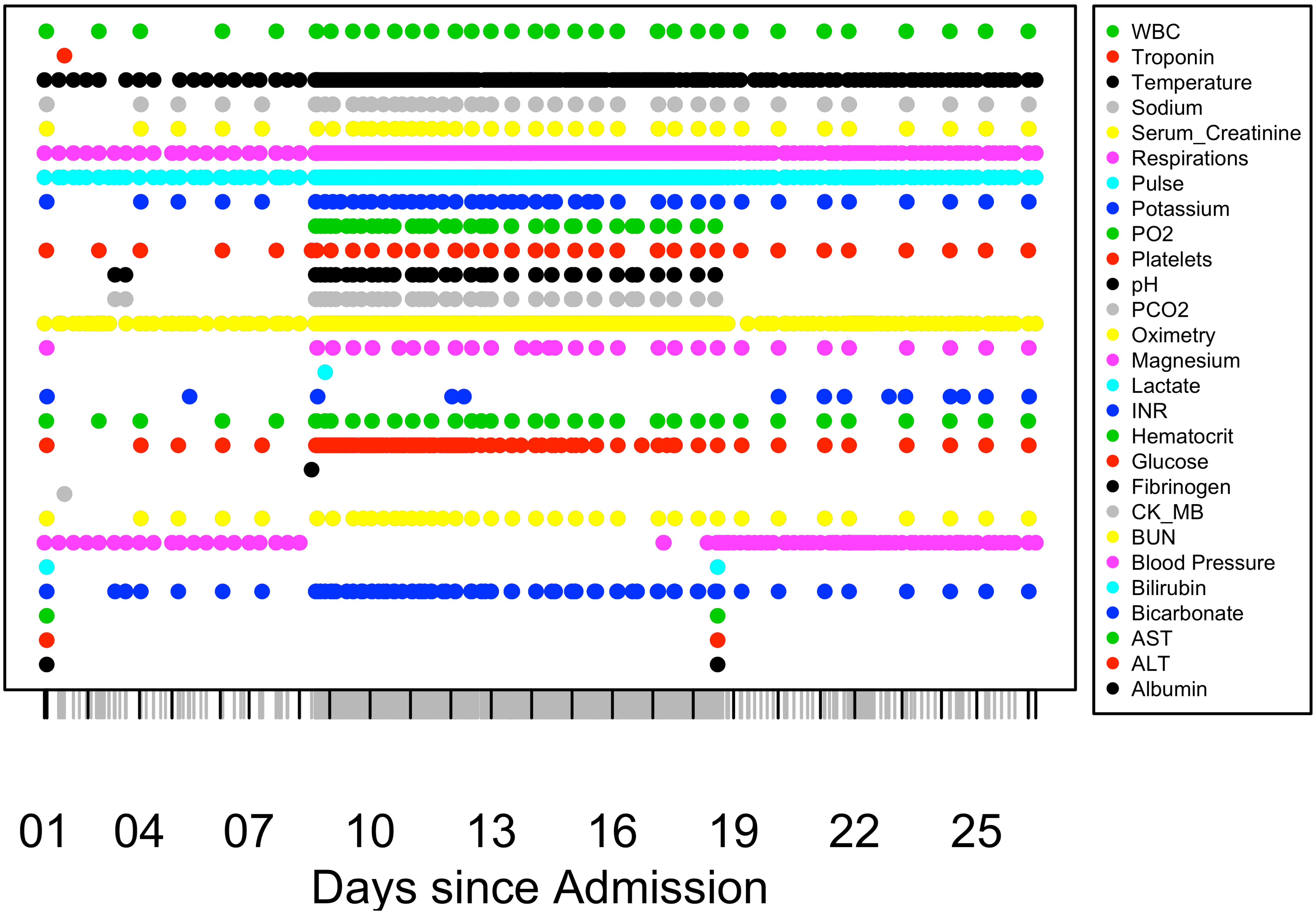
Early Warning Scores

National Early Warning Score (NEWS)*

PHYSIOLOGICAL PARAMETERS	3	2	1	0	1	2	3
Respiration Rate	≤8		9 - 11	12 - 20		21 - 24	≥25
Oxygen Saturations	≤91	92 - 93	94 - 95	≥96			
Any Supplemental Oxygen		Yes		No			
Temperature	≤35.0		35.1 - 36.0	36.1 - 38.0	38.1 - 39.0	≥39.1	
Systolic BP	≤90	91 - 100	101 - 110	111 - 219			≥220
Heart Rate	≤40		41 - 50	51 - 90	91 - 110	111 - 130	≥131
Level of Consciousness				A			V, P, or U

Can we do better?

Missingness in Motivating Example



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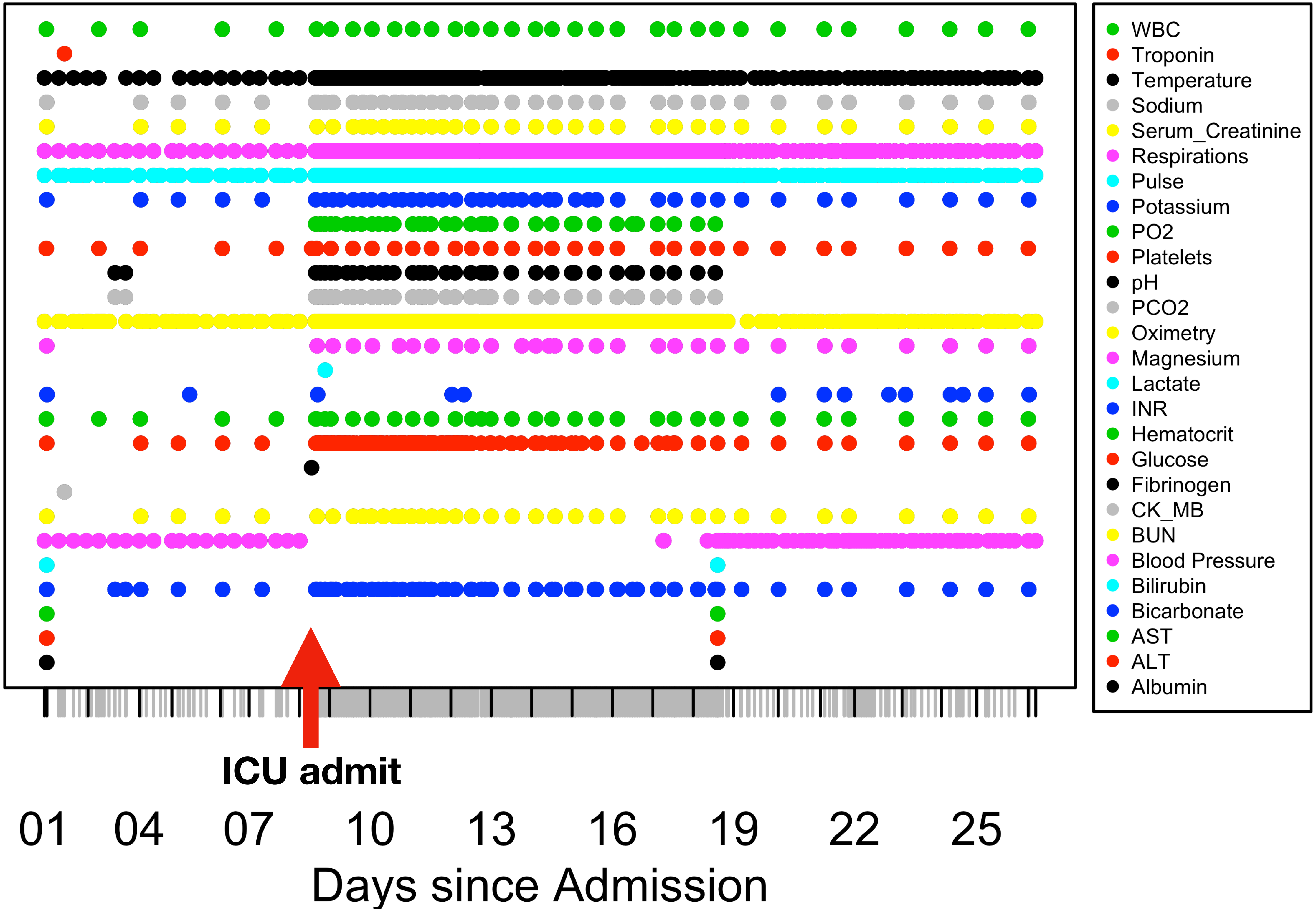
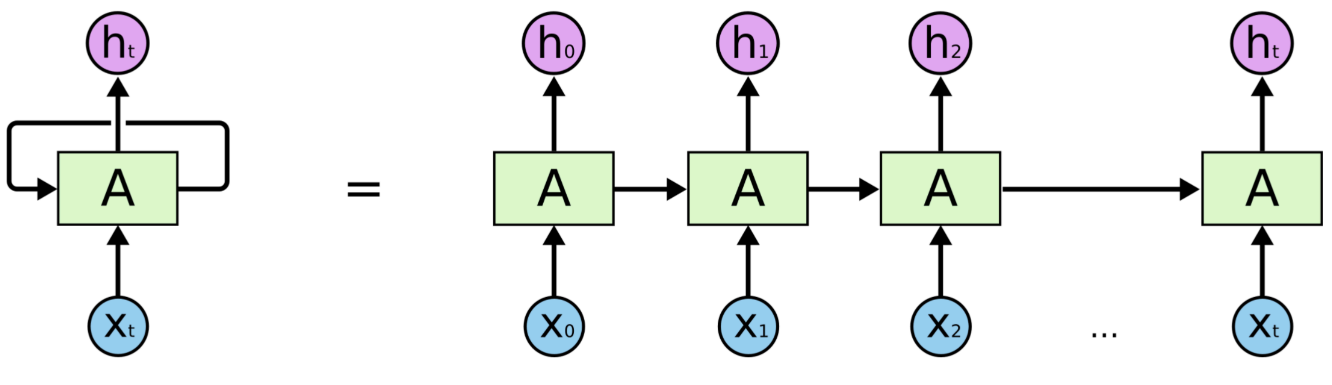


Model Main Idea

- Goal: detect onset of sepsis before it occurs.
- Data:
    1. Physiological time series (labs/vitals).
    2. Baseline admission info/comorbidities.
    3. Medication administration times.
- Multivariate time series classification: update a risk score (probability encounter is / will become septic).
- **<u>Recurrent Neural Networks (RNNs)</u>**: flexible functions, rich representational power for sequences of arbitrary length. But:
    - Requires a **complete** dataset with no missing values.
    - Requires **regularly** spaced inputs.
- **<u>Multi-output Gaussian Processes</u>**: model for multivariate time series.
    - Seamlessly handles **irregularly** spaced observation times.
    - Imputes missing values on a regular grid, along with an estimate of **<u>uncertainty</u>**.



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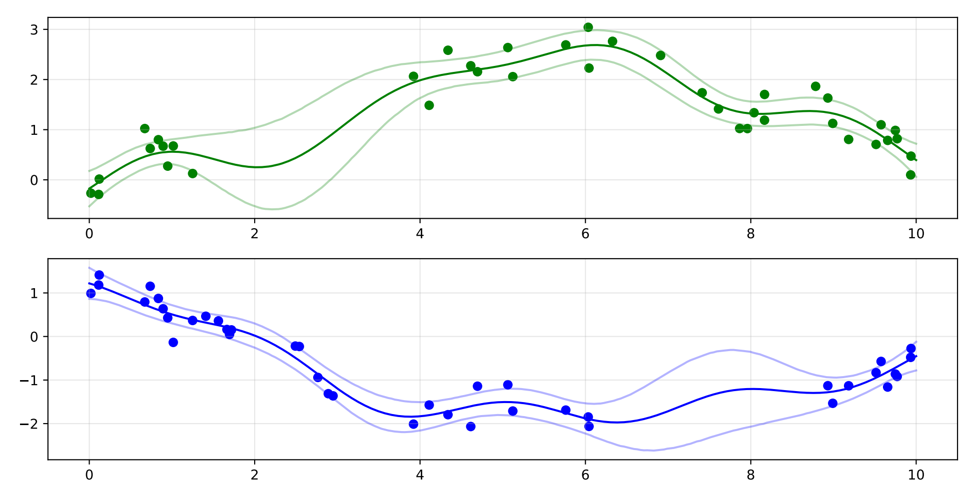
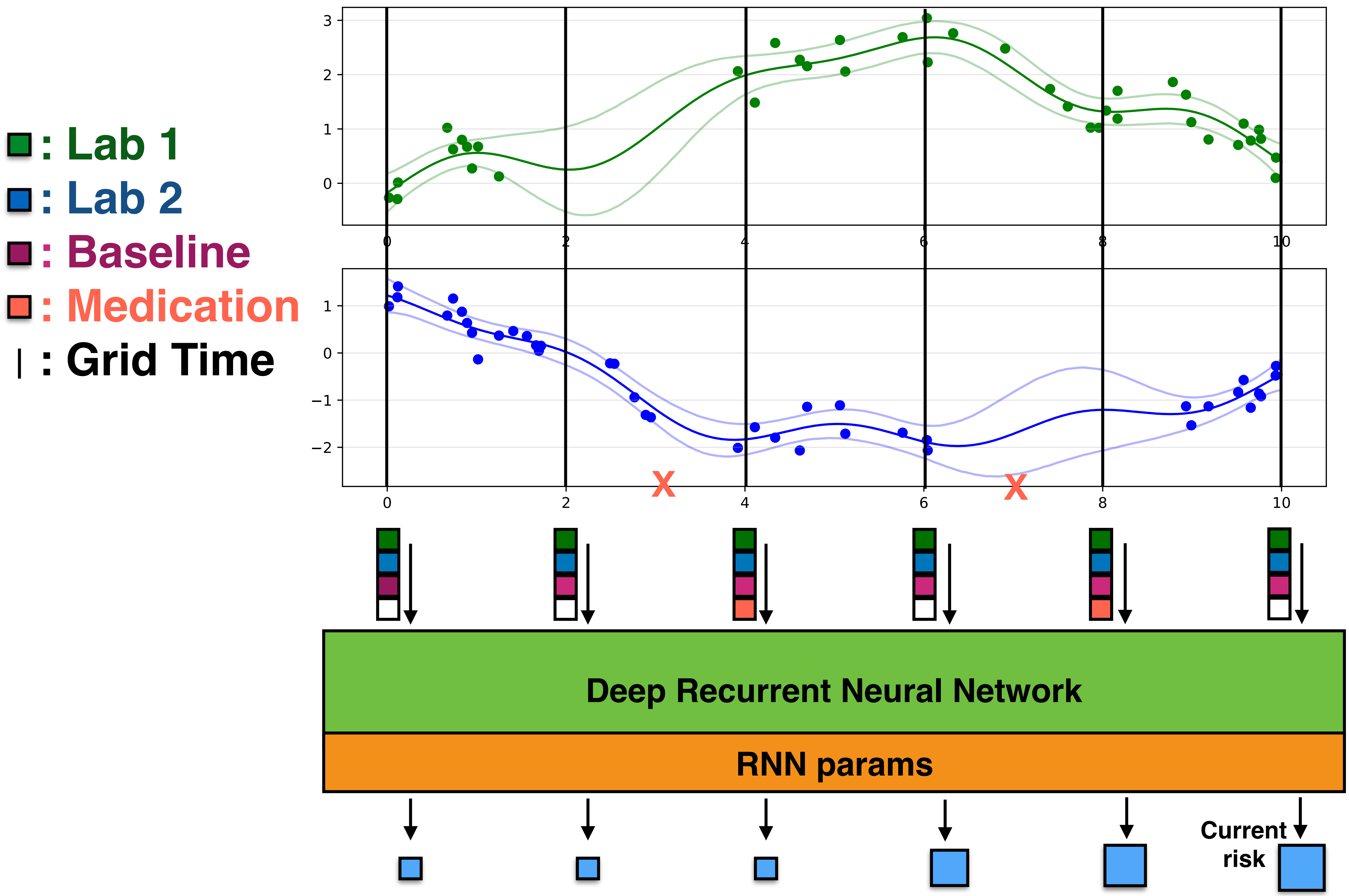


<u>Futoma</u>, Hariharan, Heller
ICML 2017

Model Schematic



MGP Overview

- **Gaussian process**: prior distribution over functions:

$$f_i(t) \sim \mathcal{GP}(\mu(t), K(t, t'))$$

"True" function value at time t

Observation times

T_i x T_i covariance matrix

$$\mathbf{t}_i = (t_{i1}, \ldots, t_{iT_i})$$

$$f_i(\mathbf{t}_i) \sim \mathcal{N}(\mu(\mathbf{t}_i), K(\mathbf{t}_i, \mathbf{t}_i))$$

Mean function (0)

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- **Multitask GP**: extension to multivariate time series.

"True" value, patient *i*, variable *m*, time *t*

M x M covariance matrix, between variables

$k^t(t,t') = e^{-|t-t'|}$

Correlation function, between observation times

$$\mathrm{cov}(f_{im}(t), f_{im'}(t')) = K^M_{mm'} k^t(t,t')$$

Observed value, patient *i*, variable *m*, time *t*

$$y_{im}(t) \sim \mathcal{N}(f_{im}(t), \sigma^2_m)$$

Noise level, variable *m*

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(Completely observed)
M time series, T_i x M matrix

$$\mathrm{vec}([\mathbf{y}_{i1}, \mathbf{y}_{i2}, \ldots, \mathbf{y}_{iM}]) \equiv \mathbf{y}_i \sim \mathcal{N}(\mathbf{0}, \Sigma_i)$$
$$\Sigma_i = K^M \otimes K^{T_i} + D \otimes I,$$

T_i x T_i correlation matrix

M x M diagonal matrix, noise levels

(In practice, only evaluate this at observed measurements)

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- Define some regularly spaced (e.g. every hour) reference times, shared across all encounters.

X_i shared reference times $\rightarrow$ $\mathbf{x}_i = (x_{i1}, x_{i2}, \ldots, x_{iX_i})$

$$\text{vec}(\mathbf{Z}_i) \equiv \mathbf{z}_i$$

X_i x M matrix, latent values at **x**_i

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Given **y**_i, conditional normal posterior:

X_i x T_i correlation matrix

$$\mu_{z_i} = (K^M \otimes K^{X_i T_i})\Sigma_i^{-1}\mathbf{y}_i$$
$$\Sigma_{z_i} = (K^M \otimes K^{X_i}) - (K^M \otimes K^{X_i T_i})\Sigma_i^{-1}(K^M \otimes K^{T_i X_i})$$

X_i x X_i correlation matrix

- MGP posterior for Z_i: the M labs at X_i times, maintains **uncertainty**.

