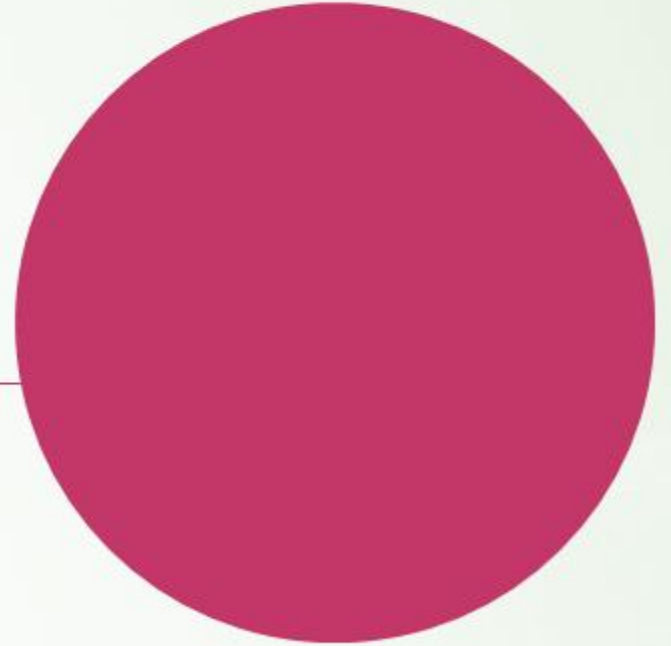


# Session 2: Acute Inflammation – Part 1

Abstract 1: Impact of Innate Immunity,  
Endothelial Damage, and Metabolic Biomarkers  
on COVID-19 Severity and Mortality

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# Immune, Vascular, and Metabolic Pathways involved in Severe COVID-19

T-cell

Joseph Rocco  
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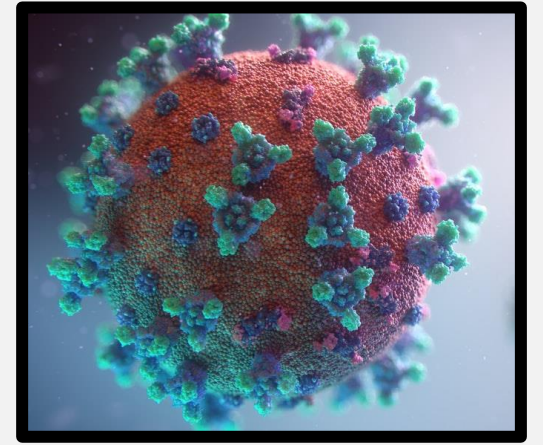
Mentor: Inhi Sereti  
Macrophage

IL-1 $\beta$

XIAP

4

# Background



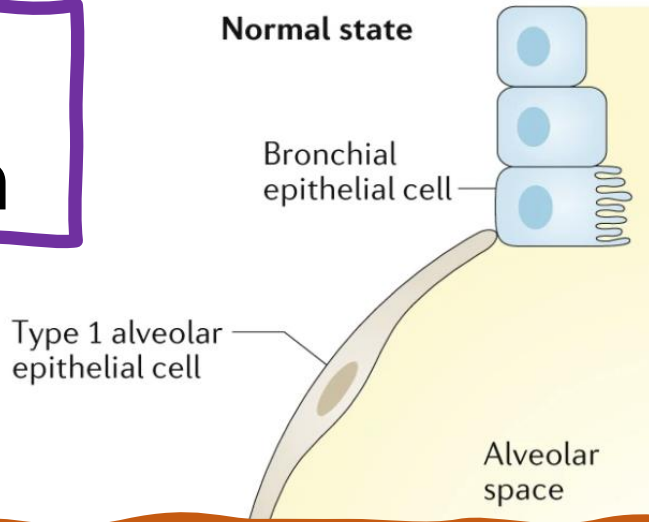
## **SARS-CoV-2 / Coronavirus disease 2019**

- A disease that needs no introduction

# COVID-19 Pathogenesis

## Metabolic:

- Irisin, Leptin



## Cytokines:

- IL1 $\beta$ , IL2, IL4, IL6, IL7, IL8, IL10, IL12, IL13, IL27, IFN $\gamma$ , TNF $\alpha$

