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A Machine Learning Understanding of Sepsis

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Sepsis

- *"A life-threatening organ dysfunction caused by a dysregulated host response to infection"* *

- WHO (2017) estimated that there were 48.9 million cases and 11 million sepsis-related deaths worldwide, which accounted for almost 20% of all global deaths.

- Sepsis was initially presumed to be an extreme body-wide inflammatory response, manifesting clinically as multisystem organ dysfunction.

- However, more recent evidence demonstrates that the pathophysiological response is more complex and variable. **

* The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), 2016 [link]
** Severe sepsis and septic shock. N Engl J Med. 2013 [link]

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Host Risk Factors

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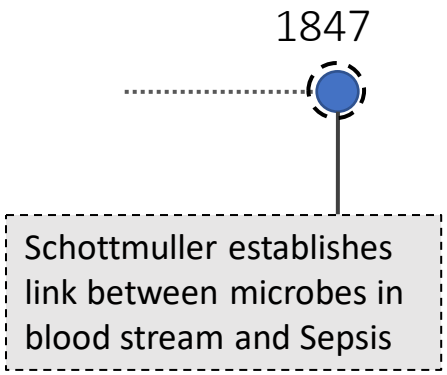
Sepsis Timeline



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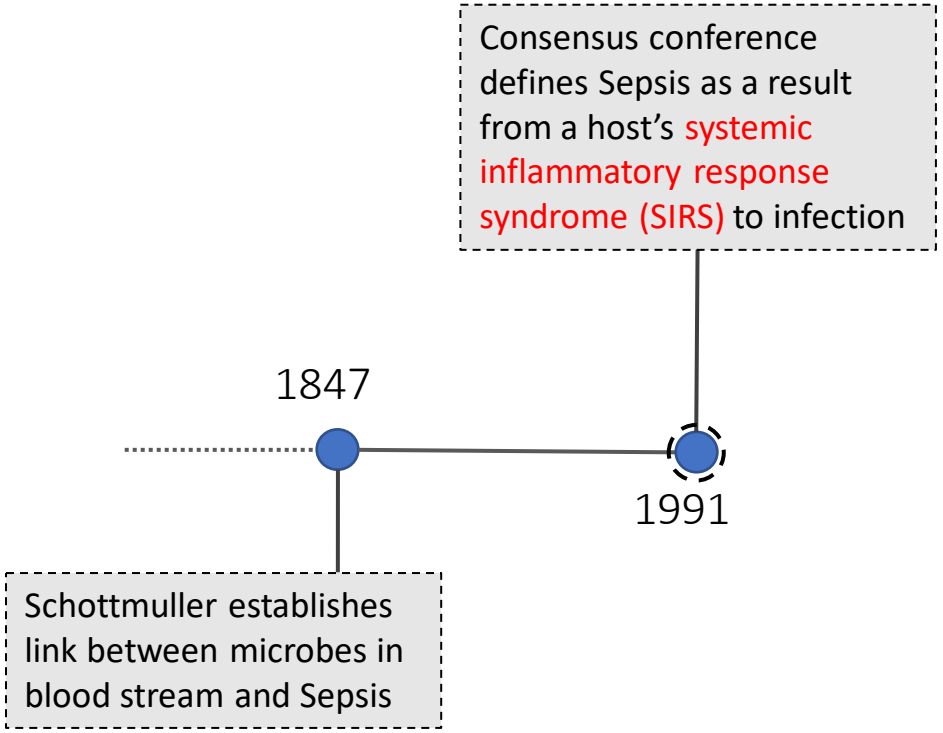