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$$p(\mathbf{z}_i | \mathbf{y}_i, \theta)$$

MGP parameters to learn, shared across all encounters

$$\theta = (K^M, \{\sigma^2_m\}^M_{m=1}, l)$$

$$\mu_{z_i} = (K^M \otimes K^{X_i T_i}) \Sigma_i^{-1} \mathbf{y}_i$$
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MGP-RNN

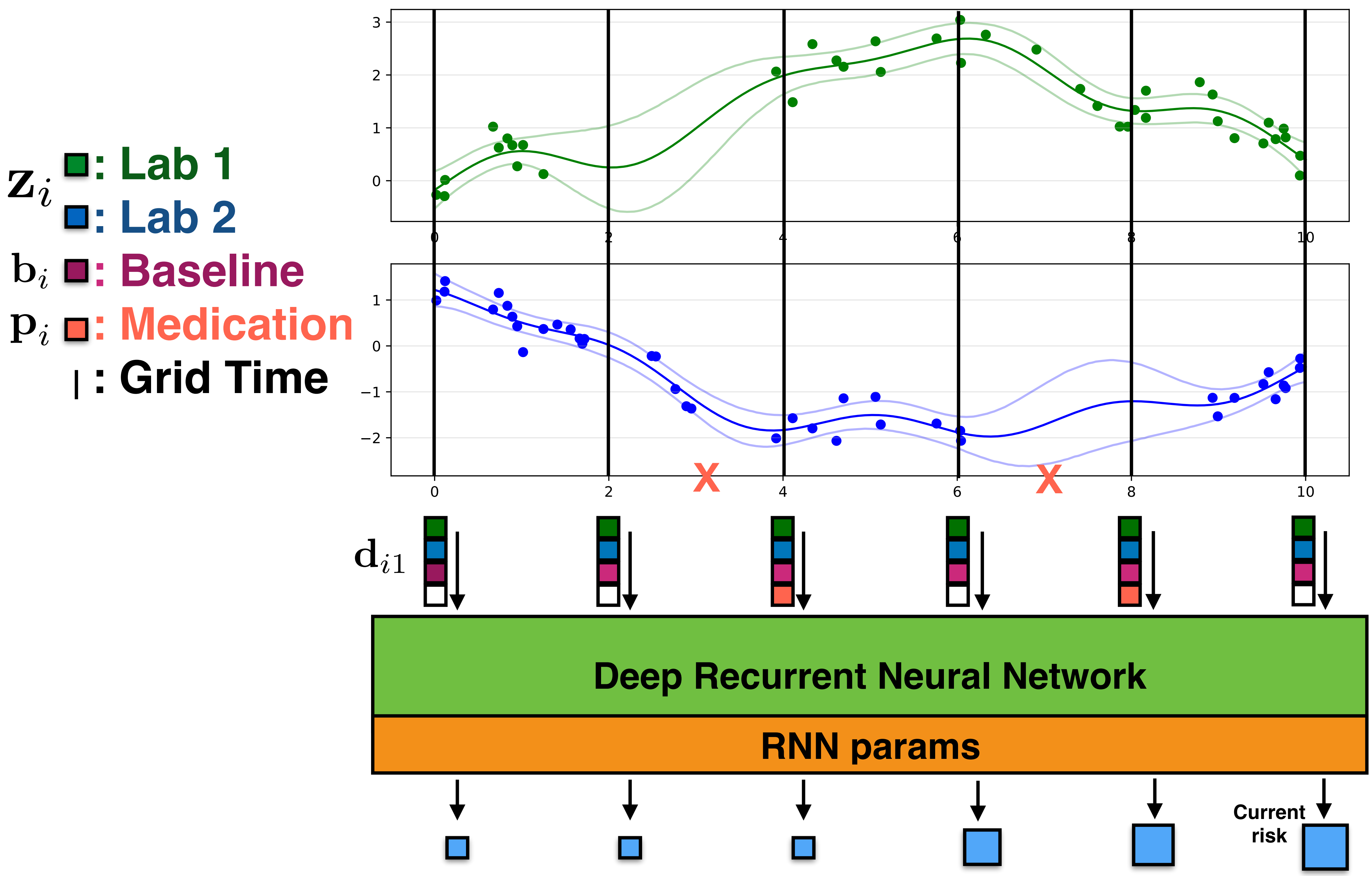
- RNN input: latent values Z_i, baseline covariates, medication indicators.

$$\mathbf{d}_{ij} = [\mathbf{z}_{ij}^\top, \mathbf{b}_i^\top, \mathbf{p}_{ij}^\top]^\top$$

Latent series values

Baseline Covariates

Medications Indicators



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- To learn RNN parameters: optimize loss comparing model predictions to true label.

$$\text{Loss} \rightarrow l(\overset{\substack{\text{RNN prediction}\\\downarrow}}{f}(\underset{\substack{\uparrow\\\text{RNN input matrix}}}{\mathbf{D}_i}; \underset{\substack{\uparrow\\\text{RNN Parameters}}}{\mathbf{w}}), \overset{\text{label}}{o_i})$$

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- Instead, optimize expected loss with respect to MGP posterior on **z**_i. Overall learning problem:

$$\boxed{\mathbf{w}^*, \theta^* = \text{argmin}_{w,\theta} \sum_{i=1}^{N} \mathbb{E}_{z_i \sim N(\mu_{z_i}, \Sigma_{z_i}; \theta)}[l(f(\mathbf{D}_i; \mathbf{w}), o_i)]}$$

Learn MGP parameters discriminatively!

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stochasticity from sampling appears to help with overfitting

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Uncertainty for inputs (physiological time series) propagated through to outputs

Risk score for new patient *i'*

$$\boxed{\mathbb{E}_{z_{i'} \sim N(\mu_{z_{i'}}, \Sigma_{z_{i'}}; \theta^*)} [f(\mathbf{D}_{i'}; \mathbf{w}^*)]}$$

Learning & Computation

- End-to-end learning of MGP, RNN with reparameterization trick for MGP
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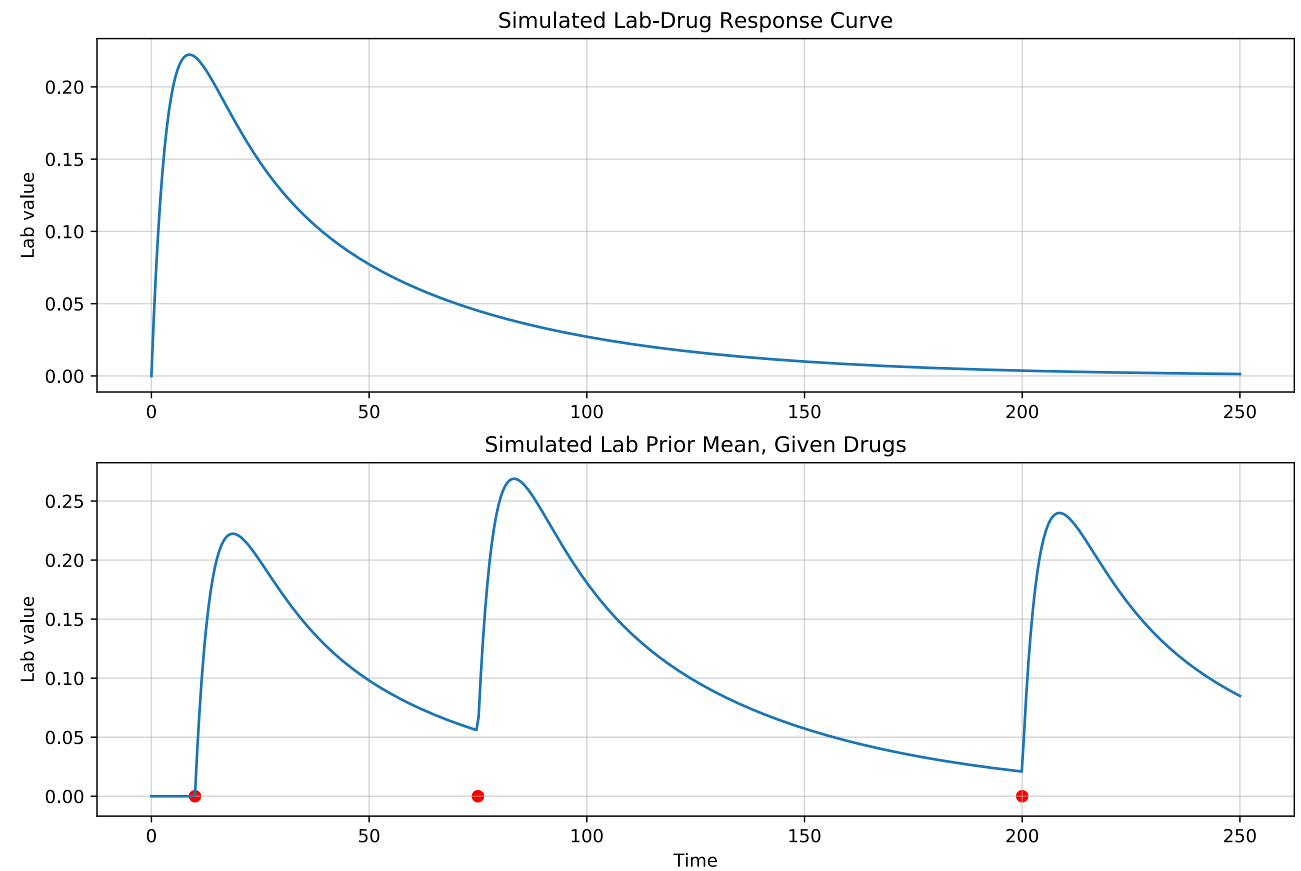
  - One option: Cholesky decomposition (R lower triangular), but cubic complexity to compute
  - Another option: use matrix square root, $\Sigma_z^{1/2}$
- Lanczos method: iterative method to approximate $\Sigma_z^{1/2}\xi, \;\; \xi \sim N(0, I)$ **(Chow & Saad, SIAM SISC 2014)**
- Conjugate gradient: related iterative method for solving linear systems with symmetric, positive definite matrices. Use to approximate matrix-vector products $\Sigma_i^{-1}\mathbf{v}$ (in computing μ_{z_i} and $\Sigma_{z_i}\mathbf{v}$)
- Backprop **through** Lanczos / conjugate gradient / Cholesky

Improving the MGP

- More flexible mean function: extend zero-mean prior means to depend on administration of drugs.

$$\mu_m(t) = \sum_{p=1}^{P} \sum_{t_p<t} f_{pm}(t - t_p)$$

$$f_{pm}(t) = \sum_{l=1}^{L} \alpha_{lpm} e^{-\beta_{lpm} t}$$



- More flexible kernel: extend separable kernel in Multitask GP (Q=1) to sum of separable kernels (related to Linear Model of Coregionalizaton)

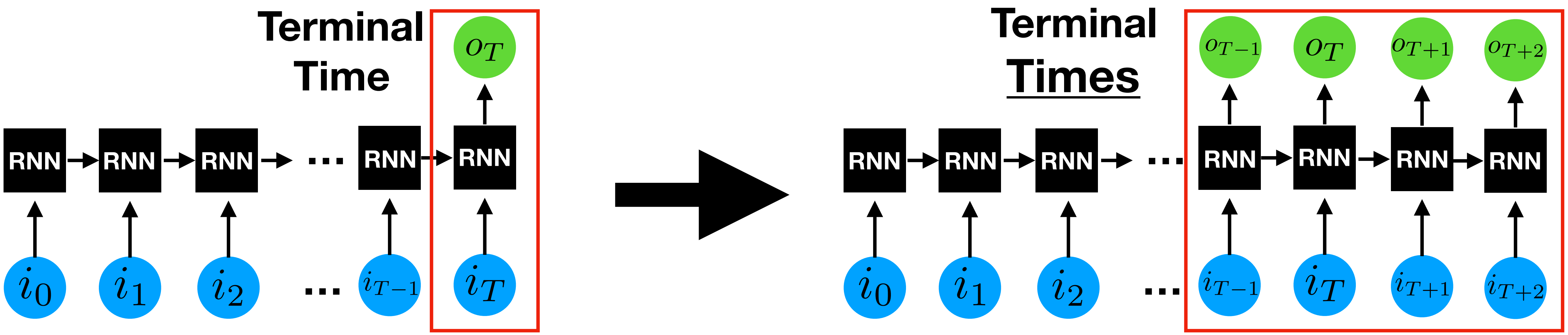
$$\mathrm{cov}(f_{im}(t), f_{im'}(t')) = \sum_{q=1}^{Q} K_q^M(m, m') k_q^t(t, t')$$

-

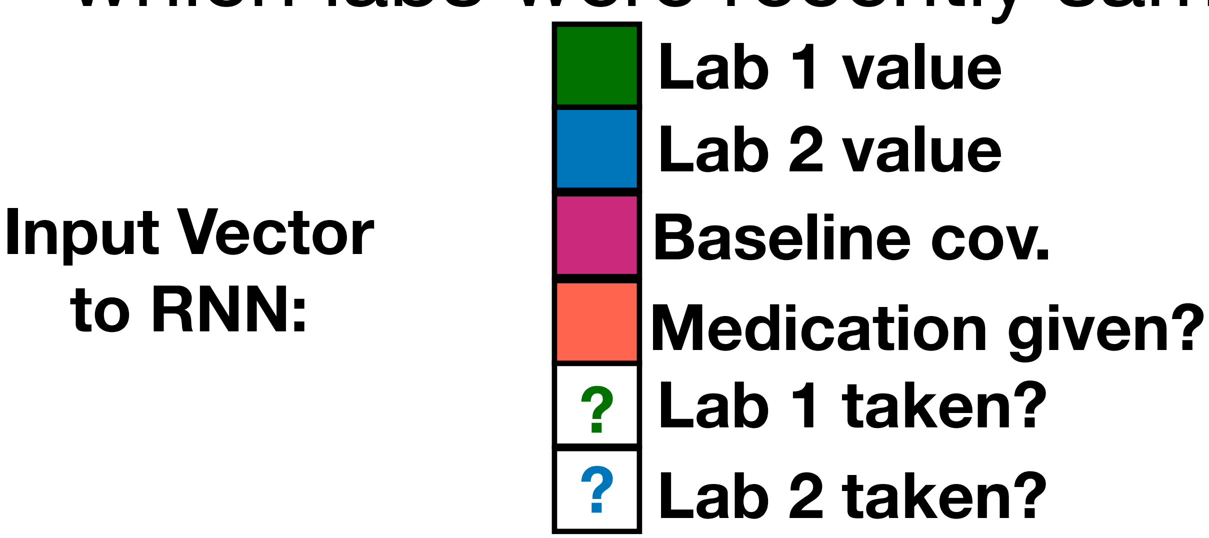
Futoma et al MLHC 2017

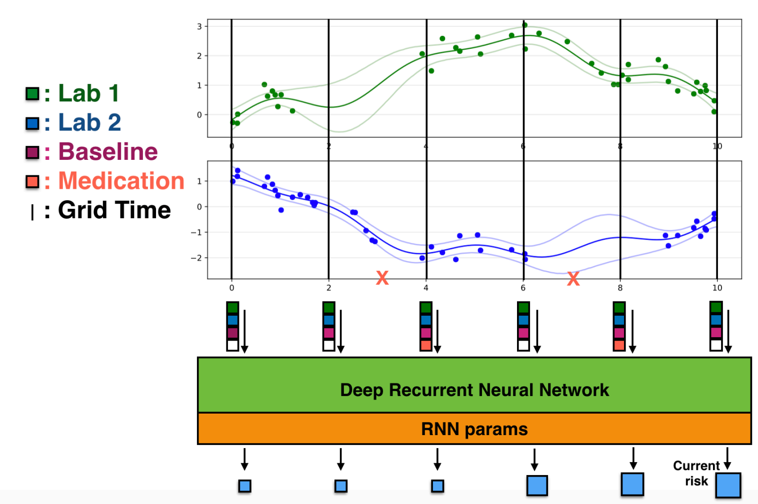
Improving the RNN

- Target replication: classification loss depends on multiple outputs instead of last time point.



- Missingness indicators: directly model pattern of informative missingness in the RNN by passing indicator vector with which labs were recently sampled.





Experiments & Results

Dataset

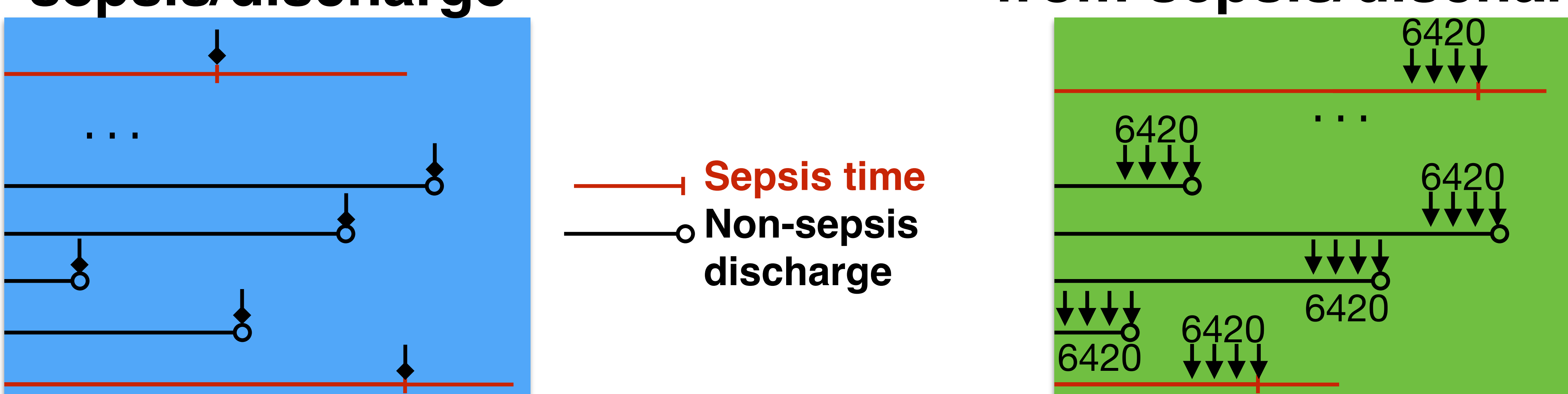
- **49,312** inpatient encounters at Duke Hospital over 18 months, 21.4% with a sepsis event; no specific inclusion/exclusion criteria.
- **34** physiological variables (5 vitals, 29 labs).
  - At least one value for each vital in 99% of encounters.
  - Some labs rarely measured (2-4%), most measured 20-80% of the time.
- **35** baseline covariates (e.g. age, transfer status, comorbidities).
- **10** medication classes (e.g. antibiotics, IV fluids, vasopressors, opioids).
- Mean length of stay 121.7 hours (sd: 108.1); highly variable.