## Innate Biomarkers:

- CRP, Serum Amyloid A, sCD14, Pentraxin-3, Elastase

## Complement:

- C1q, C3a, C5a, CH50, C1C-C1q, C1C-C3d

## Vascular:

- sICAM-1/3, sVCAM, E-selectin, P-selectin

## Coagulopathy:

- D-dimer, TFPI, TPO, ATIII, PAD-4, TM

# Soluble Biomarkers in COVID-19

- **128-patients** admitted consecutively
  - Provincial and Regional Center
- **All SARS-CoV-2 PCR positive**
- **Mild-Moderate** (n=60)
- **Severe-Critical** (n=68)
  - Hypoxia or organ failure
- Plasma/Serum samples from admission



<b>Characteristic (N = 128)</b>	<b>Mild-Moderate (N = 60)</b>	<b>Severe-Critical (N = 68)</b>	<b>P-value</b>
Age – years	53 (43-62)	67 (56.8-84.2)	<b>&lt;0.001</b>
Female – no. (%)	32 (53.3)	34 (50)	0.8
<b>Race – no. (%)</b>			>0.9
Caucasian	57 (100)	65 (97)	
BMI (kg/m <sup>2</sup> )	24.3 (22.2-26.0)	25.6 (23.1-27.3)	0.11
Symptoms to Lab (Days)	9.0 (7.0-13.5)	15.0 (10.0-30.2)	<b>&lt;0.001</b>
Total neutrophil count	3.48 (2.71-4.57)	3.64 (2.36-5.55)	0.6
Total lymphocyte count	1.39 (0.86-1.89)	1.1 (0.66-1.61)	<b>0.05</b>
<b>Treatment – no. (%)</b>			
Antibiotics	2 (3.3)	17 (25)	
Tocilizumab	2 (3.3)	11 (16.2)	
Steroids	0 (0)	5 (7.5)	

# Soluble Biomarkers - Analyses

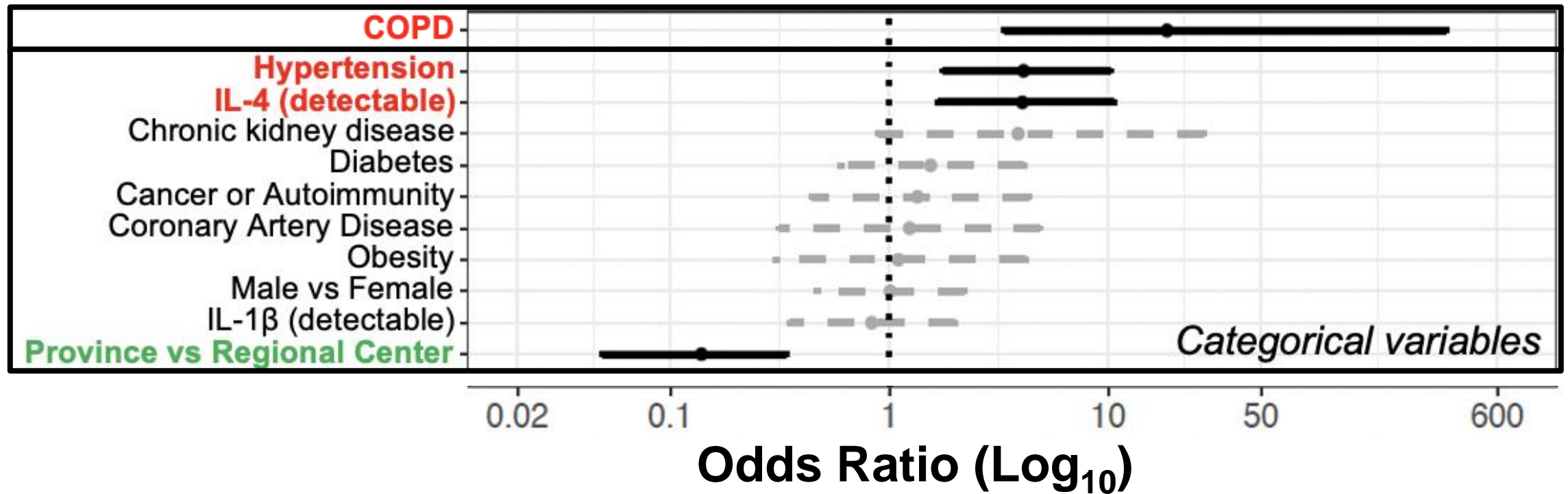
- ❖ Mild-Mod vs Severe-Crit → Logistic regression  
→ Control for symptoms to lab draw
- ❖ In-Hospital Mortality → Logistic regression  
→ Control for symptoms to lab draw
- ❖ Multivariable regression (Severity)
- ❖ Correlation Networks, Decision Tree Analysis