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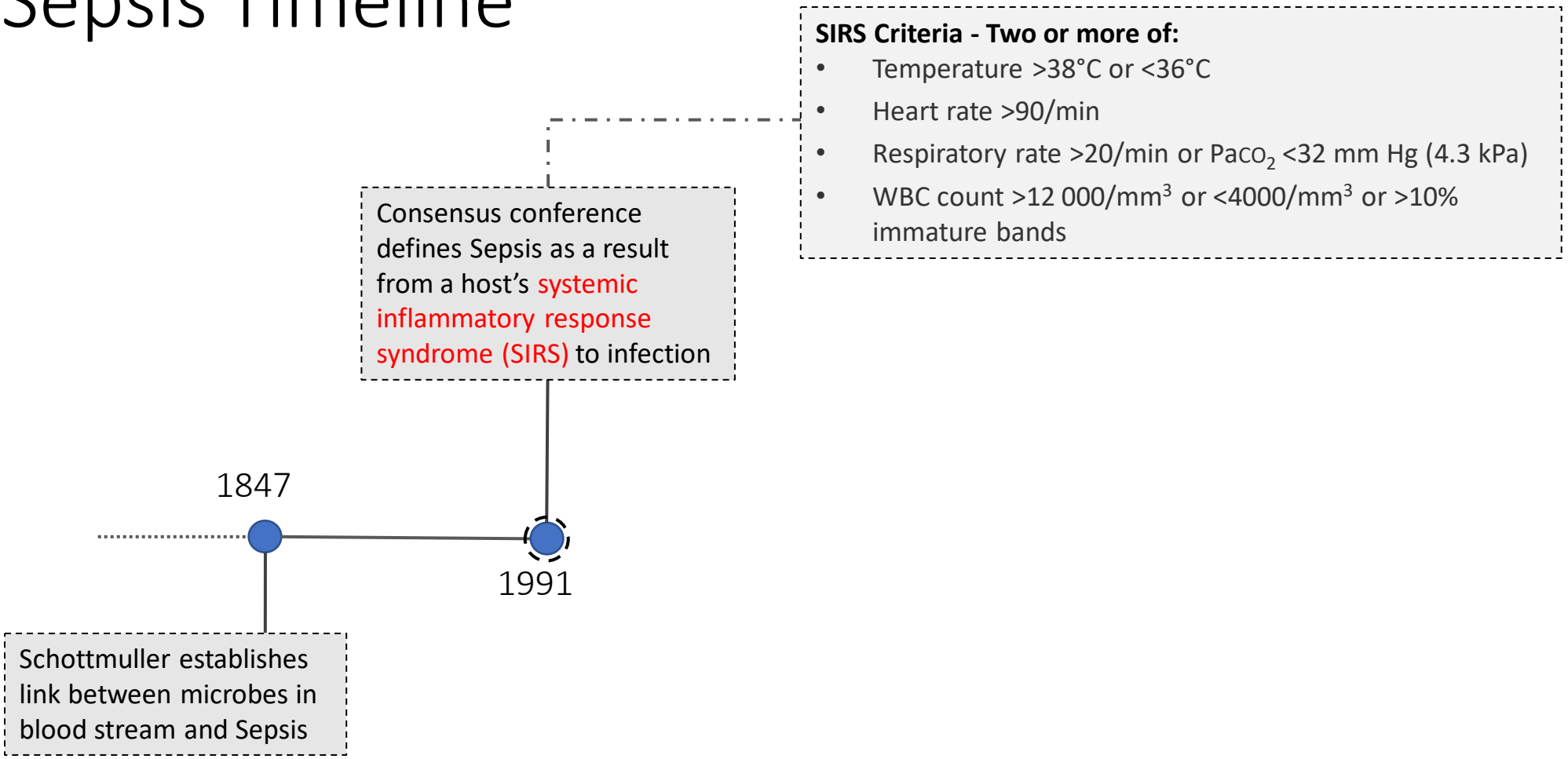