Experimental Setup

- Compare metrics hours in advance of sepsis/discharge:
  - **AU-ROC:** Area under ROC curve / C-statistic.
  - **AU-PR:** Area under Precision Recall curve.
  - **Precision (PPV):** At fixed sensitivity.

Train: up to sepsis/discharge

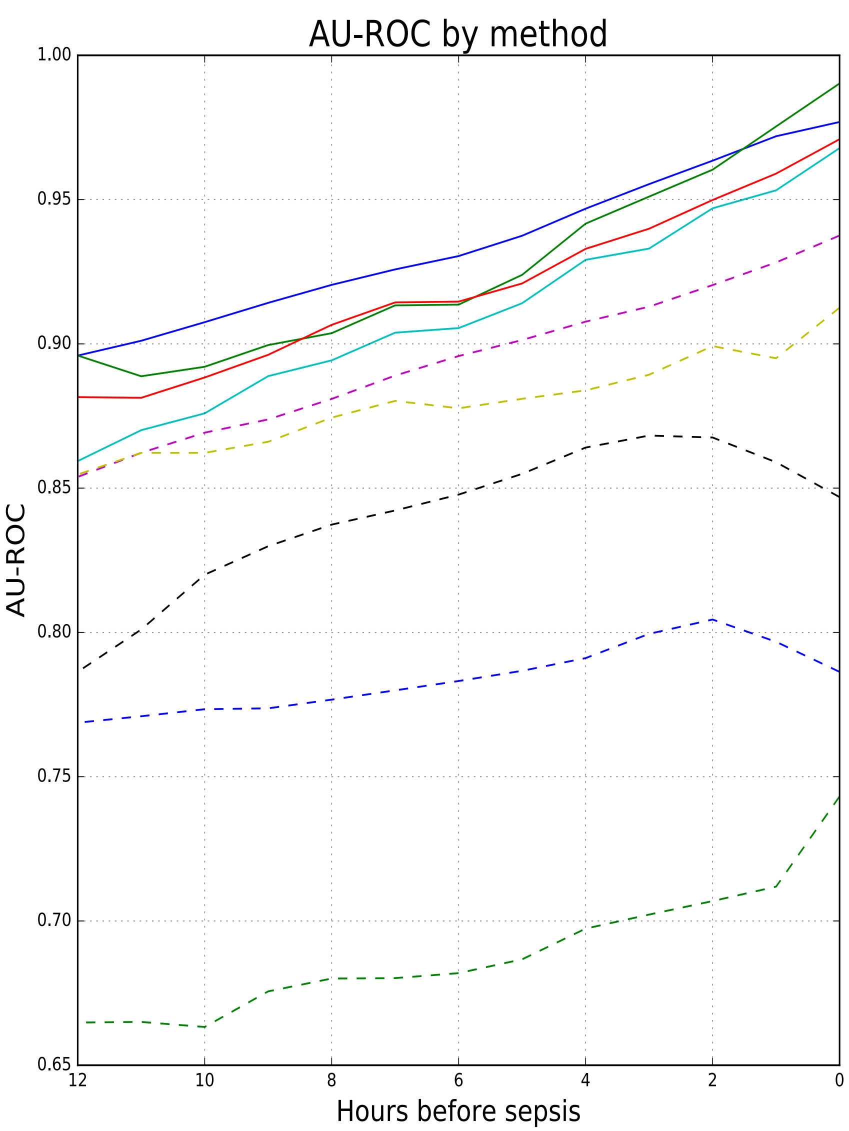
Test: vary # hours from sepsis/discharge

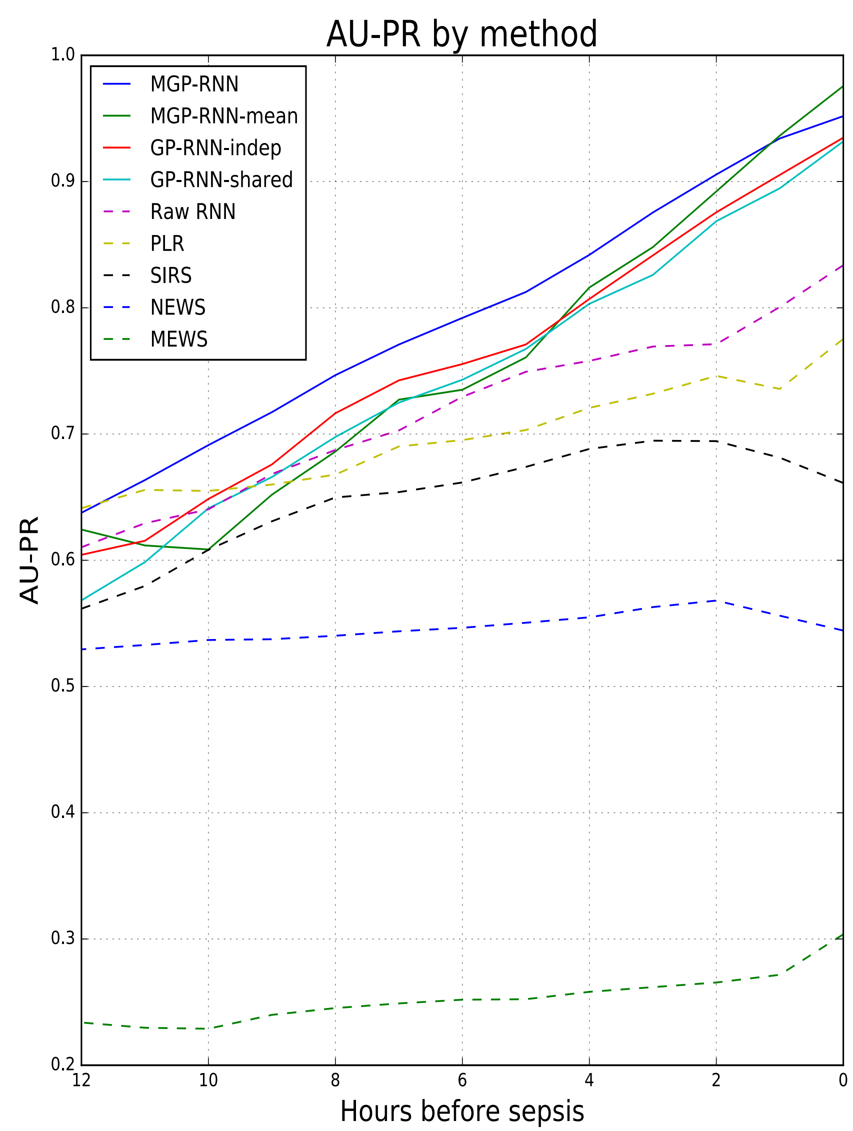


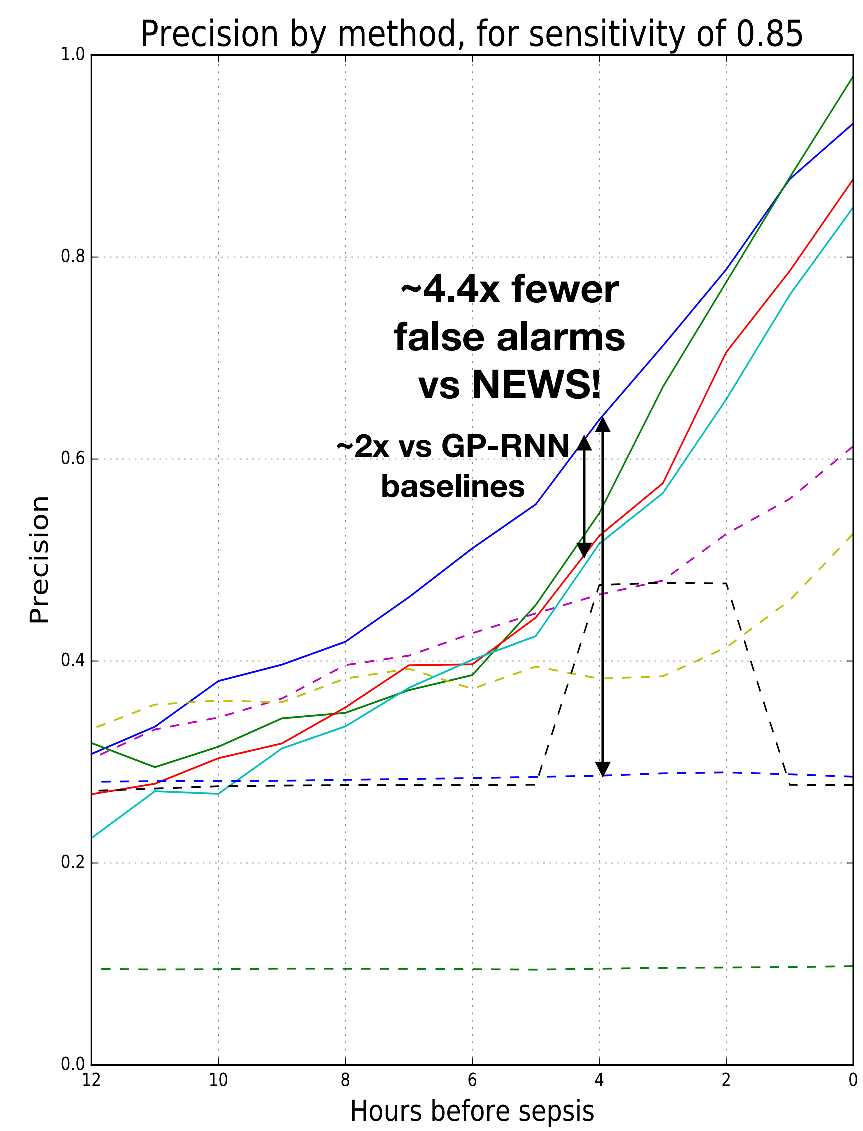
Results

Just μ_z — Different GP for each var — Different GP for each var; Shared length scale

- **MGP-RNN**, **MGP-RNN-mean**, **GP-RNN-indep**, **GP-RNN-shared:** variations on our approach [solid colors]
- **Raw RNN**: trained on raw data with no GP (missing: carry forwards last observed value)
- **PLR**: Penalized logistic regression, same imputation as Raw RNN
- **SIRS**, **NEWS**, **MEWS**: clinical scores

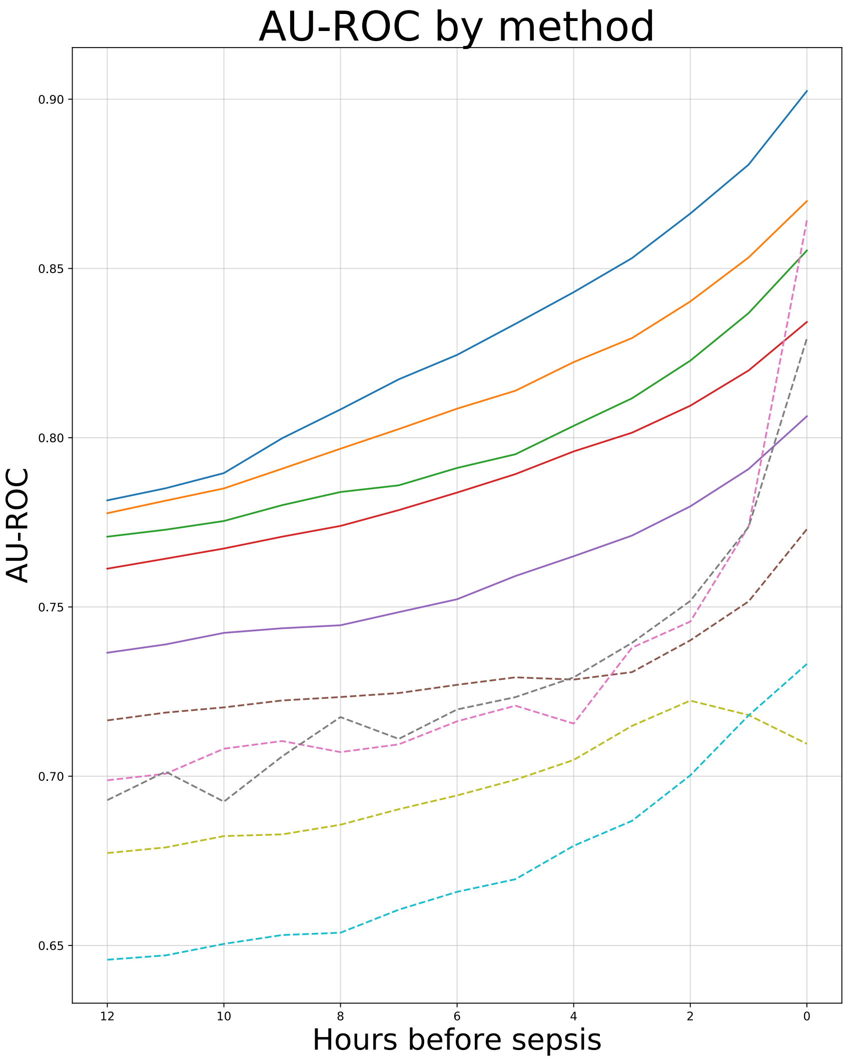


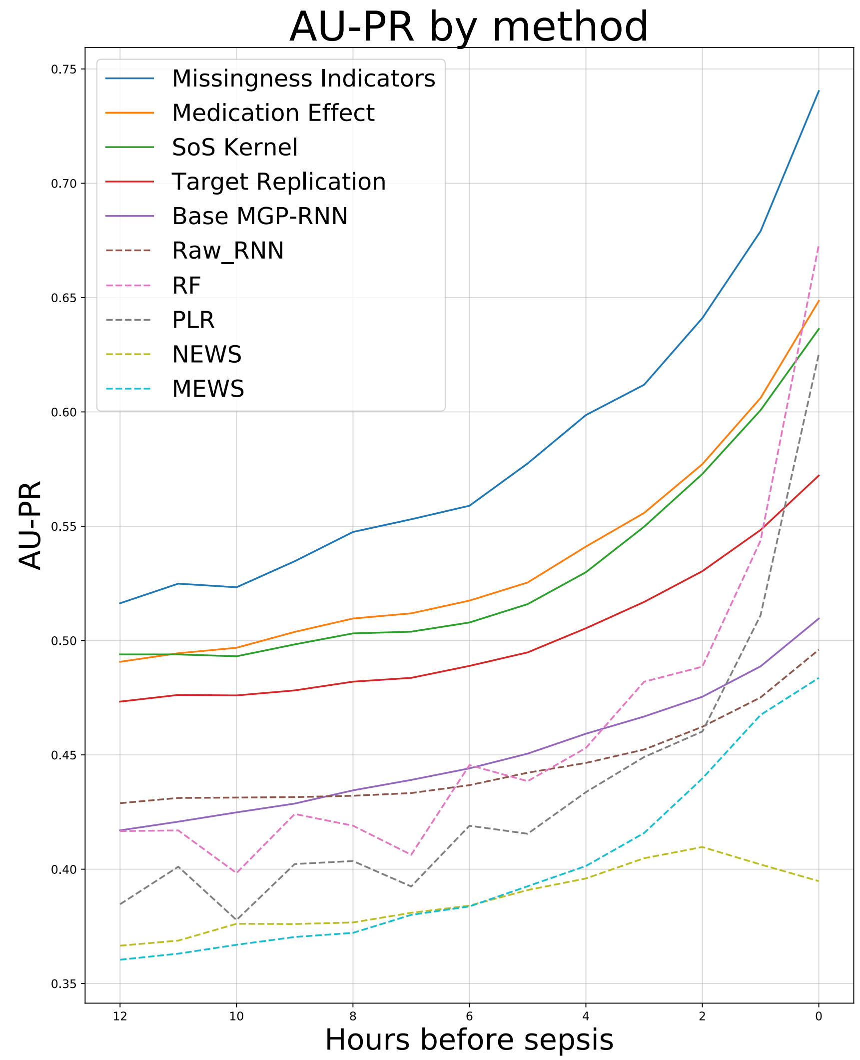


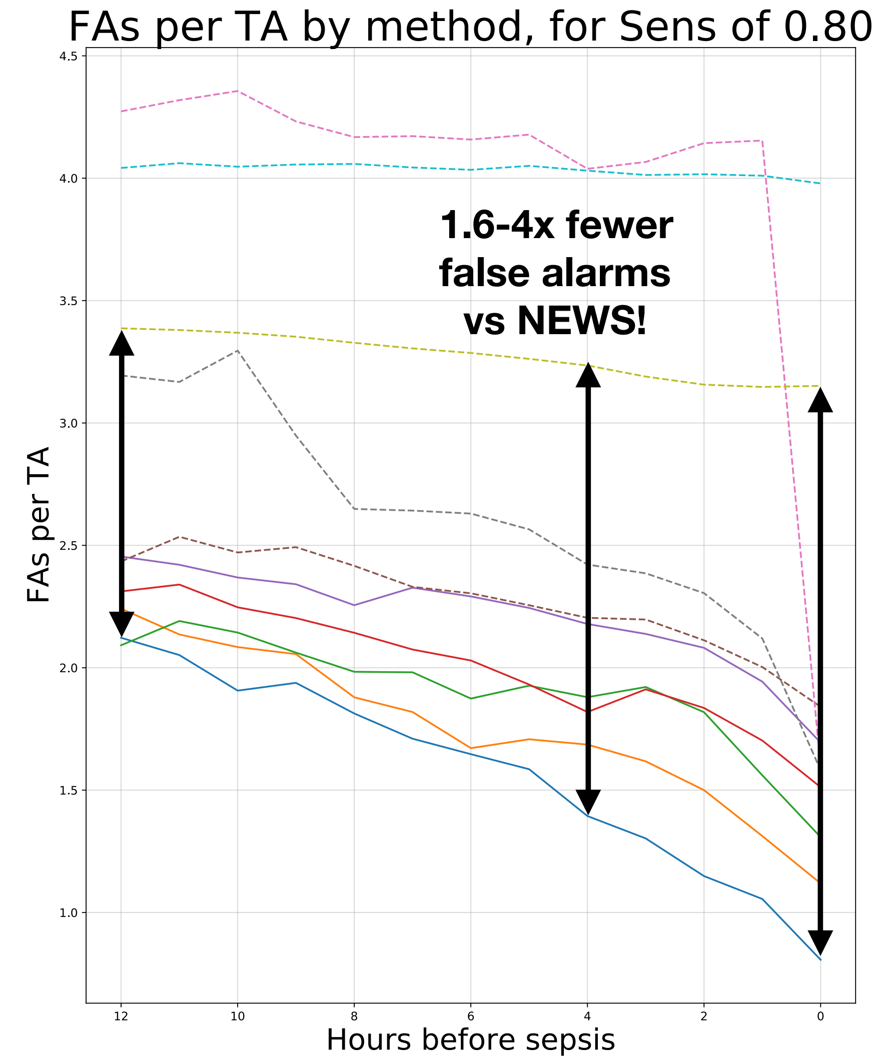


Additional Results

- **Solid lines:** 5 MGP-RNN versions, adding in each extension sequentially.
    - Base; Target replication; SoS kernel; Med effects; Missing Indicators
- **Dashed lines:** RNN, Random Forest, Penalized Logistic Regression (impute with last observation carried forward); NEWS, MEWS clinical scores