# Clinical Characteristics - Categorical

## Severe-Critical Disease

← Less likely      More likely →

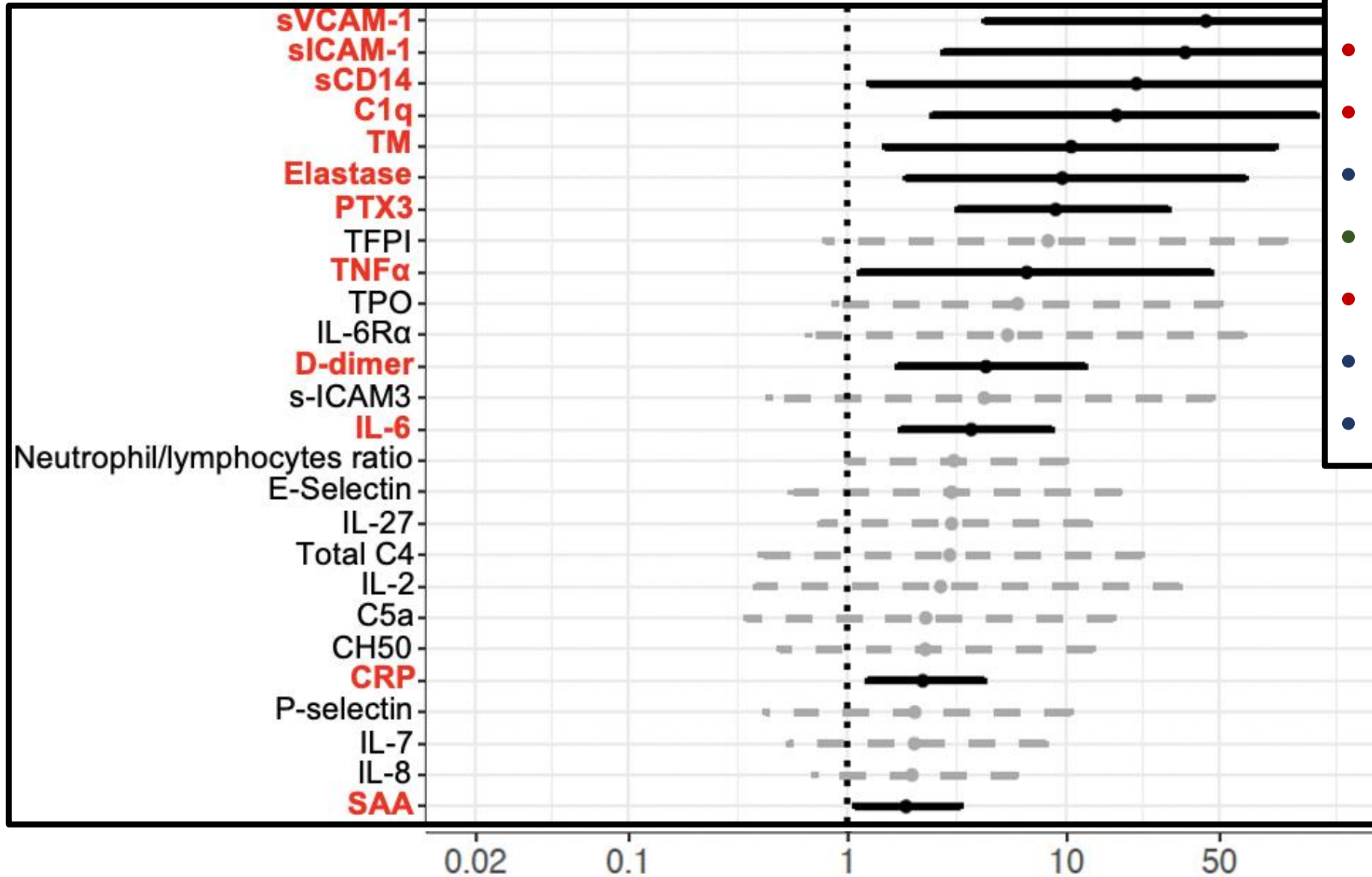


**Comorbidities: COPD, Hypertension**

# Severe-Critical Disease

← Less likely

More likely →