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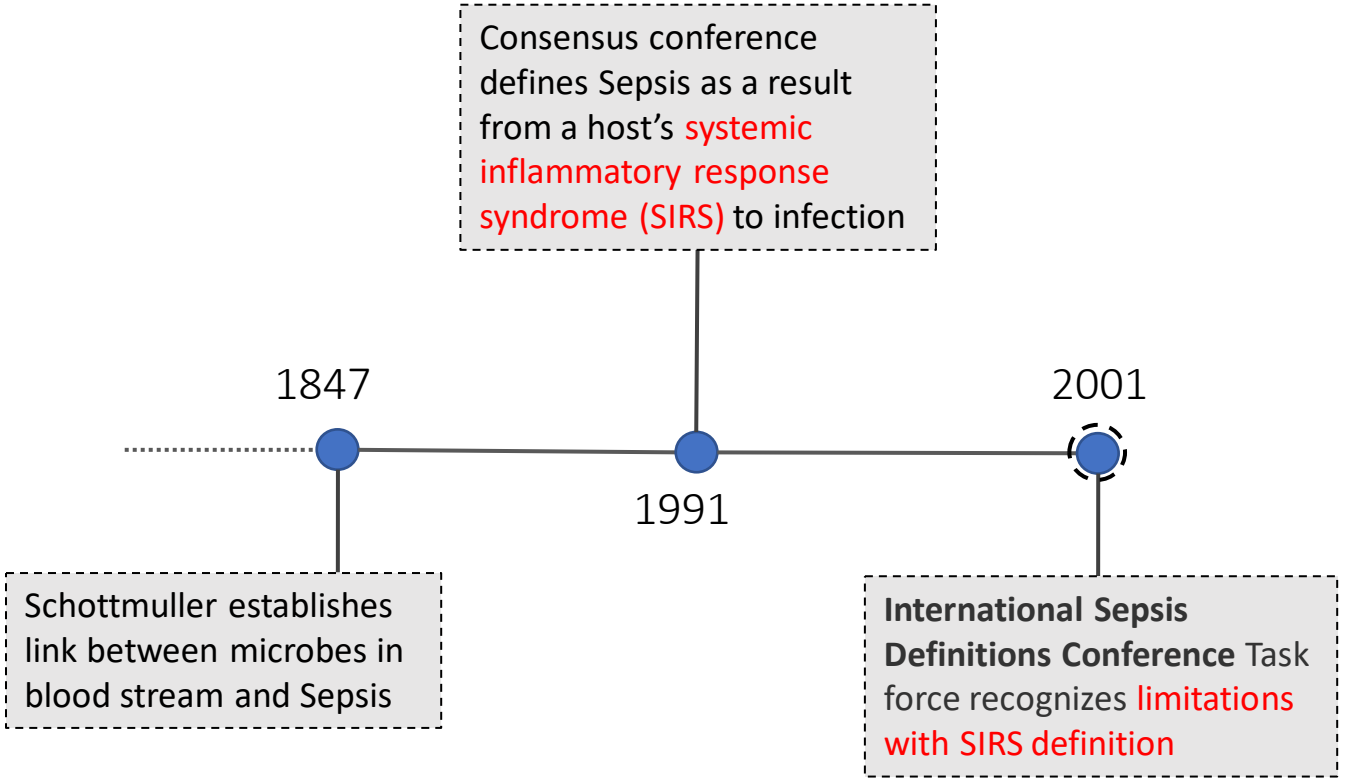