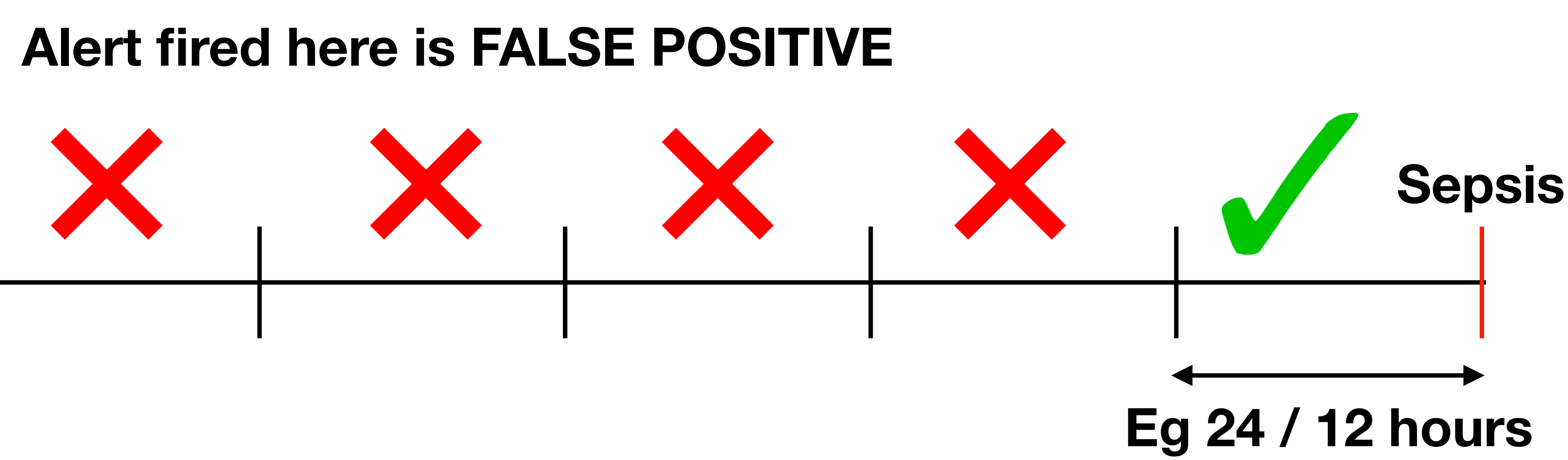


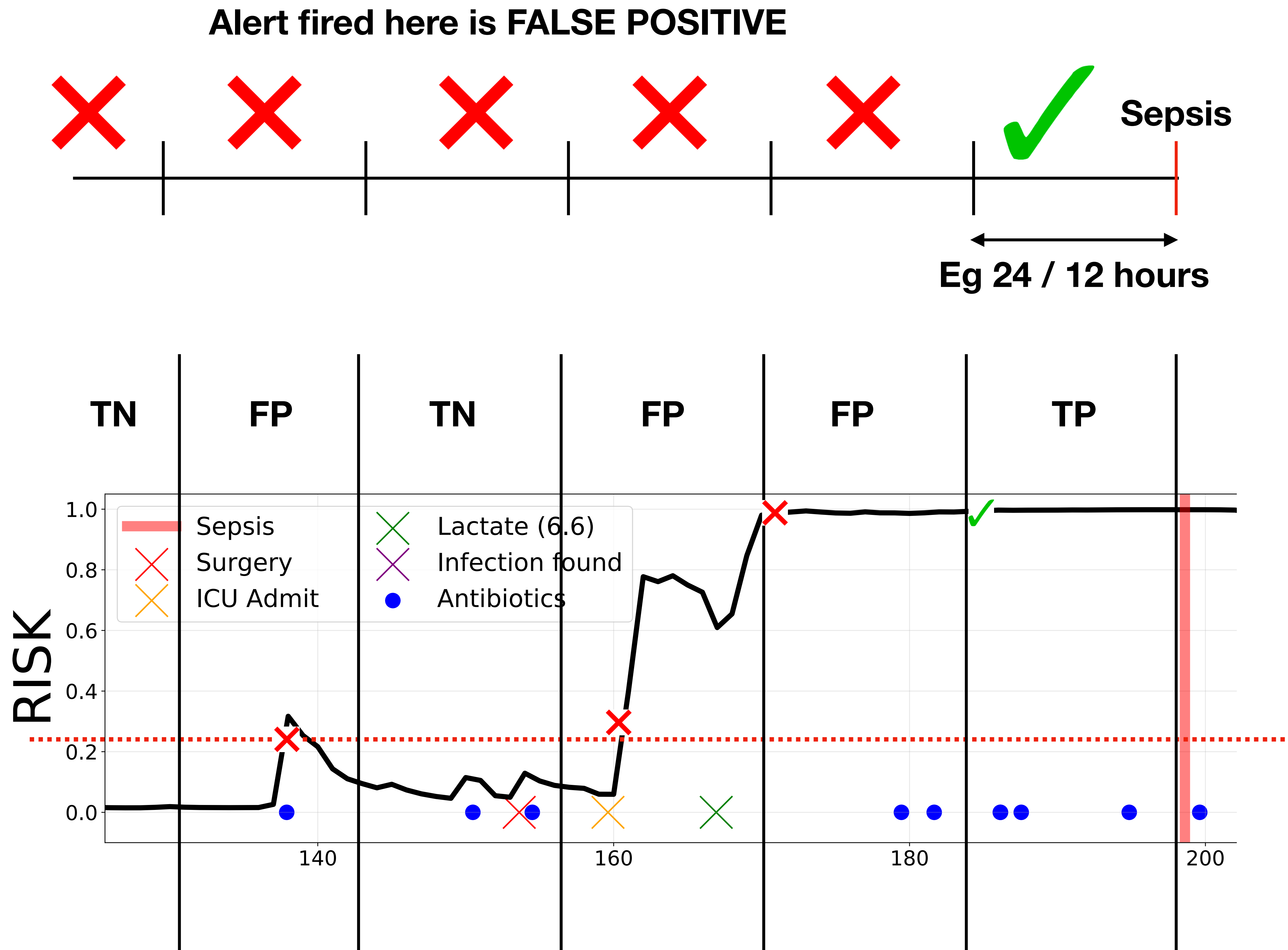




“Real-time” Validation

- More closely mimics actual use case
- More accurate estimate of what this might look like in real setting
- Better penalize alerts fired off way too early
- Ignore encounters septic within first hour (can’t detect that any earlier than definition would)
- We’re looking at risk score **only** before time of sepsis; if model hasn’t caught it by that time, the definition would kick in and catch it anyways
    - This is to catch cases where model only picks up on sepsis after definition is met; at which point it’s not actually helpful
- Metrics will depend on this window size!

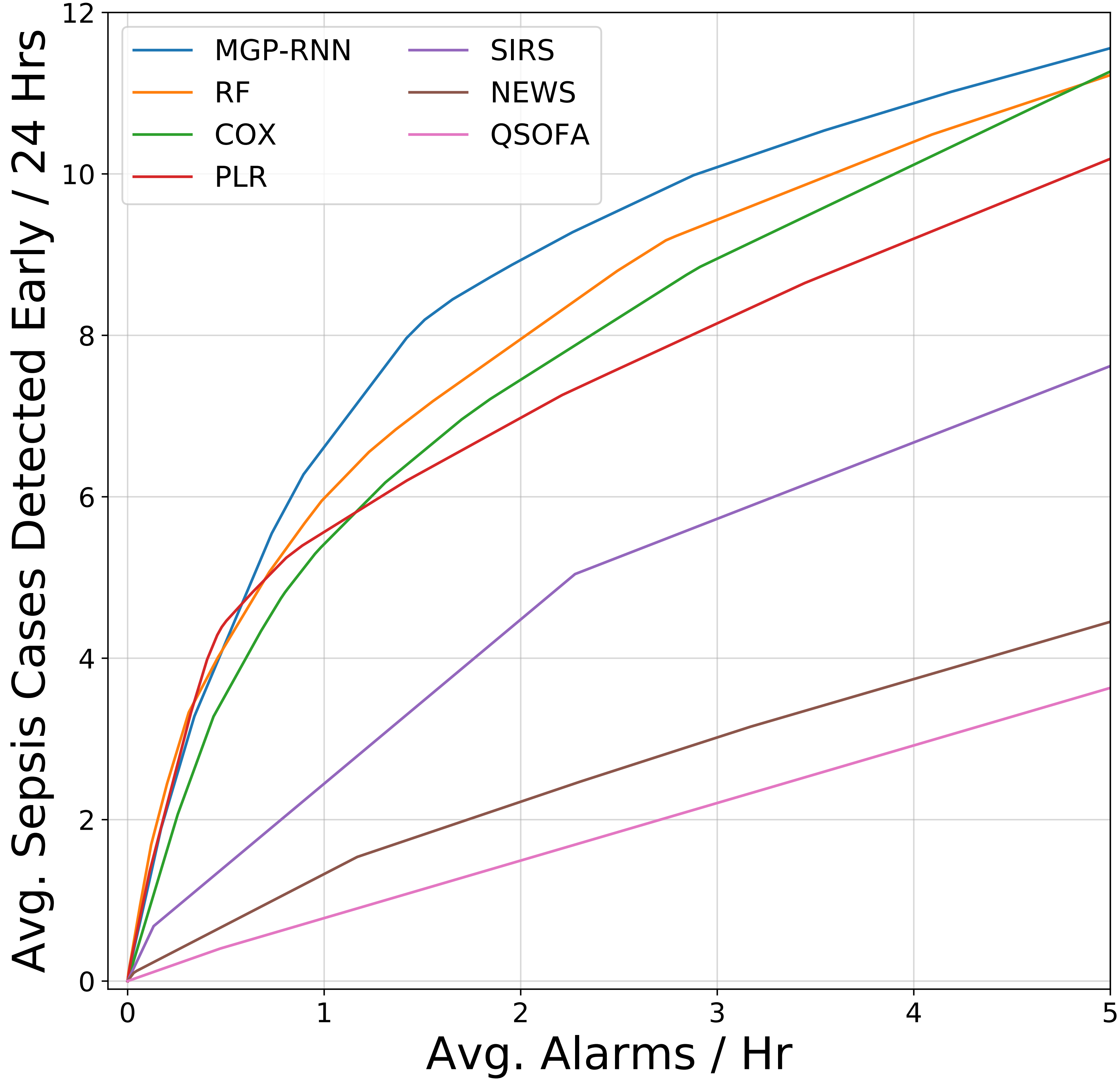


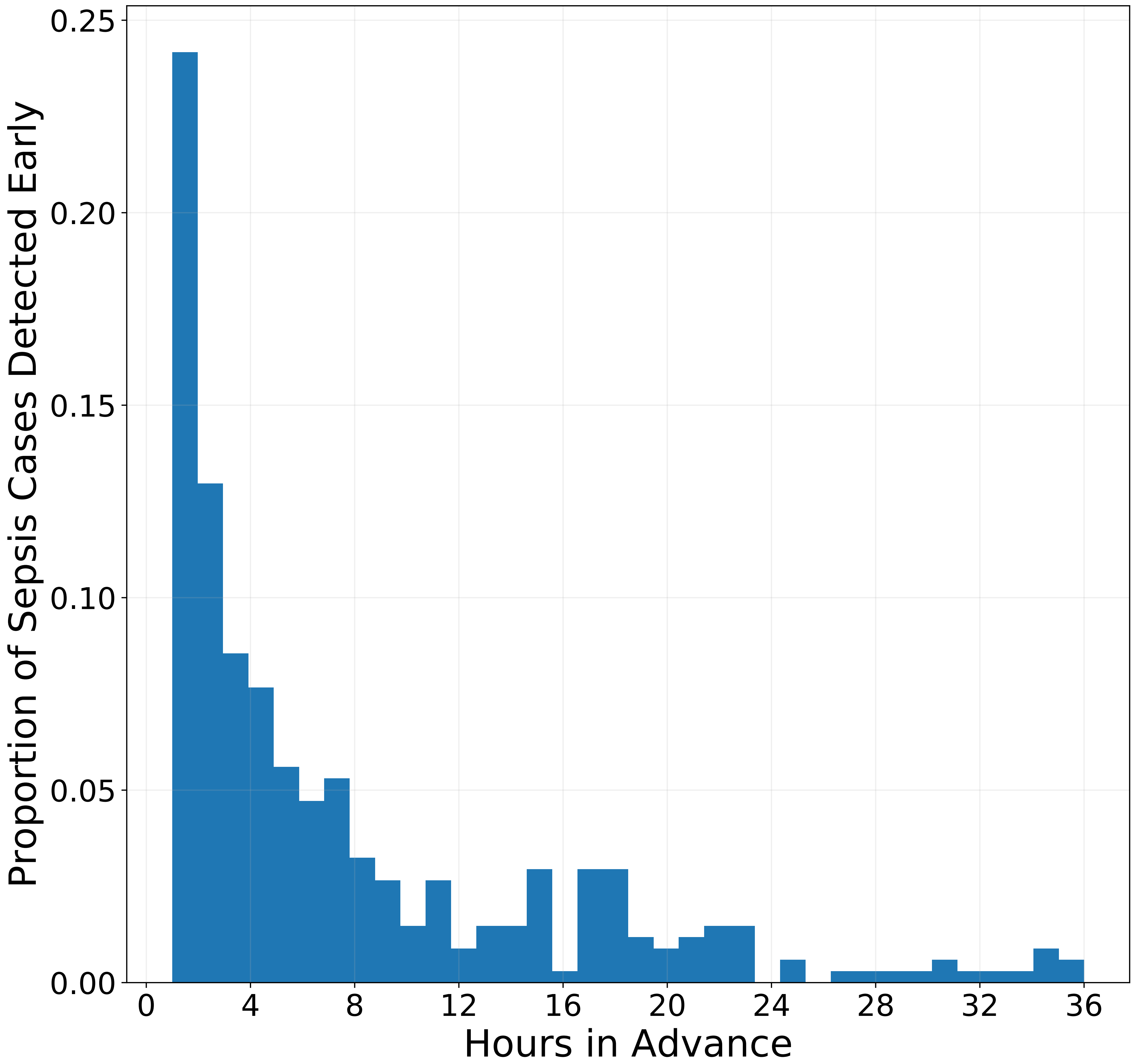


1. To build out metrics, take max risk score in a bin as that window's overall risk

2. To get "hours early", take first time within bin that risk score crosses threshold

“Real-Time” Results




Proportion of Sepsis Cases Detected Early
Hours in Advance
0.00
0.05
0.10
0.15
0.20
0.25
0
4
8
12
16
20
24
28
32
36

In the Real World…

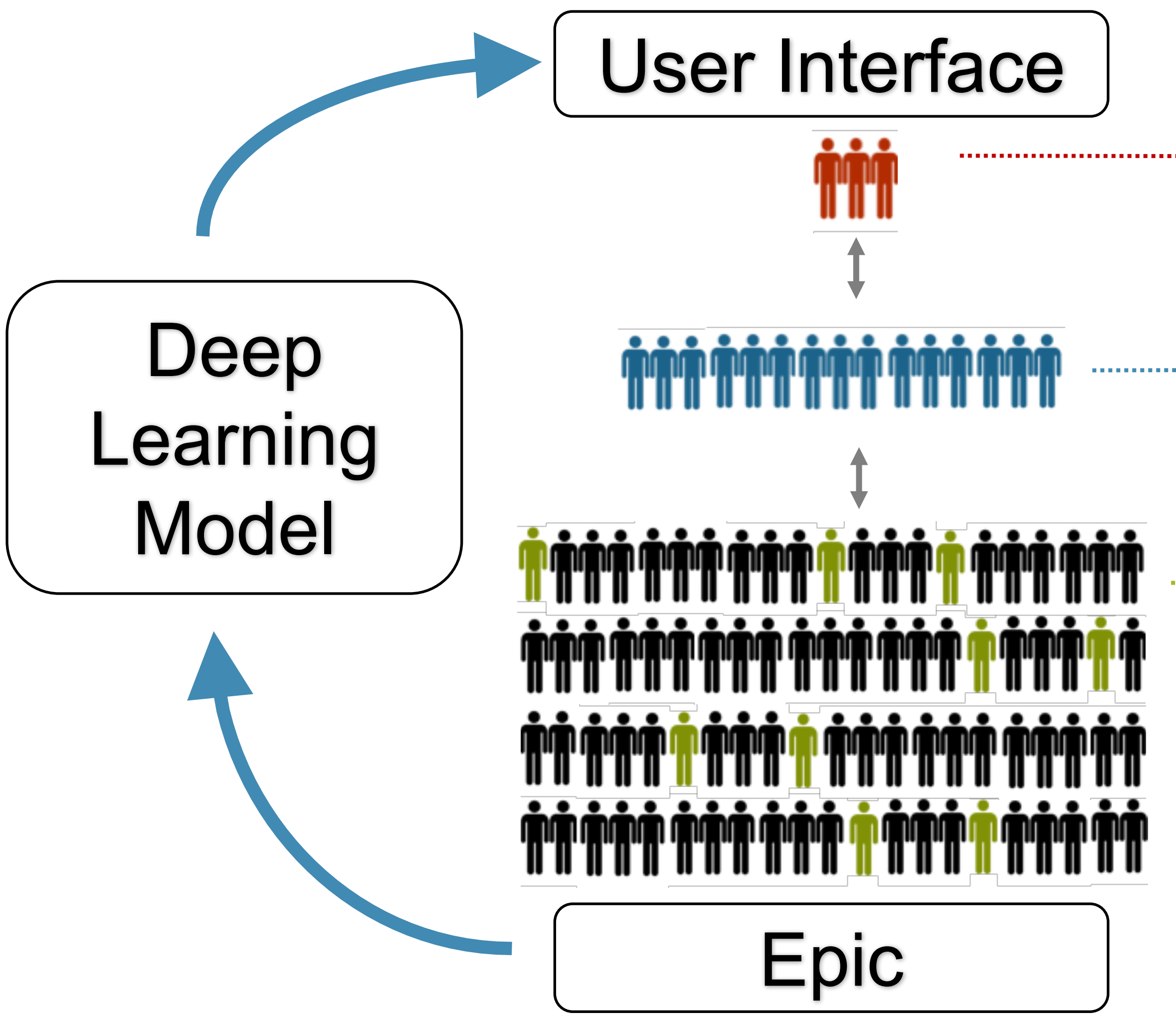
…does it work? Let's find out!