## Strongest:

- sVCAM-1
- sICAM-1
- sCD14
- C1q
- Thrombomodulin
- Elastase
- Pentraxin-3

## Significant:

- TNF $\alpha$
- D-dimer
- CRP
- SAA
- IL-6

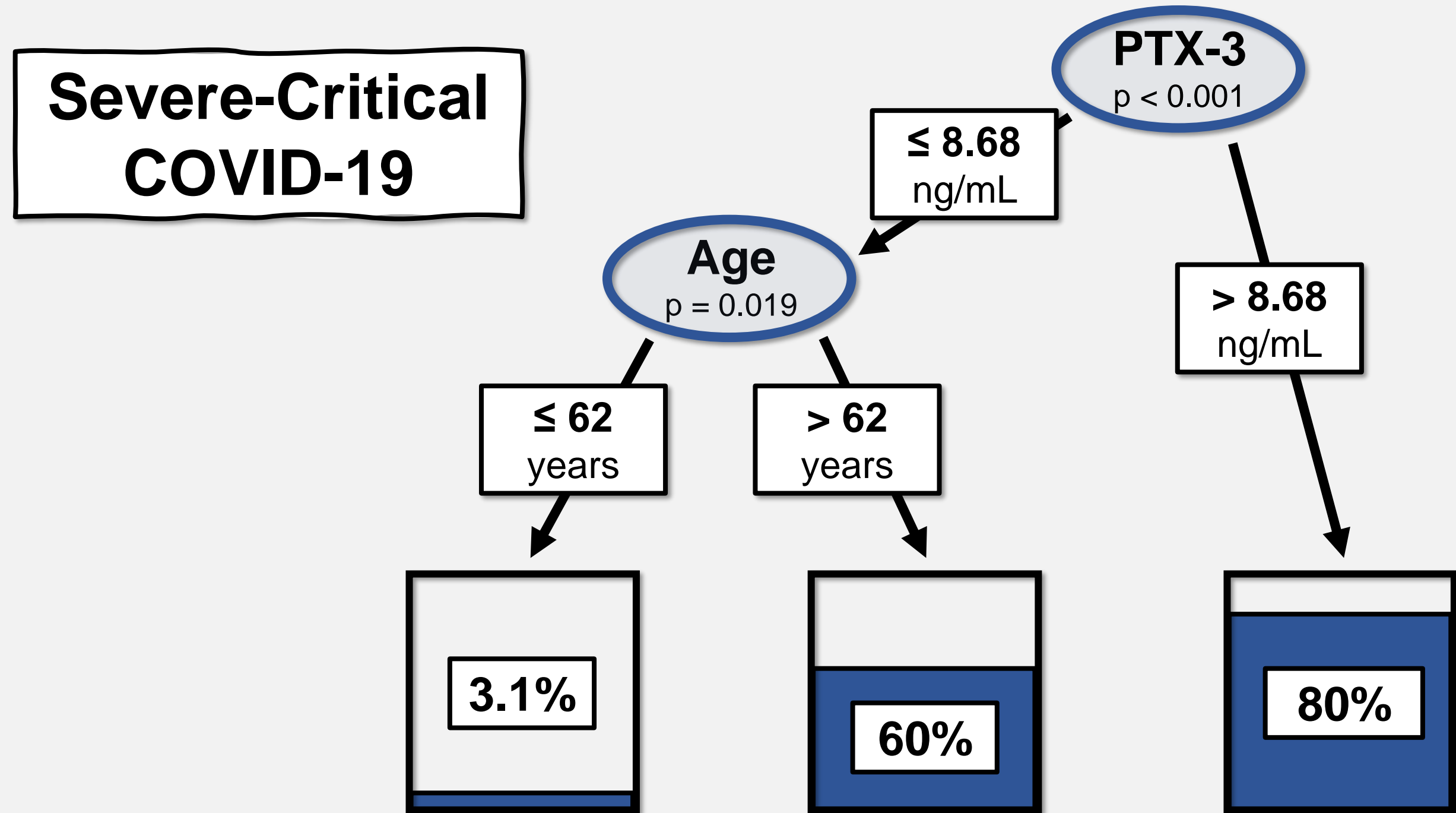
Irisin → associates with protection from severe COVID-19