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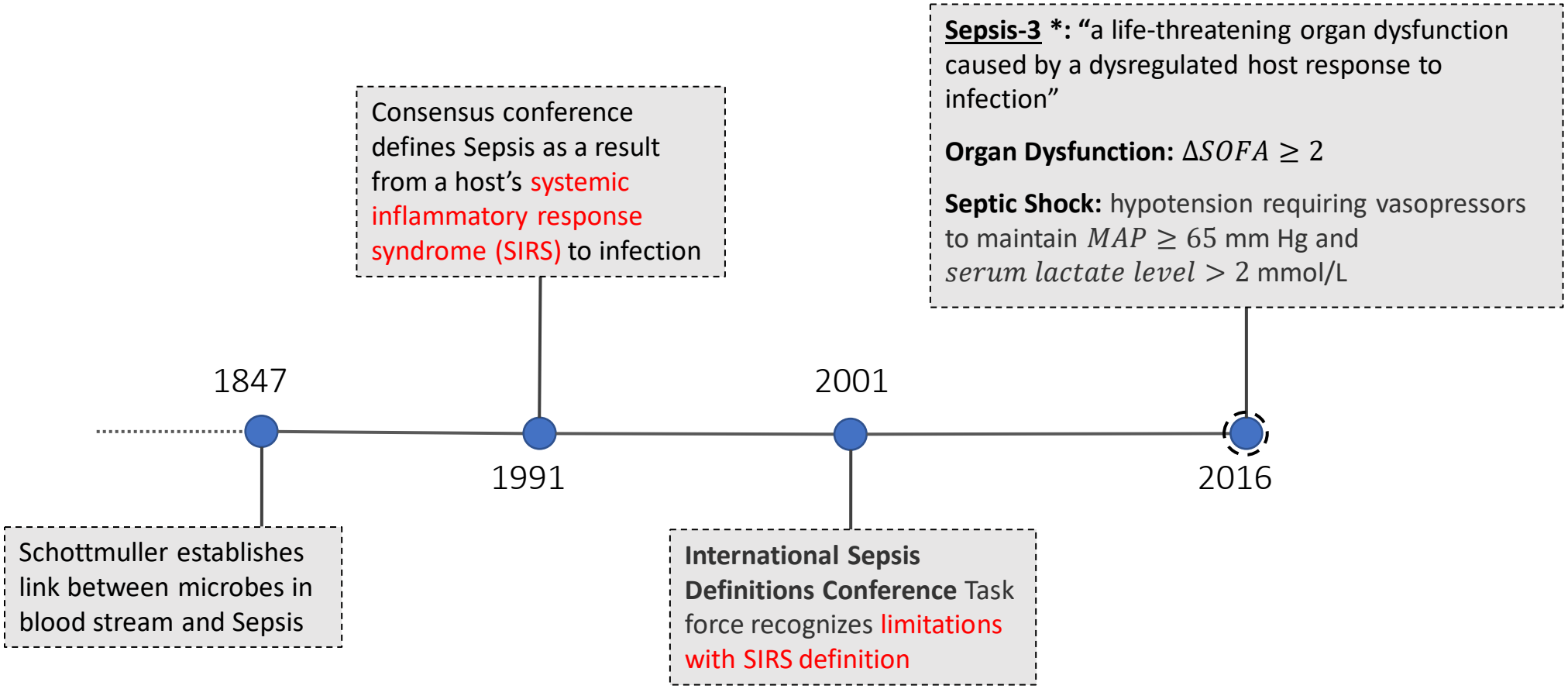

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Problems & Goals

- Effective treatment plans and preventive measures for patients at risk is **dependent on early and accurate diagnosis of the condition**.

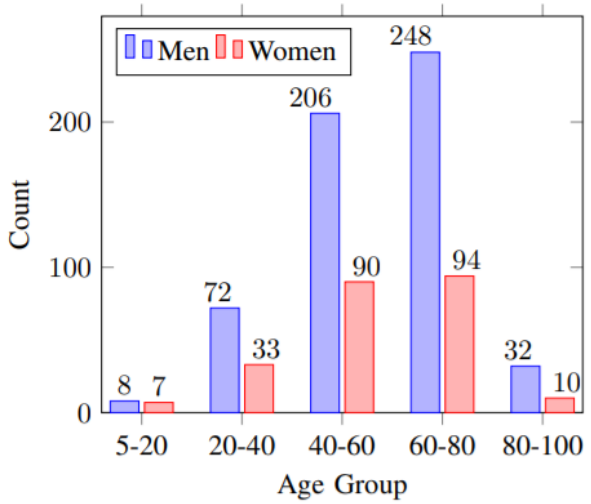
- As a result, in this work, we aim to:
  1. **Build a prognostic system** for sepsis, utilizing recorded clinical parameters of patients, and enabling technologies such as machine learning.