- **Sepsis Rapid Response Team** (RRT): Fast-responding team to help coordinate care for patients with suspected sepsis.
  - Cardiac care unit nurses, pharmacists, hospitalists, respiratory therapists, administrators (logistics).
- Patients at high risk, or that meet the sepsis definition, will be reviewed by a care nurse.
- It's **live** in the Duke ER!
  - Goal: evaluate effect of using the app on **clinical outcomes** (in-hospital mortality).
  - Secondary outcomes: compliance to completing 3, 6 hour bundles on time.

SepsisWatch

Duke Institute for Health Innovation

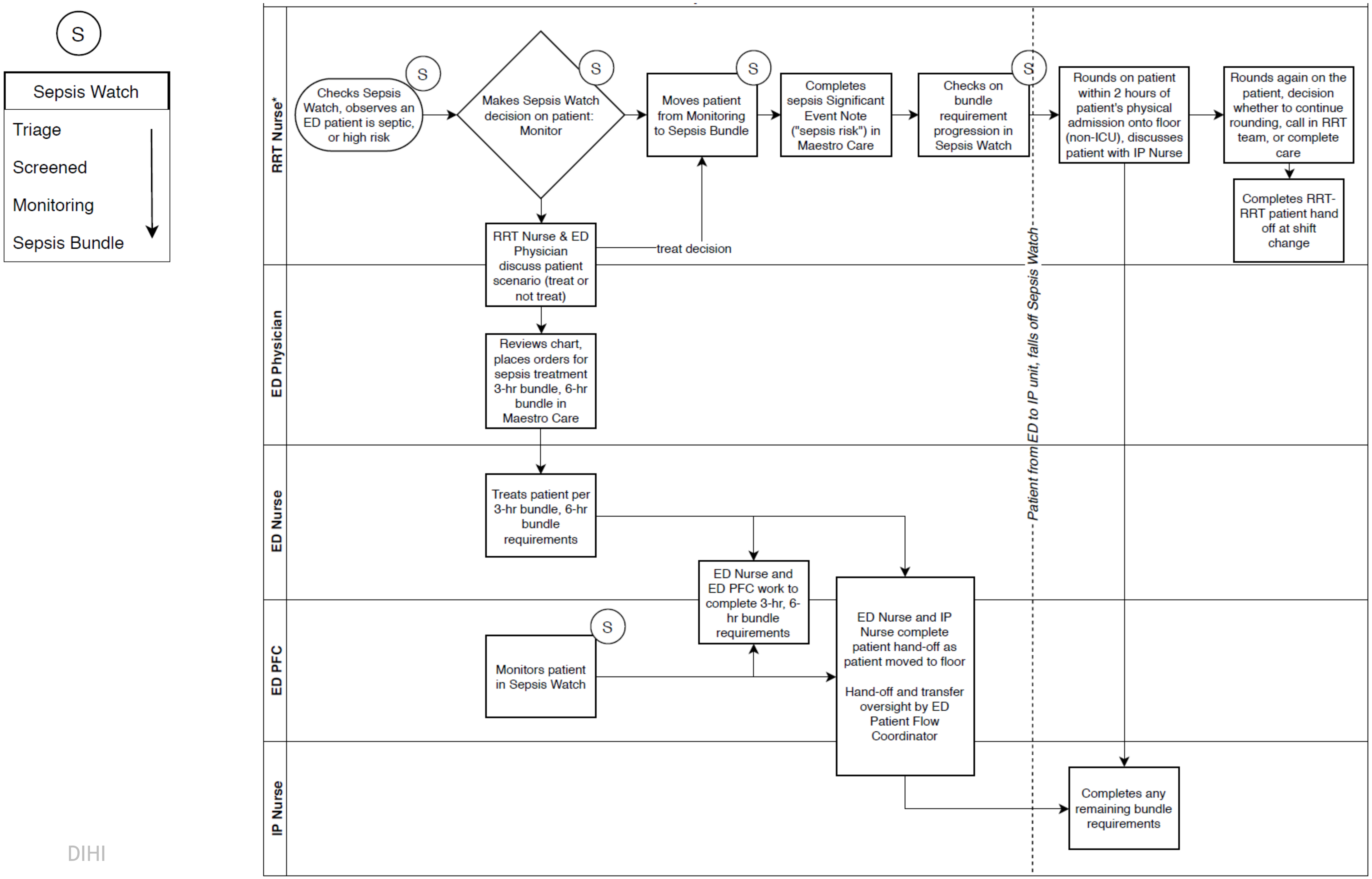
Workflow Overview



- *Leverage Sepsis Care Team*
  RRT nurses and hospitalists
- *Support primary providers*
  …<u>without</u> causing alarm-fatigue
- *Improve patient care over entire cycle*
  high risk through treatment

Actual Workflow…

Duke Institute for Health Innovation

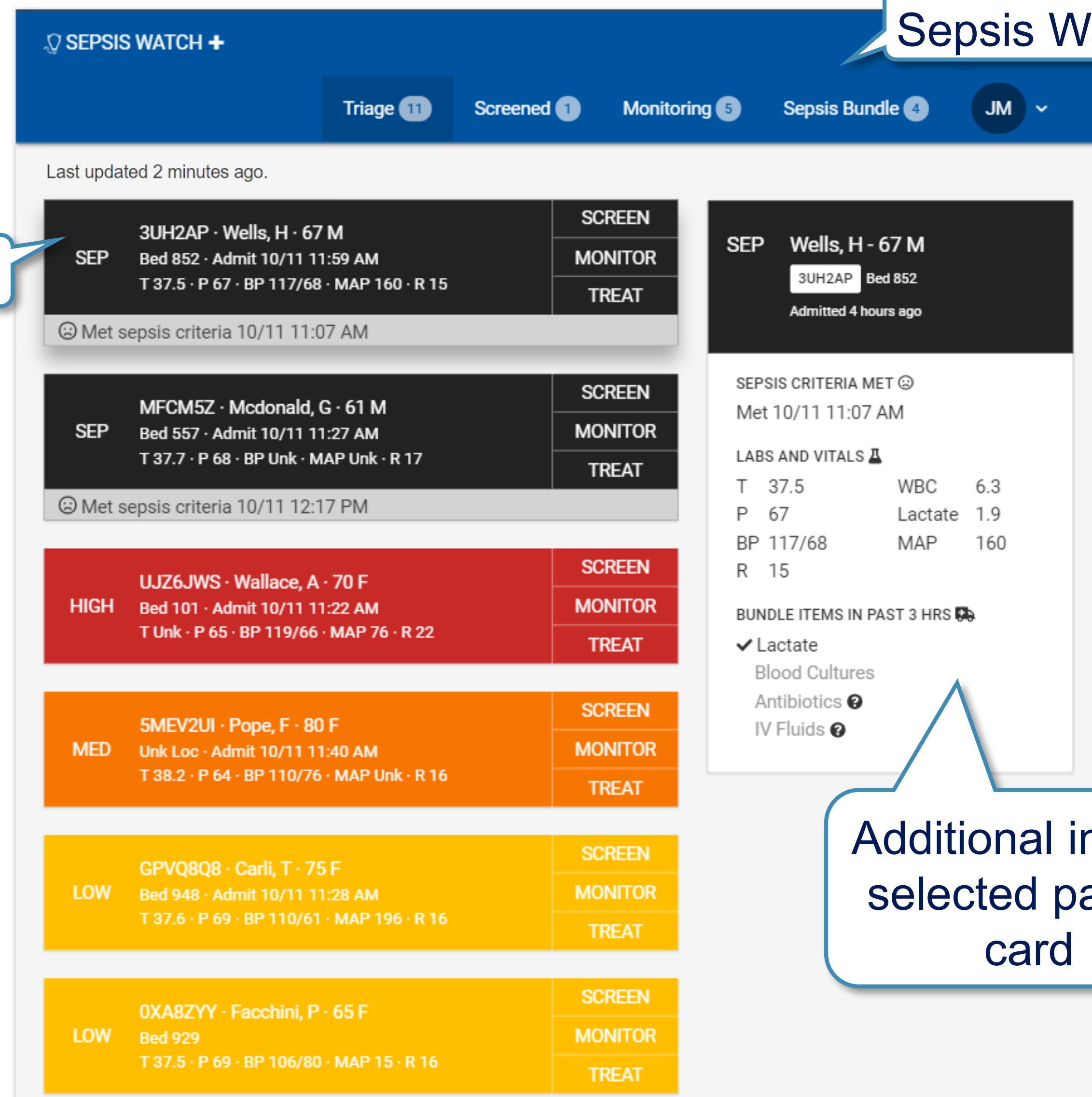


*An RRT or patient consult is the top priority of the RRT nurse

Sepsis Watch Web Application

Patient “card”

Each “card” represents a single patient at Duke Hospital



Sepsis Watch tabs

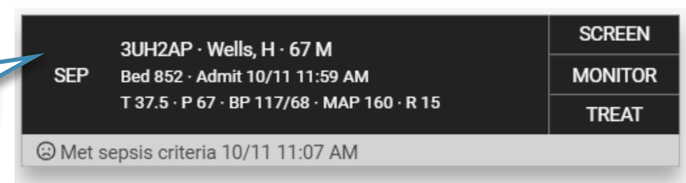
There are four Sepsis Watch tabs. These tabs are meant to help organize patients and prioritize patient care. We are currently viewing the “**Triage**” tab

Additional info on selected patient card

When you tap on a patient card, you can see more info about that patient on the right-hand side of the screen

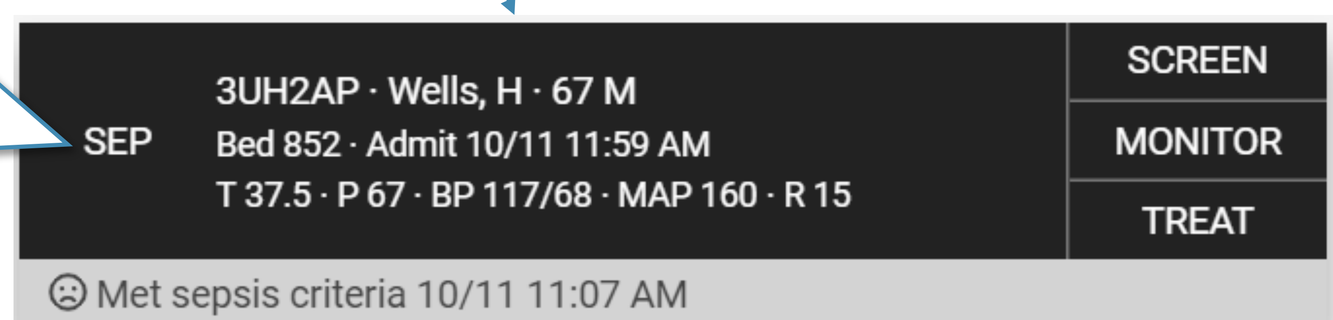
Each card shows information on one patient

Patient “card”



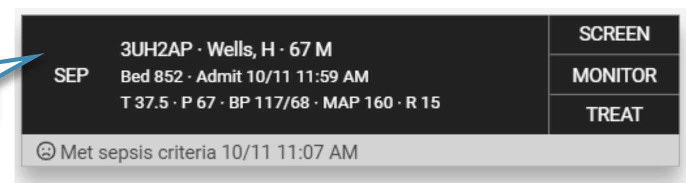
Sepsis status

- **SEP** = meets sepsis criteria
- **HIGH** = high risk of sepsis
- **MED** = medium risk of sepsis
- **LOW** = low risk of sepsis

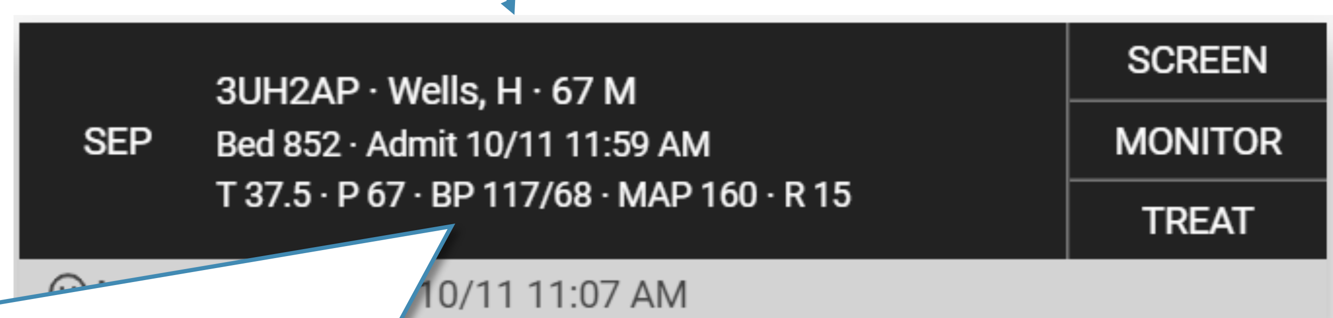


Each card shows information on one patient

Patient "card"



Sepsis Watch shows the most recently filed data on a patient, and refreshes with any new data from Maestro every 5 minutes



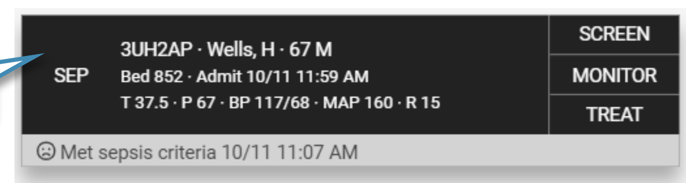
Patient MRN **Name (Last, First Initial)** **Age** **Sex**

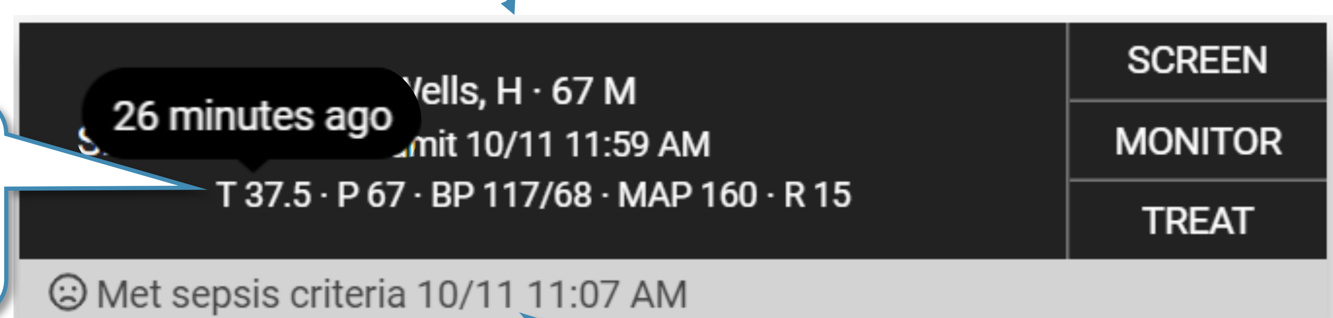
Bed Location **Admission Date and Time**

T *(temperature)* **P** *(pulse)* **BP** *(blood pressure)* **MAP** *(mean arterial pressure)* **R** *(respirations)*

Each card shows information on one patient

Patient "card"



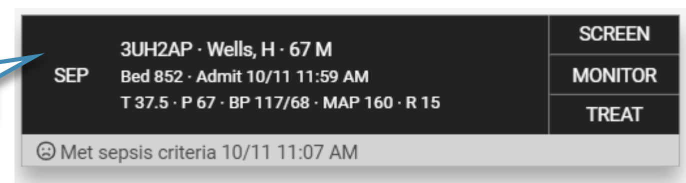


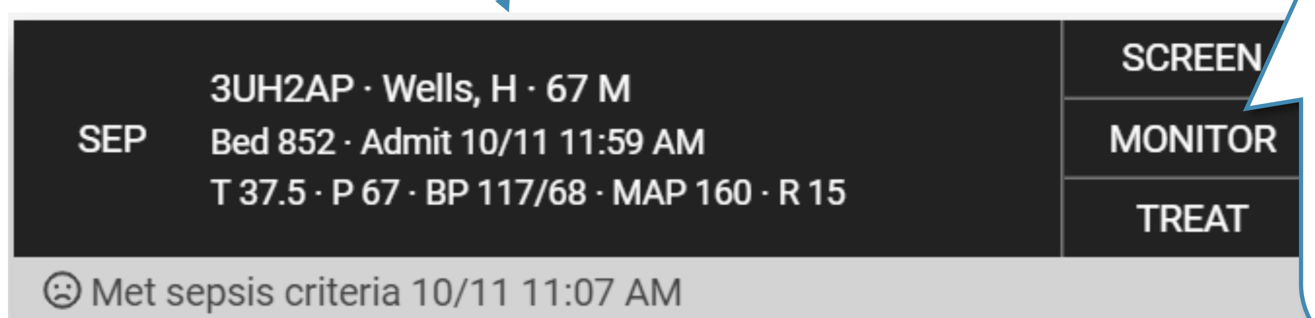
Tap a data point to see how long ago it was filed in Maestro

Black cards also show the time when patient met the criteria for sepsis

Each card shows information on one patient

Patient "card"