## Severe-Critical Disease

### Multivariable Logistic Regression:

- ❖ Age - OR 1.143
- ❖ D-dimer - OR 107.6
- ❖ IL-6 - OR 61.7

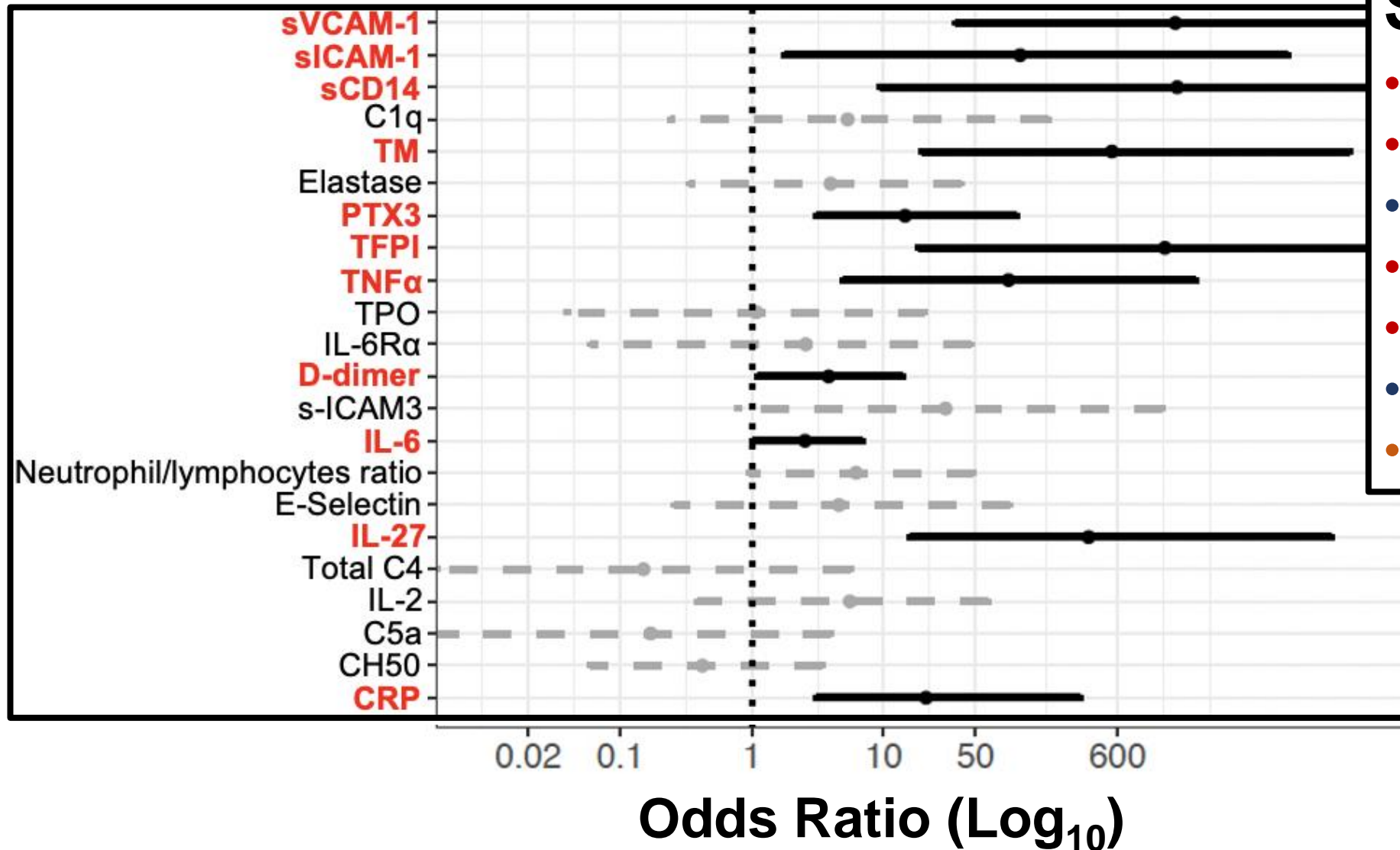