  2. **Predict two outcomes** for Sepsis patients to cover factors influencing Sepsis:
     1. *Sepsis Severity* - Classification of the severity into `Sepsis, Severe Sepsis, or Septic Shock`
     2. *Comorbidity Severity* – Predicting a bucket of `Charlson Comorbidity Index (CCI)`

  3. **Analyze and interpret predictions** to harmonize consistencies and/or contradictions between elements of human knowledge and that of a model.

Dataset

1. Data of 800 patients, collected and provided by Amrita Institute of Medical Sciences (AIMS).
2. Each patient record consists of around 80 features that can be categorized as
    1. On Admission Parameters – Age, Gender, etc.
    2. Clinical Parameters – Heart Rate, Temperature, PH, etc.
    3. Organ Failure Parameters – ASOFA (on admission), NSOFA (after 72 hr. in ICU)
3. Sepsis Severity Distribution:
    1) Sepsis (34%)
    2) Severe Sepsis (54.3%)
    3) Septic Shock (11.7%)
4. Comorbidity Severity Distribution:
    1) Mild (26.3%), if CCI < 3
    2) Moderate (33.6%), if $3 \leq$ CCI ≤ 4
    3) Severe (40.1%), if CCI ≥ 5



Dataset and Code used for experiments can be found here - https://bitbucket.org/GowriSrinivasa/interpretsepsis

Models & Evaluation

COMPARISON OF 5 FOLD CROSS VALIDATION METRICS FOR *Sepsis Severity* CLASSIFICATION

Model	Label	Pre.	Rec.	F1	Acc. (± std)
AdaBoost	1	0.77	0.78	0.77	
	2	0.89	0.81	0.85	0.82 (± 0.037)
	3	0.48	0.67	0.56	
	Avg	0.80	0.78	0.79	
GradientBoosting	1	**0.82**	0.80	0.81	
	2	**0.93**	0.88	**0.91**	**0.92 (± 0.016)**
	3	0.52	0.67	**0.58**	
	Avg	0.85	0.83	0.84	
Linear SVM	1	0.66	0.54	0.60	
	2	**0.93**	0.42	0.58	0.64 (± 0.05)
	3	0.24	**0.90**	0.38	
	Avg	0.76	0.52	0.56	
Random Forest	1	**0.82**	**0.89**	**0.85**	
	2	0.86	**0.94**	0.90	**0.93 (± 0.02)**
	3	**0.89**	0.38	0.53	
	Avg	0.85	0.85	0.84	

COMPARISON OF 5 FOLD CROSS VALIDATION METRICS FOR *Comorbidity Severity* CLASSIFICATION

Model	Label	Pre.	Rec.	F1	Acc. (± std)
AdaBoost	1	0.87	**0.94**	**0.91**	
	2	**0.77**	0.49	0.60	0.81 (± 0.02)
	3	0.69	0.90	**0.78**	
	Avg	0.77	0.76	0.75	
GradientBoosting	1	0.88	0.91	0.90	
	2	0.72	**0.56**	**0.63**	**0.82 (± 0.05)**
	3	**0.71**	0.85	0.77	
	Avg	0.76	0.76	0.76	
Linear SVM	1	0.72	0.88	0.79	
	2	0.65	0.34	0.45	0.57 (± 0.05)
	3	0.67	0.87	0.76	
	Avg	0.68	0.68	0.66	
Random Forest	1	**0.91**	0.88	0.89	
	2	0.74	0.52	0.61	**0.85 (± 0.04)**
	3	0.69	**0.91**	**0.78**	
	Avg	0.77	0.76	0.74	

Interpretations & Insights

TOP FEATURES AND PERMUTATION FEATURE IMPORTANCES

Feature	Importance	± std
Was Lactate Measured?	0.145	0.023
ASOFA	0.114	0.025
NSOFA	0.025	0.016
SOFA diff	0.025	0.0077
SBP	0.02145	0.014
PLR	0.021	0.0087

IMPORTANCES OF SIRS CRITERIA FEATURES

Feature	Importance	± std
Temperature	-0.00083	0.005
Heart rate	0.006	0.004
Respiratory rate	0.009	0.005
White blood cell count	0.015	0.008

Finding #1

SOFA scores & change in SOFA score are the most important features for the model.