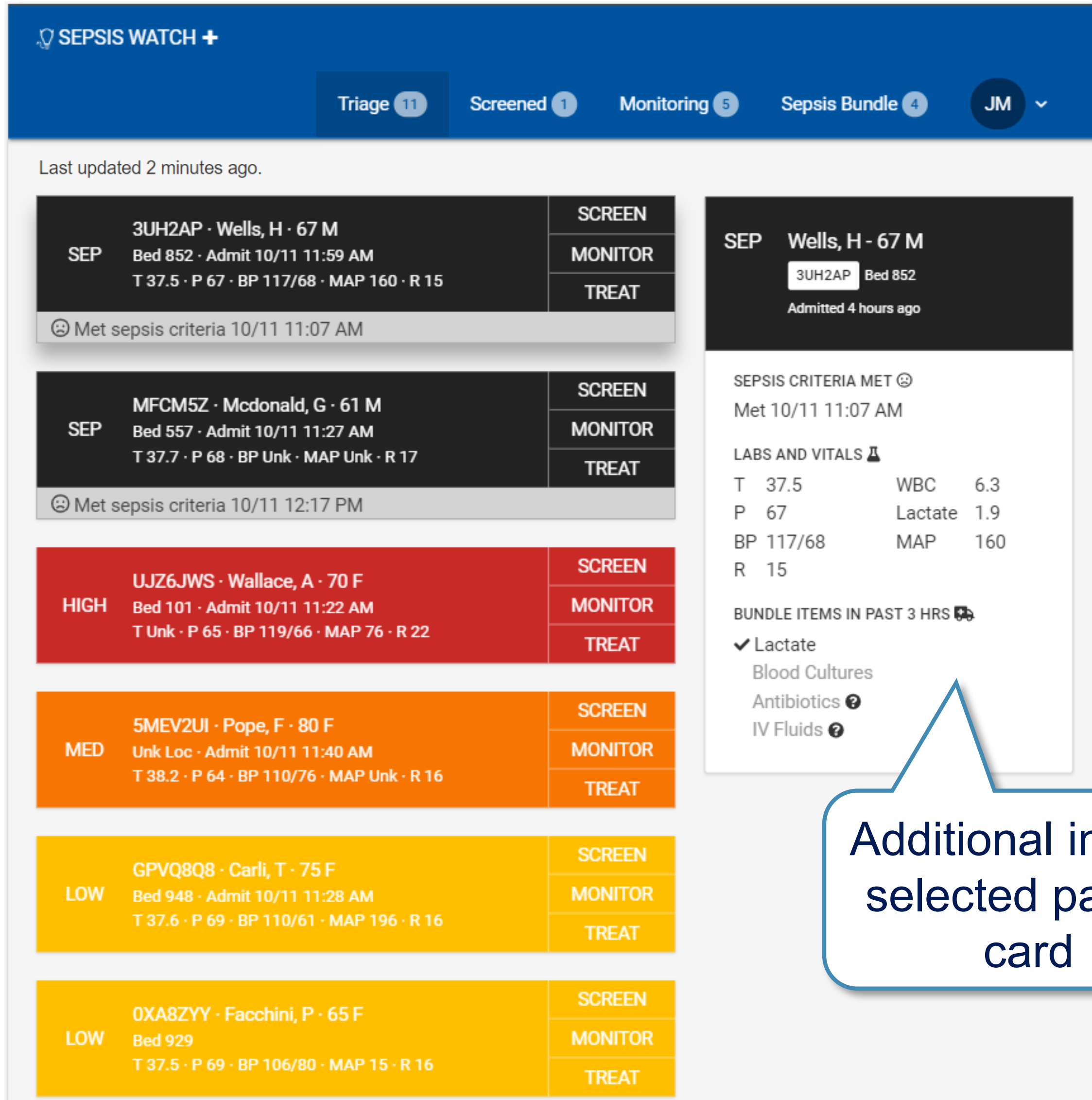




Sepsis Treatment Decision Buttons

- **SCREEN**→ moves patient to Screened tab
- **MONITOR**→ moves patient to Monitoring tab
- **TREAT**→ moves patient to Sepsis Bundle tab

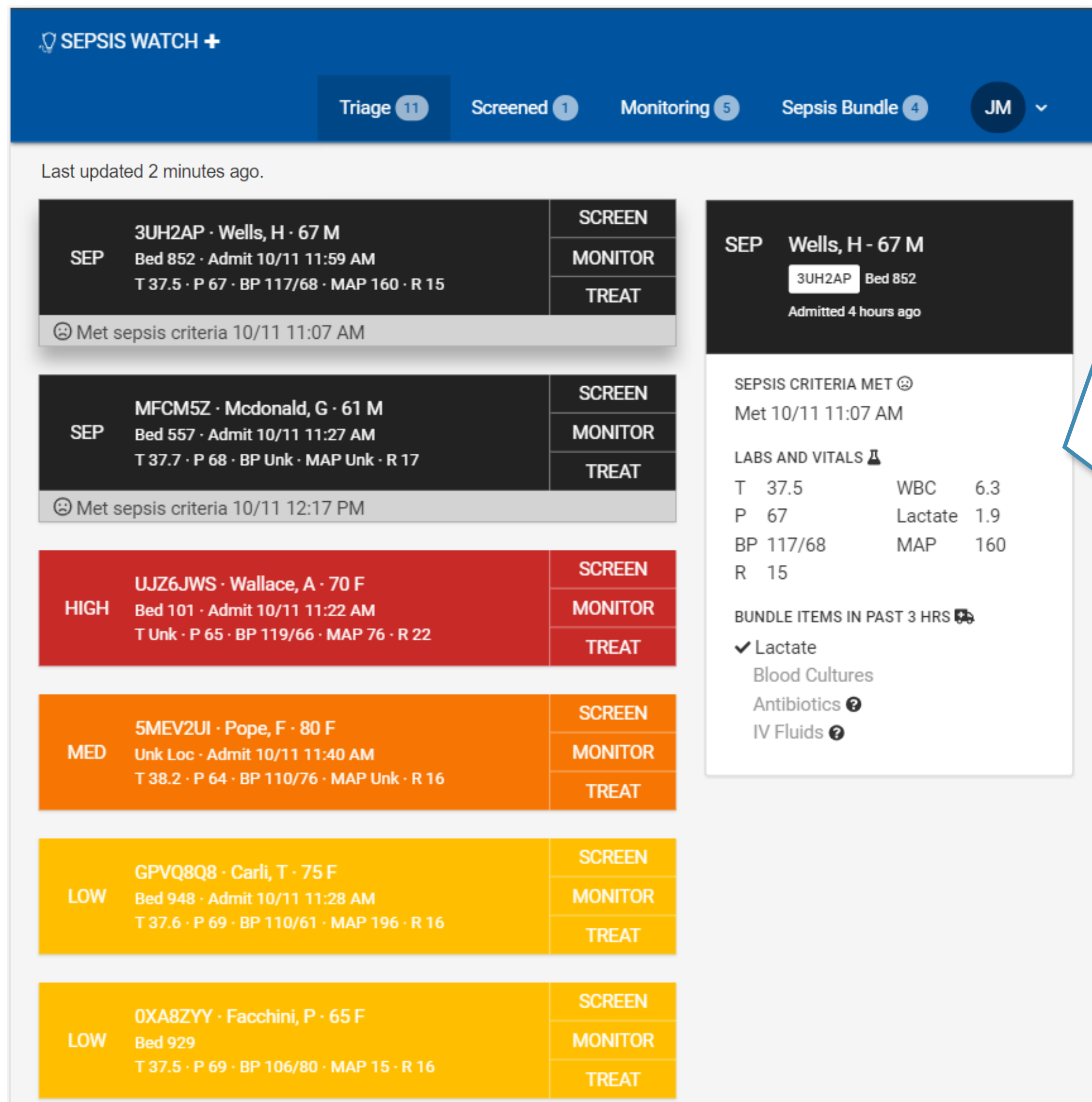
Additional Information Pane



Additional info on selected patient card

When you tap on a patient card, you can see more info about that patient on the right-hand side of the screen

Additional Information Pane



Sepsis Criteria Met

Time when patient met sepsis criteria (black cards only)

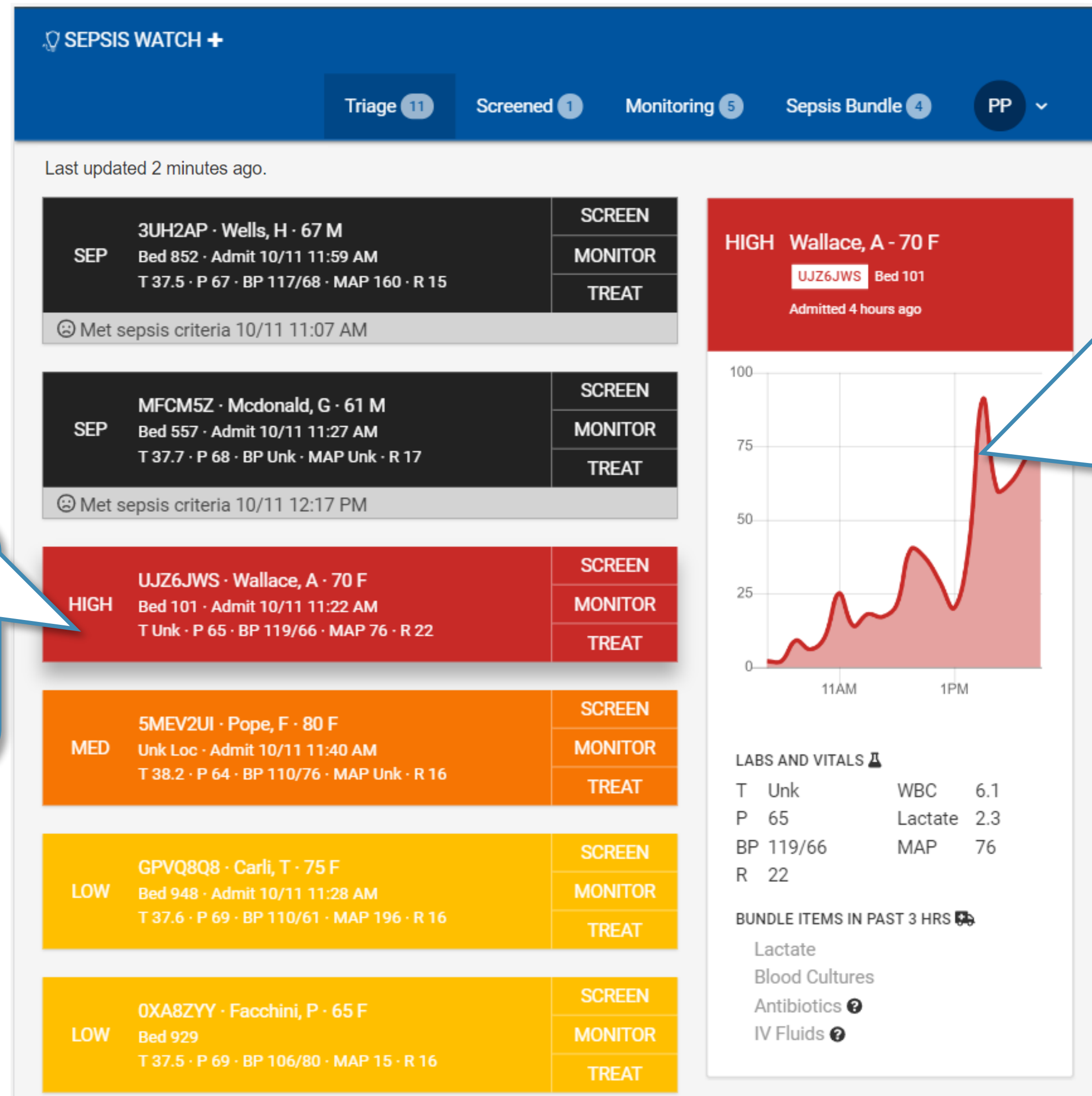
Labs and Vitals

Temperature, Pulse, Blood Pressure, Respirations, White Blood Cell Count, Lactate level, Mean Arterial Pressure

Bundle Items in Past 3 Hrs

Indicates whether any of the bundle requirements have been acted on in the last 3 hours

Additional Information Pane



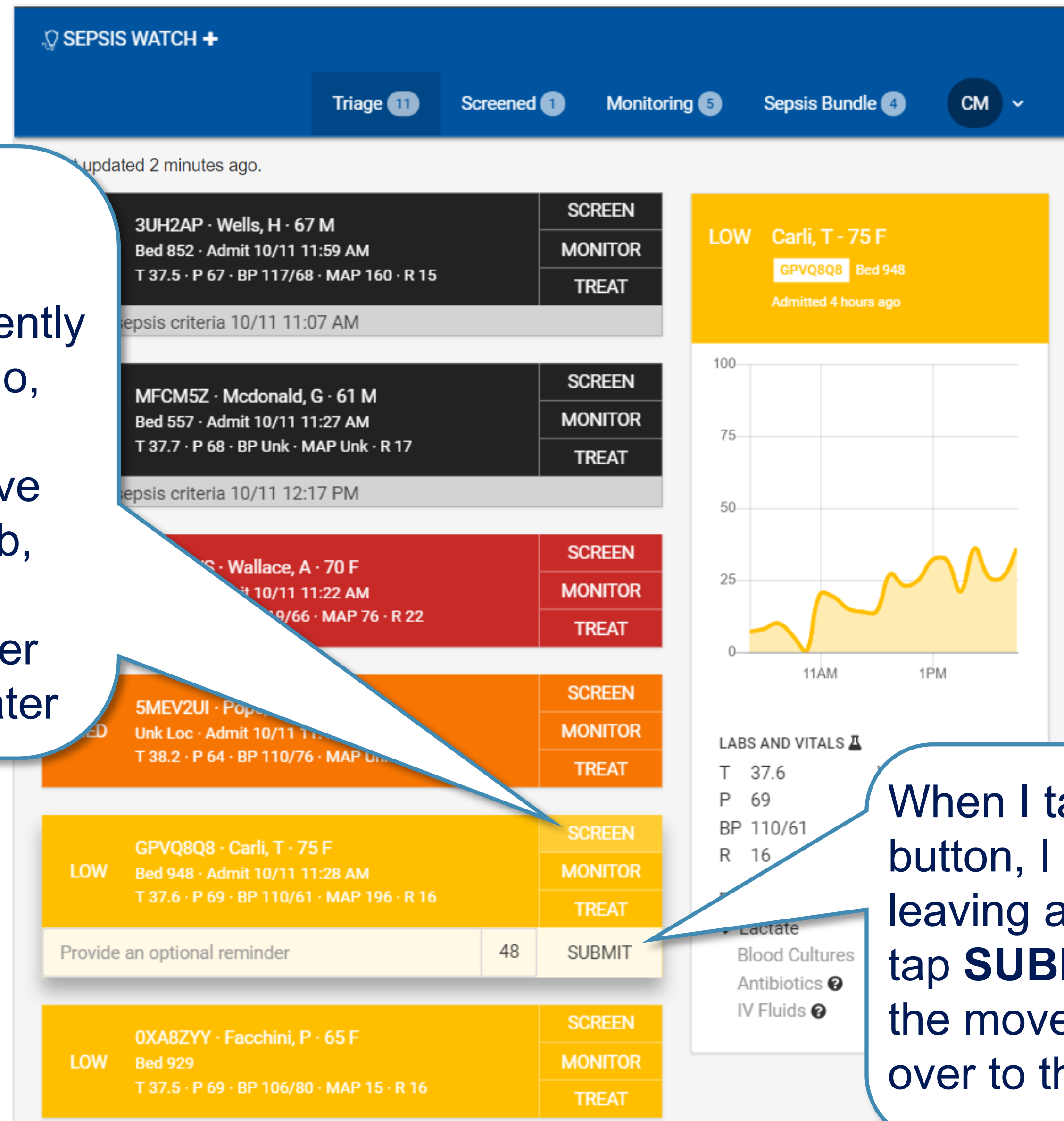
You can tell this patient card is selected because it has shadowing

For HIGH, MED, or LOW risk of sepsis patients, the additional info pane shows a historical trend of the patient's risk score. This patient became a high risk of sepsis patient just after 1pm

Move patient from Triage tab to Screened tab

1

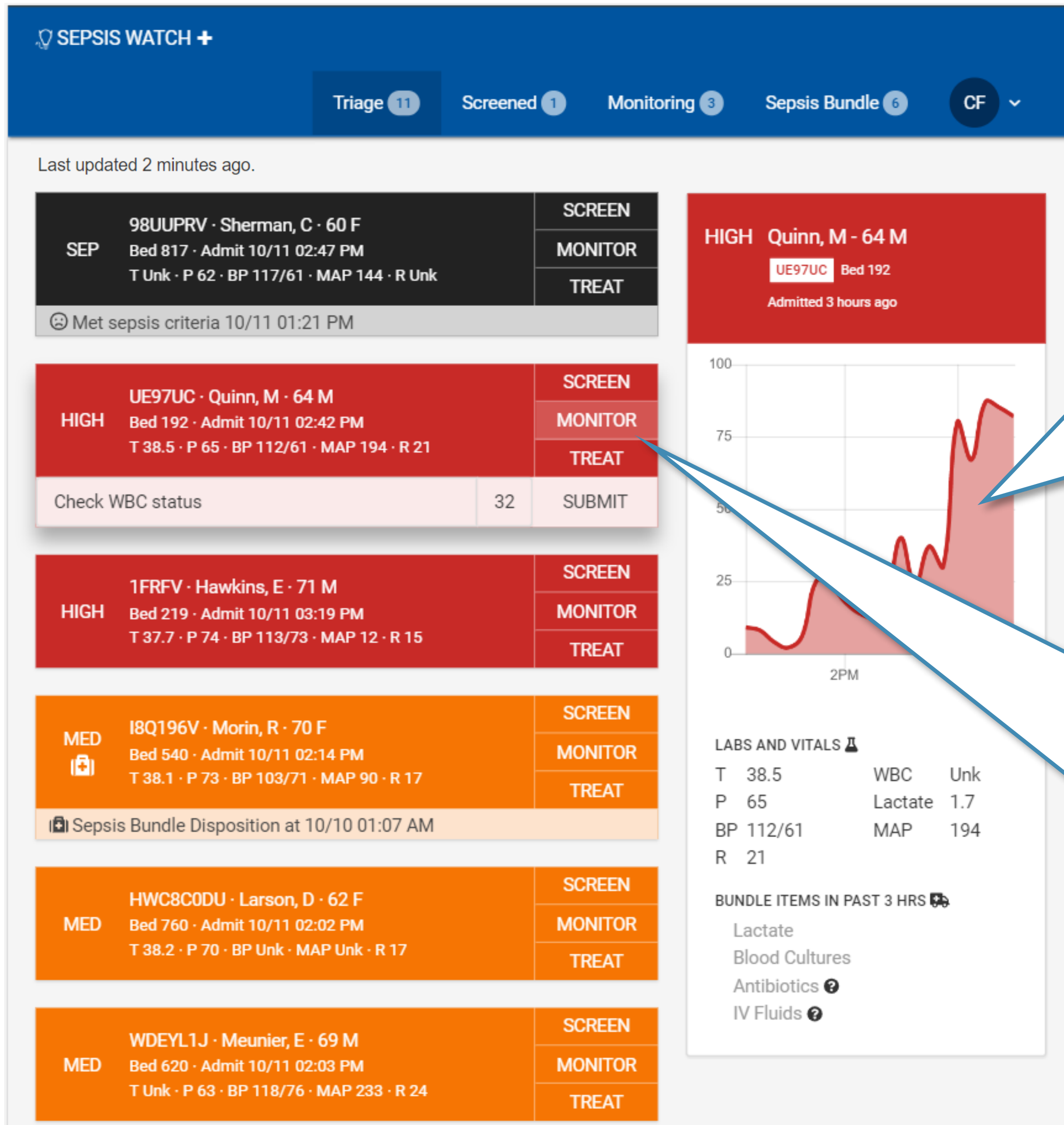
After reviewing this patient's information, I assess that she is currently at low risk for sepsis. So, I'm going to tap the **SCREEN** button to move her to my **Screened** tab, so I can focus on other patients. I'll check on her on the **Screened** tab later