# Severe-Critical COVID-19



# In-Hospital Mortality

← Less likely

More likely →

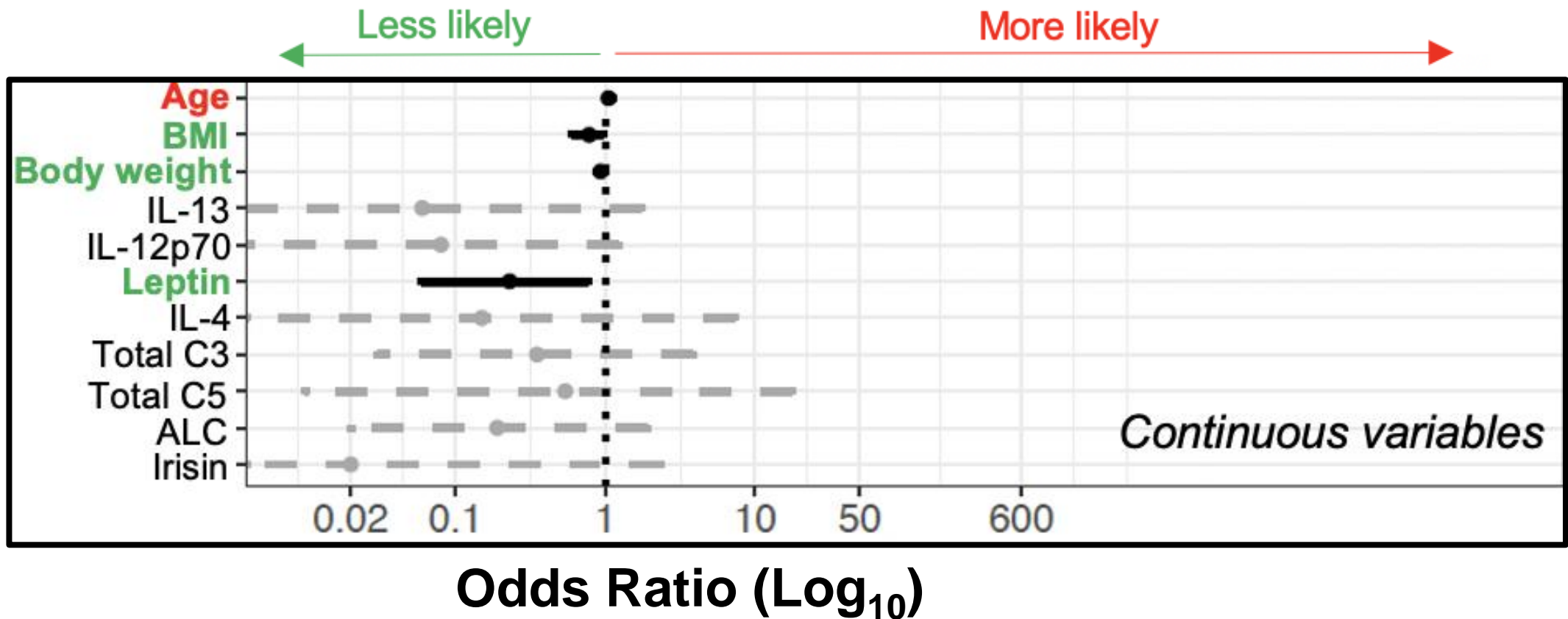


- Strongest:**
- sVCAM-1
  - sICAM-1
  - sCD14
  - Thrombomodulin
  - TFPI
  - IL-27
  - TNFα