Finding #2

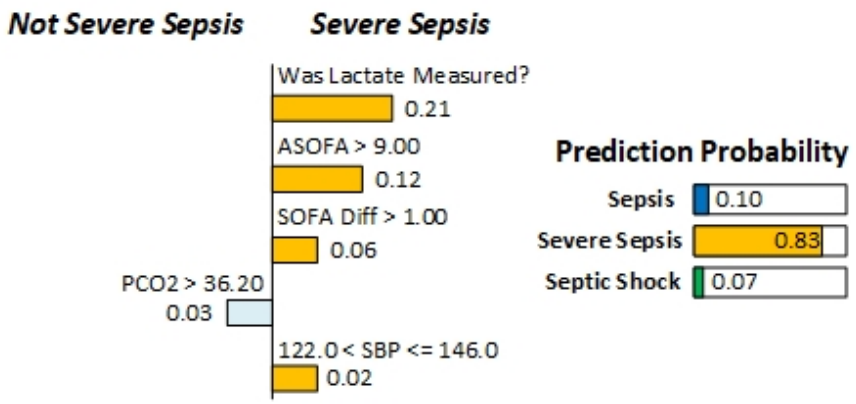
Systolic Blood Pressure, a direct indicator of hypotension for Septic Shock patients, is also important.

Finding #3

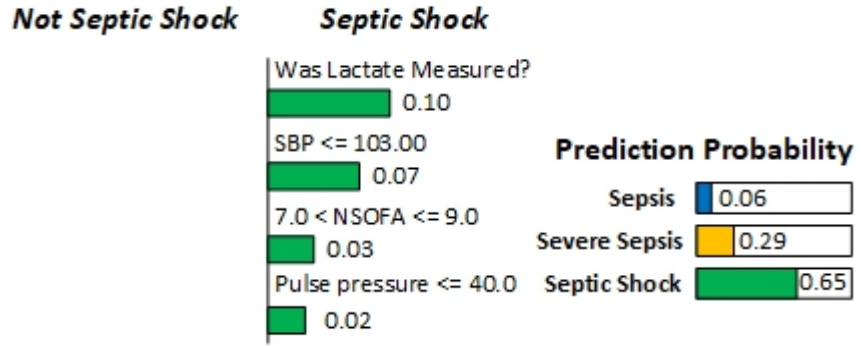
SIRS related features less helpful to predict Sepsis.

Consistent with the latest recommendations from the Third International Consensus Definitions for Sepsis and Septic Shock (2016)!!

Interpretations & Insights



Patient X – Severe Sepsis



Patient Y – Septic Shock

Patient X Model Insights

1. ASOFA > 9.0 => Severe Sepsis
2. SOFA Diff > 1.00 => Severe Sepsis
3. Systolic Blood Pressure range [122, 146] => Not Septic Shock

Patient Y Model Insights

1. SBP <= 103 => Hypotension => Septic Shock
2. Arterial Pulse Pressure <= 40 => Septic shock

Again, consistent with the latest recommendations and insights from experts and the task force!!

Summary

- Sepsis is amongst the leading causes of death in the world.
- Effective treatment plans for patients at risk is dependent on early and accurate diagnosis of the condition.
- We propose a novel 2 phase prognostic scoring system by predicting two complementary outcomes in sepsis patients - *Sepsis Severity* and *Comorbidity Severity*.
- We interpret and explain multiple patient predictions and map machine understanding to published domain knowledge used in the field.
- Lastly, we open-source the code, model, and preprocessed data - https://bitbucket.org/GowriSrinivasa/interpretsepsis