2

When I tap the **SCREEN** button, I have the option of leaving a reminder. Then, I tap **SUBMIT** to complete the move of this patient over to the **Screened** tab

Move high risk patient to Monitoring tab



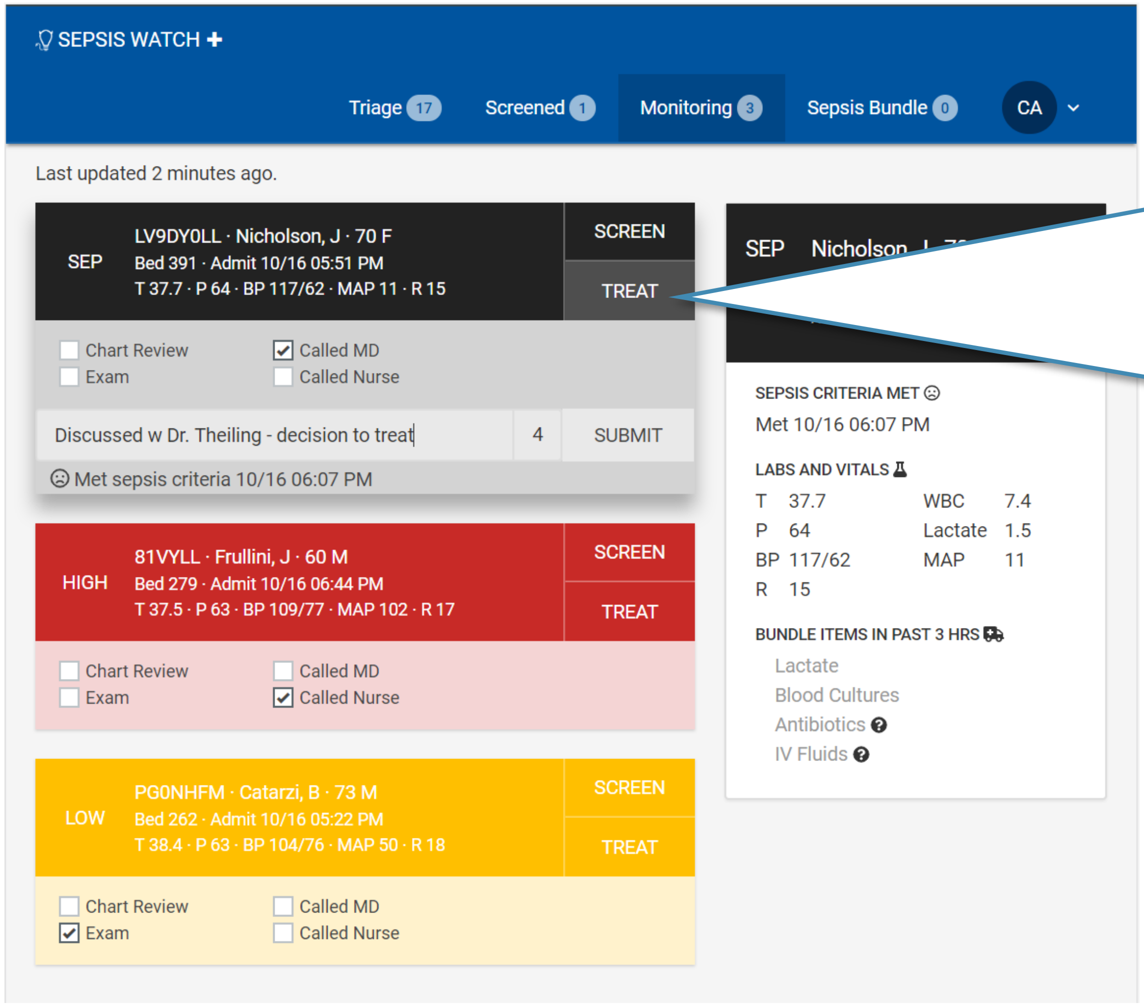
1

After assessing this patient, I see his sepsis risk score has spiked recently, and I want to keep a close watch on him…

2

…so I tap the **MONITOR** button and decide to add a comment “Check WBC status”. Then, I tap the **SUBMIT** button to move the patient to the **Monitoring** tab

Move patient from Monitoring tab to Sepsis Bundle tab

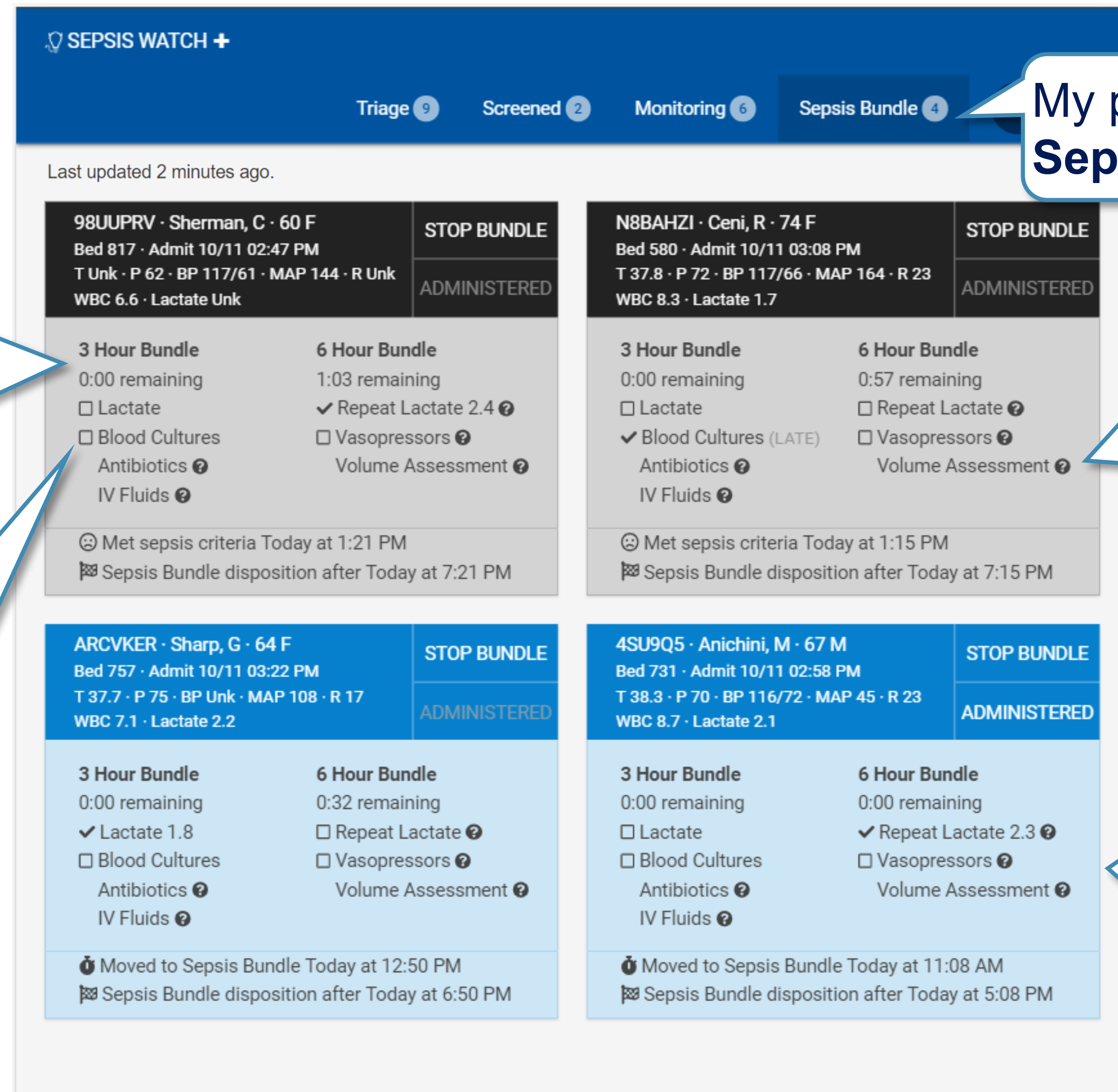


If the ED physician agrees to move forward with treating for sepsis, then I will tap **TREAT** and then **SUBMIT** to move the patient from the Monitoring tab to the **Sepsis Bundle** tab. I can also leave a comment about the interaction.

Track patient treatment on Sepsis Bundle tab

On this tab, I can see additional information on the sepsis bundle compliance treatment for the 3-hour and 6-hour bundle

The Lactate, Blood Cultures, and Vasopressors will update automatically (box will be checked) as soon as they are collected in Maestro

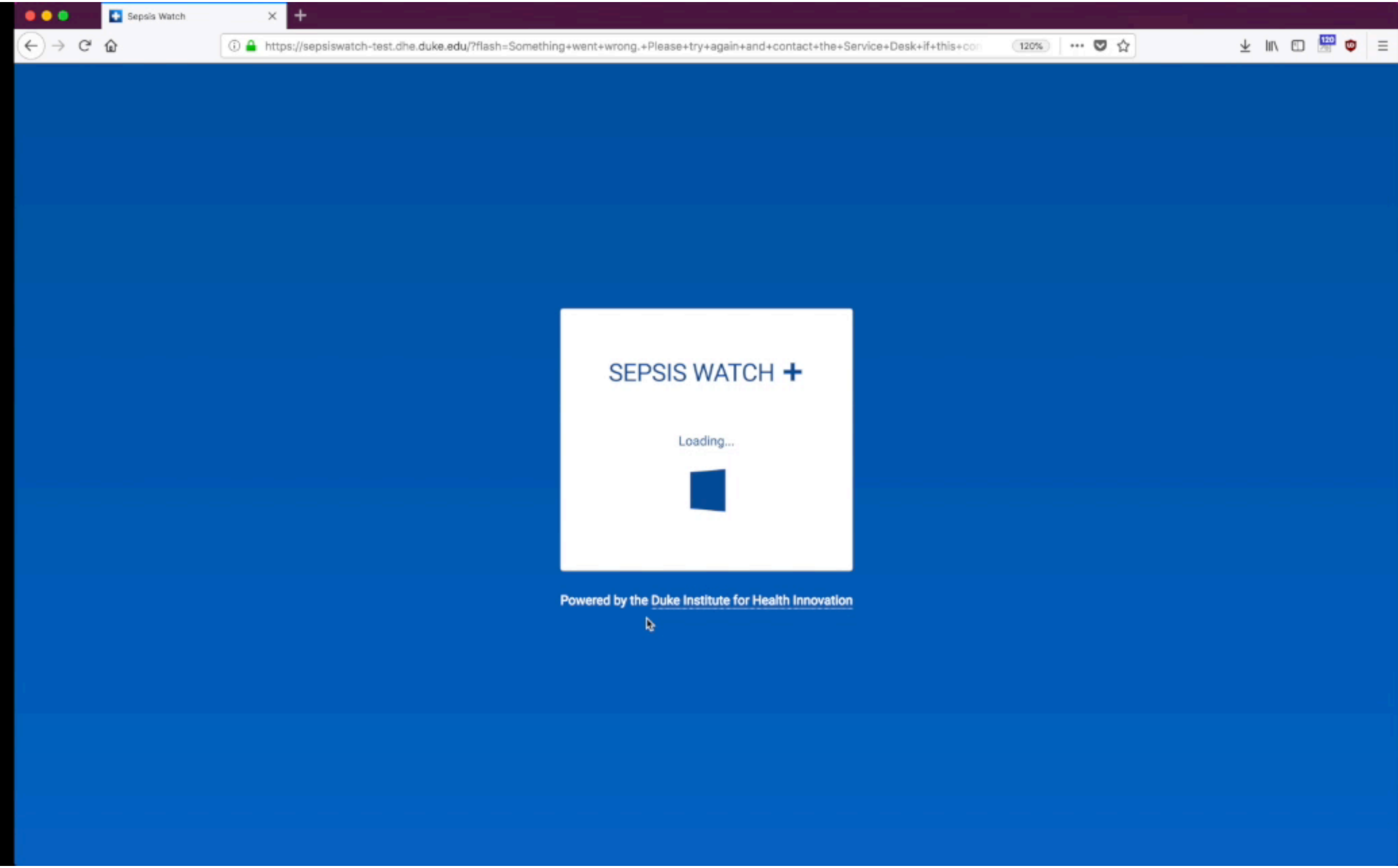


My patient now shows up on the **Sepsis Bundle** tab

Antibiotics, IV Fluids, and Volume Assessment will not auto-update, and their completion will need to be tracked in Maestro

Patients with blue cards are being treated for sepsis, but do not meet the sepsis. These are the high, medium, or low sepsis risk patients

In action!


Sepsis Watch
https://sepsiswatch-test.dhe.duke.edu/?flash=Something+went+wrong.+Please+try+again+and+contact+the+Service+Desk+if+this+co
120%
SEPSIS WATCH +
Loading...
Powered by the Duke Institute for Health Innovation

It works!

CALCULATION_TIME		VALUE
2018-12-01	0	0.11
2018-12-01	1	0.96
2018-12-01	2	0.88
2018-12-01	3	0.77
2018-12-01	4	0.82
2018-12-01	...	0.83
2018-12-01		0.85
2018-12-01		0.83
2018-12-01		0.84
2018-12-01		0.83
2018-12-02		0.83
2018-12-02		0.83
2018-12-02		0.83
2018-12-02		0.84
2018-12-02		0.84
2018-12-02		0.84
2018-12-02		0.84

OUTCOME_NAME	OUTCOME_TIME ▲ 1	
sepsis definition met	2018-12-01	1.25
sepsis definition met	2018-12-01	1.3
sepsis definition met	2018-12-01	3.5
sepsis definition met	2018-12-01	3.6
sepsis definition met	2018-12-01	5.0
sepsis definition met	2018-12-01	...
sepsis definition met	2018-12-01	
sepsis definition met	2018-12-01	
sepsis definition met	2018-12-01	
sepsis definition met	2018-12-01	
sepsis definition met	2018-12-01	
sepsis definition met	2018-12-02	
sepsis definition met	2018-12-02	
sepsis definition met	2018-12-02	
sepsis definition met	2018-12-02	
sepsis definition met	2018-12-04	
sepsis definition met	2018-12-04	
sepsis definition met	2018-12-04	
sepsis definition met	2018-12-04	
sepsis definition met	2018-12-04	

STATUS_TIME		STATUS	REMINDER	CREATED_BY	CREATED_AT
2018-12-01	1.3	4	Treatment initiated	cp178	2018
2018-12-01	7.3	3	Bundle complered	cp178	2018
2018-12-01	...	2	<null>	cp178	2018

Conclusions

- Novel model for early detection of sepsis, leveraging **deep learning** and **Gaussian processes.** We get **uncertainty** in (inputs to) deep model!
- Significantly improved performance over NEWS used at Duke.
- It works! Results of clinical trial forthcoming (need ~6 months of data), and scaling to other hospitals in Duke system (and eventually NYU!)
- Many exciting new research directions:
    - Decision theory: how to utilize risk, **and** uncertainty in risk, to make decisions.
    - Reinforcement learning: optimize the treatments themselves?
    - More realistic GP models to improve time series modeling (e.g. non-stationary)
    - Improve uncertainty quantification with Bayesian deep learning
    - Combine GP with other black box models for clinical time series
    - Practical issues around model deployment, eg how often to retrain? how to weight different data sources / do transfer learning across sites?

Acknowledgements

DIHI Team:
Mark Sendak, MD, MPP
Nathan Brajer, MD Candidate
Michael Gao, MS
Suresh Balu, MBA
Machine Learning:
Sanjay Hariharan, MS
Katherine Heller, PhD
Sepsis Clinicians:
Cara O'Brien, MD
Armando Bedoya, MD
Meredith Clement, MD
Software Developer:
Faraz Yashar

jfutoma14@gmail.com

https://github.com/jfutoma/MGP-RNN

Defining Sepsis

accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis

THE ACCP/SCCM CONSENSUS CONFERENCE COMMITTEE:
Roger C. Bone, M.D., F.C.C.P., Chairman
Robert A. Balk, M.D., F.C.C.P.
Frank B. Cerra, M.D.
R. Phillip Dellinger, M.D., F.C.C.P.
Alan M. Fein, M.D., F.C.C.P.
William A. Knaus, M.D.
Roland M. H. Schein, M.D.
William J. Sibbald, M.D., F.C.C.P.

1992

Intensive Care Med (2003) 29:530–538
DOI 10.1007/s00134-003-1662-x

EXPERT PANEL

Mitchell M. Levy
Mitchell P. Fink
John C. Marshall
Edward Abraham
Derek Angus
Deborah Cook
Jonathan Cohen
Steven M. Opal
Jean-Louis Vincent
Graham Ramsay
for the International Sepsis Definitions Conference

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference

2001

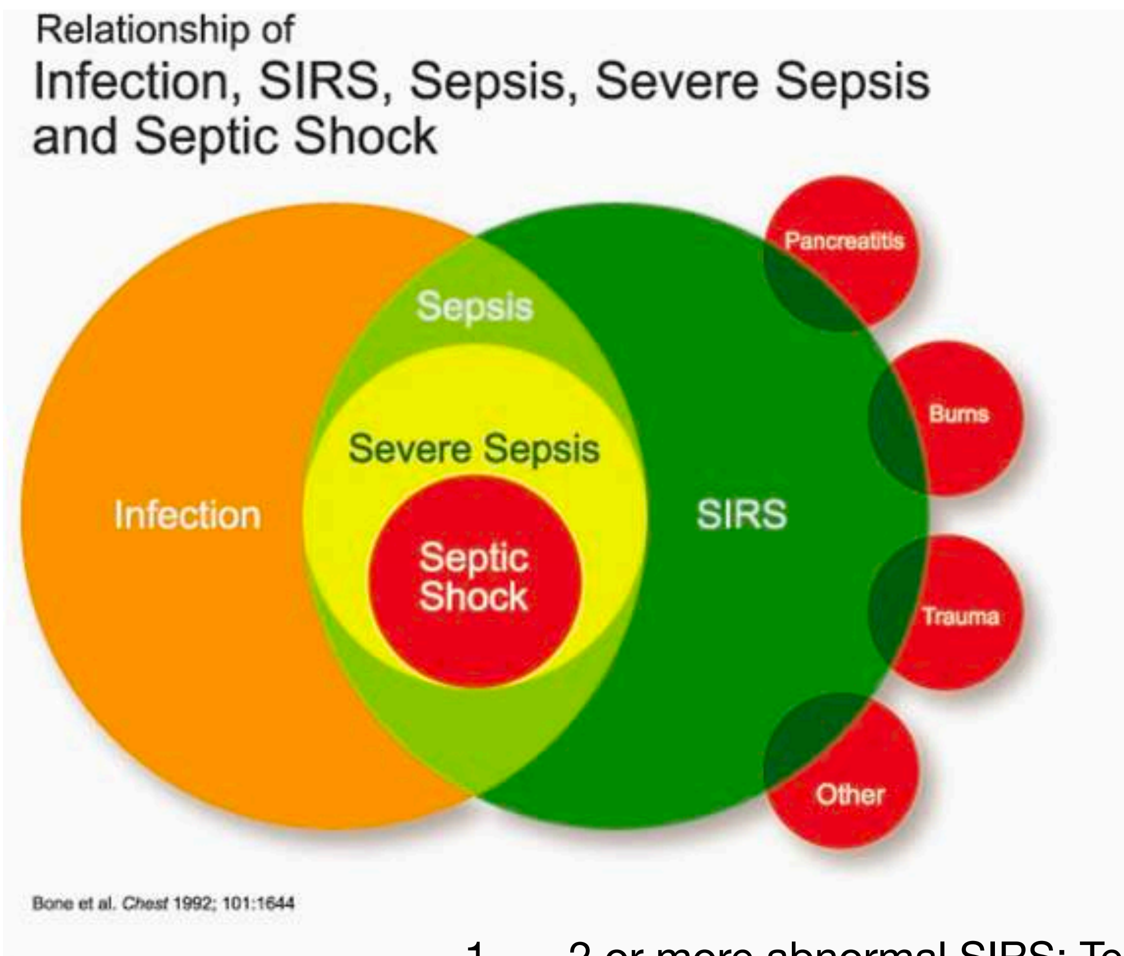
Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

2016

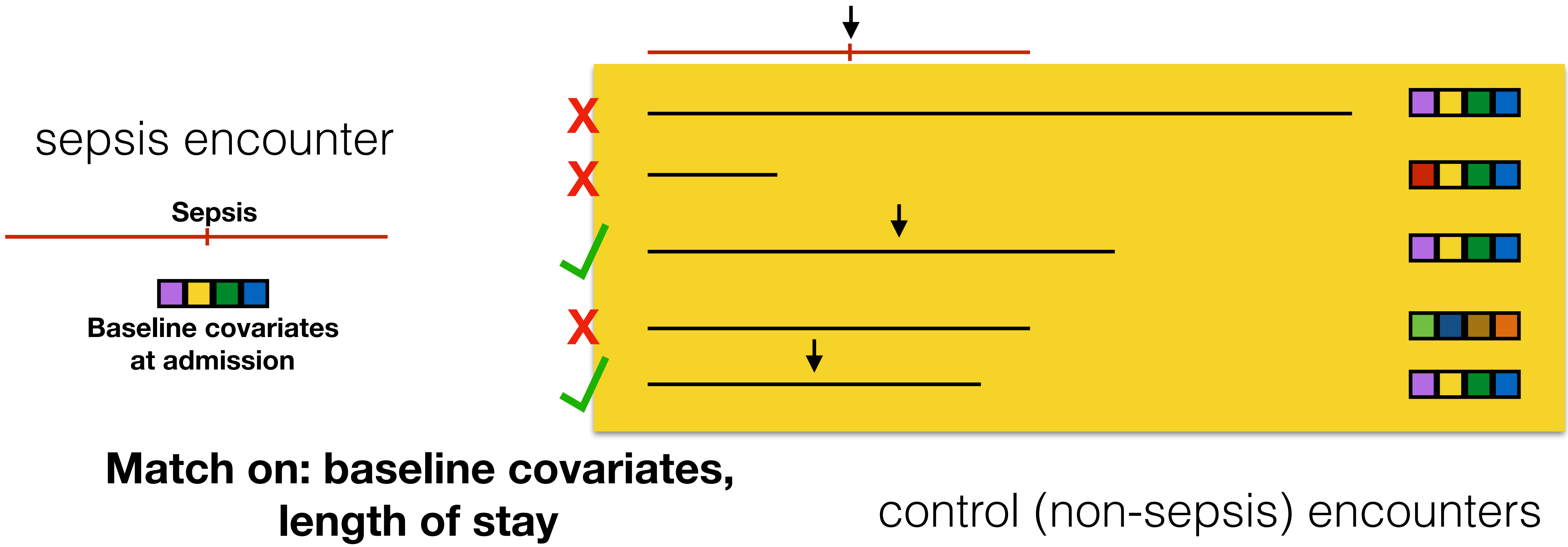


qSOFA

Our definition ("Severe Sepsis")

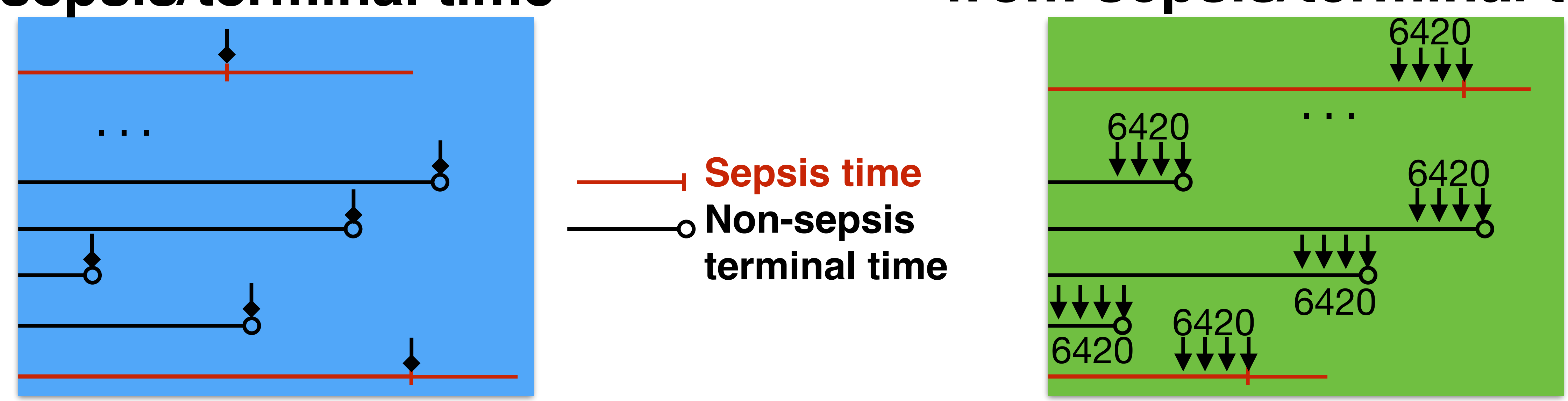
1. 2 or more abnormal SIRS: Temperature, Heart Rate, Respiration Rate, WBC Count.
2. Blood culture (suspected infection).
3. End organ damage lab.

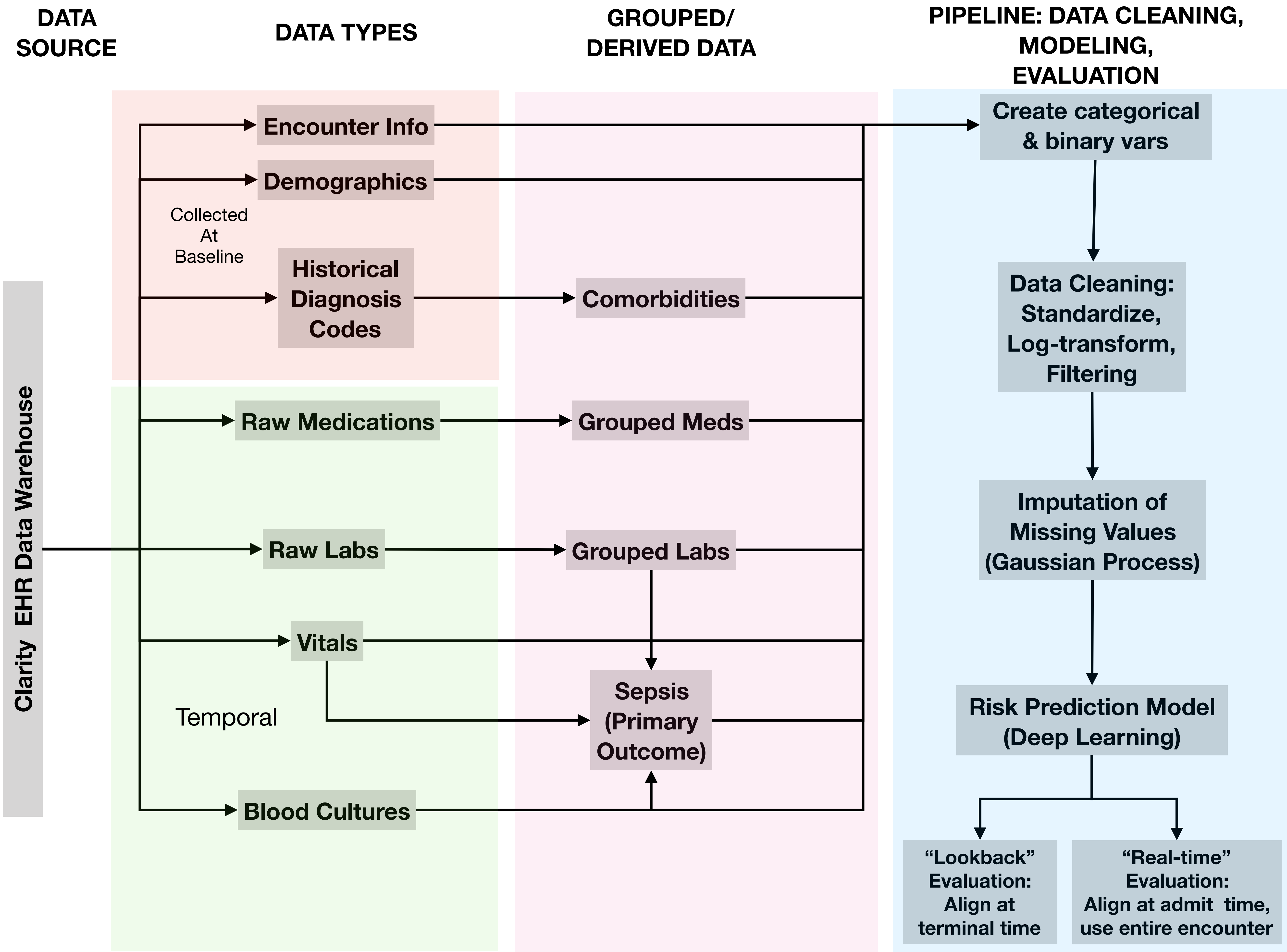
Case Control Matching & Experimental Setup

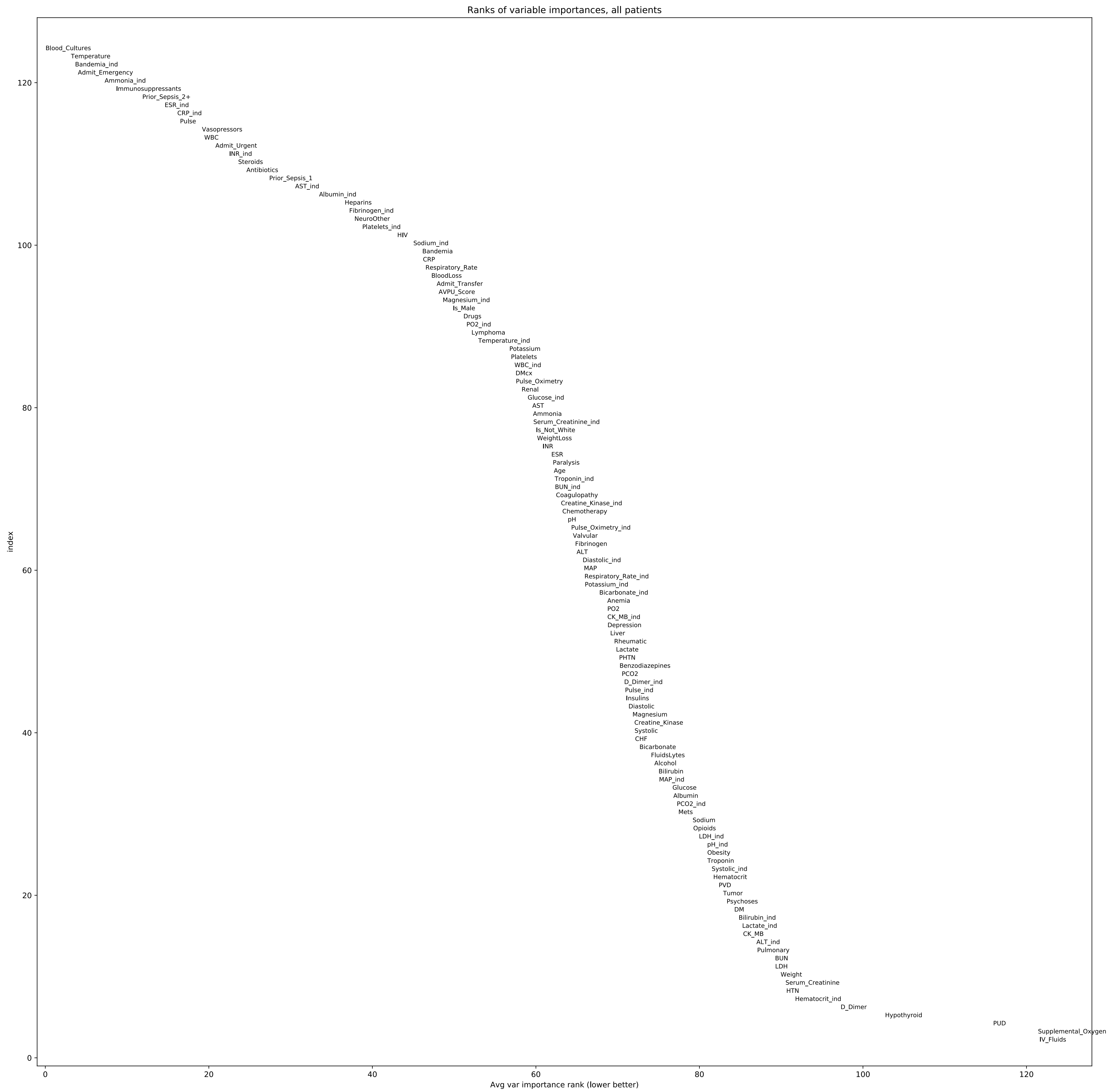


Train: up to sepsis/terminal time

Test: vary # hours from sepsis/terminal time




DATA SOURCE
DATA TYPES
GROUPED/ DERIVED DATA
PIPELINE: DATA CLEANING, MODELING, EVALUATION
Clarity EHR Data Warehouse
Encounter Info
Demographics
Collected At Baseline
Historical Diagnosis Codes
Comorbidities
Raw Medications
Grouped Meds
Raw Labs
Grouped Labs
Vitals
Temporal
Sepsis (Primary Outcome)
Blood Cultures
Create categorical & binary vars
Data Cleaning: Standardize, Log-transform, Filtering
Imputation of Missing Values (Gaussian Process)
Risk Prediction Model (Deep Learning)
"Lookback" Evaluation: Align at terminal time
"Real-time" Evaluation: Align at admit time, use entire encounter


Ranks of variable importances, all patients
index
Avg var importance rank (lower better)
0
20
40
60
80
100
120
Blood_Cultures
Temperature
Bandemia_ind
Admit_Emergency
Ammonia_ind
Immunosuppressants
Prior_Sepsis_2+
ESR_ind
CRP_ind
Pulse
Vasopressors
WBC
Admit_Urgent
INR_ind
Steroids
Antibiotics
Prior_Sepsis_1
AST_ind
Albumin_ind
Heparins
Fibrinogen_ind
NeuroOther
Platelets_ind
HIV
Sodium_ind
Bandemia
CRP
Respiratory_Rate
BloodLoss
Admit_Transfer
AVPU_Score
Magnesium_ind
Is_Male
Drugs
PO2_ind
Lymphoma
Temperature_ind
Potassium
Platelets
WBC_ind
DMcx
Pulse_Oximetry
Renal
Glucose_ind
AST
Ammonia
Serum_Creatinine_ind
Is_Not_White
WeightLoss
INR
ESR
Paralysis
Age
Troponin_ind
BUN_ind
Coagulopathy
Creatine_Kinase_ind
Chemotherapy
pH
Pulse_Oximetry_ind
Valvular
Fibrinogen
ALT
Diastolic_ind
MAP
Respiratory_Rate_ind
Potassium_ind
Bicarbonate_ind
Anemia
PO2
CK_MB_ind
Depression
Liver
Rheumatic
Lactate
PHTN
Benzodiazepines
PCO2
D_Dimer_ind
Pulse_ind
Insulins
Diastolic
Magnesium
Creatine_Kinase
Systolic
CHF
Bicarbonate
FluidsLytes
Alcohol
Bilirubin
MAP_ind
Glucose
Albumin
PCO2_ind
Mets
Sodium
Opioids
LDH_ind
pH_ind
Obesity
Troponin
Systolic_ind
Hematocrit
PVD
Tumor
Psychoses
DM
Bilirubin_ind
Lactate_ind
CK_MB
ALT_ind
Pulmonary
BUN
LDH
Weight
Serum_Creatinine
HTN
Hematocrit_ind
D_Dimer
Hypothyroid
PUD
Supplemental_Oxygen
IV_Fluids