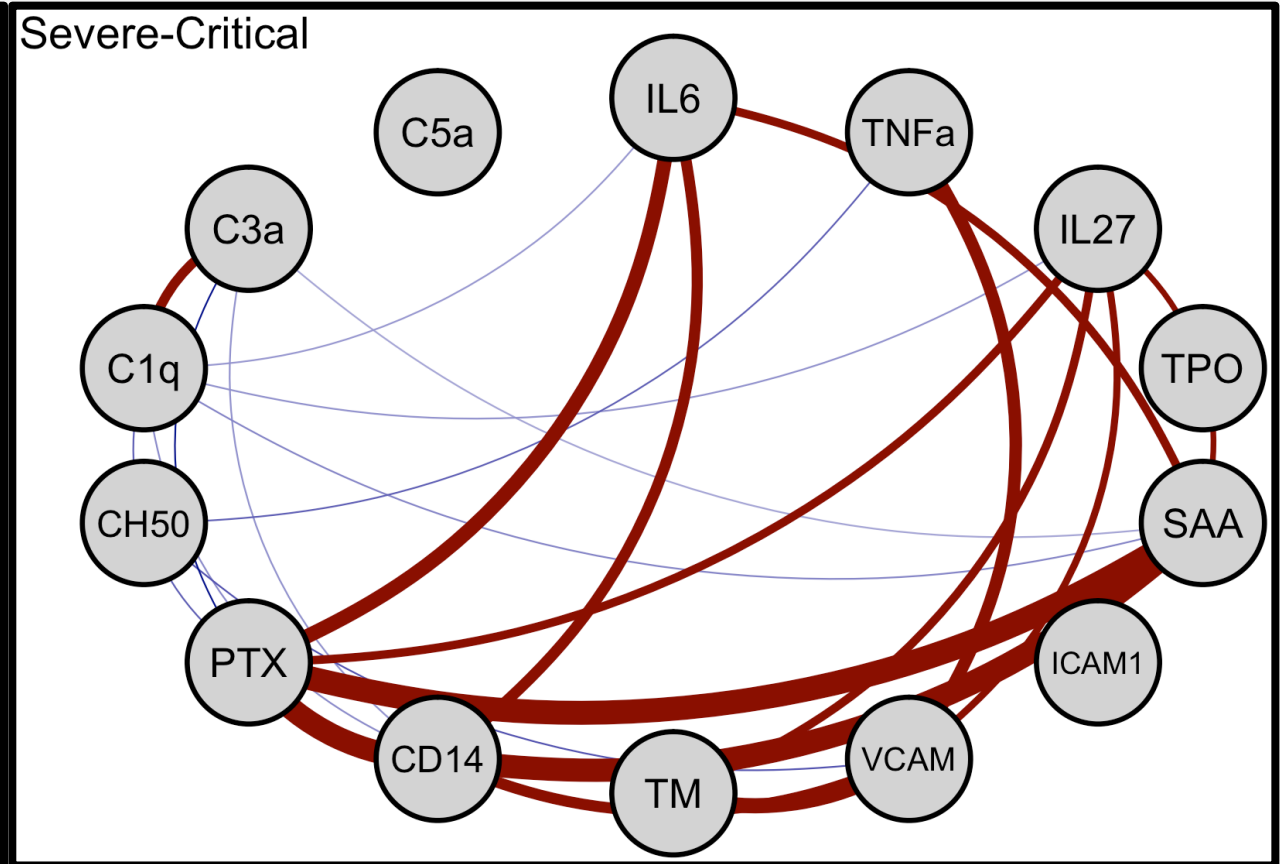
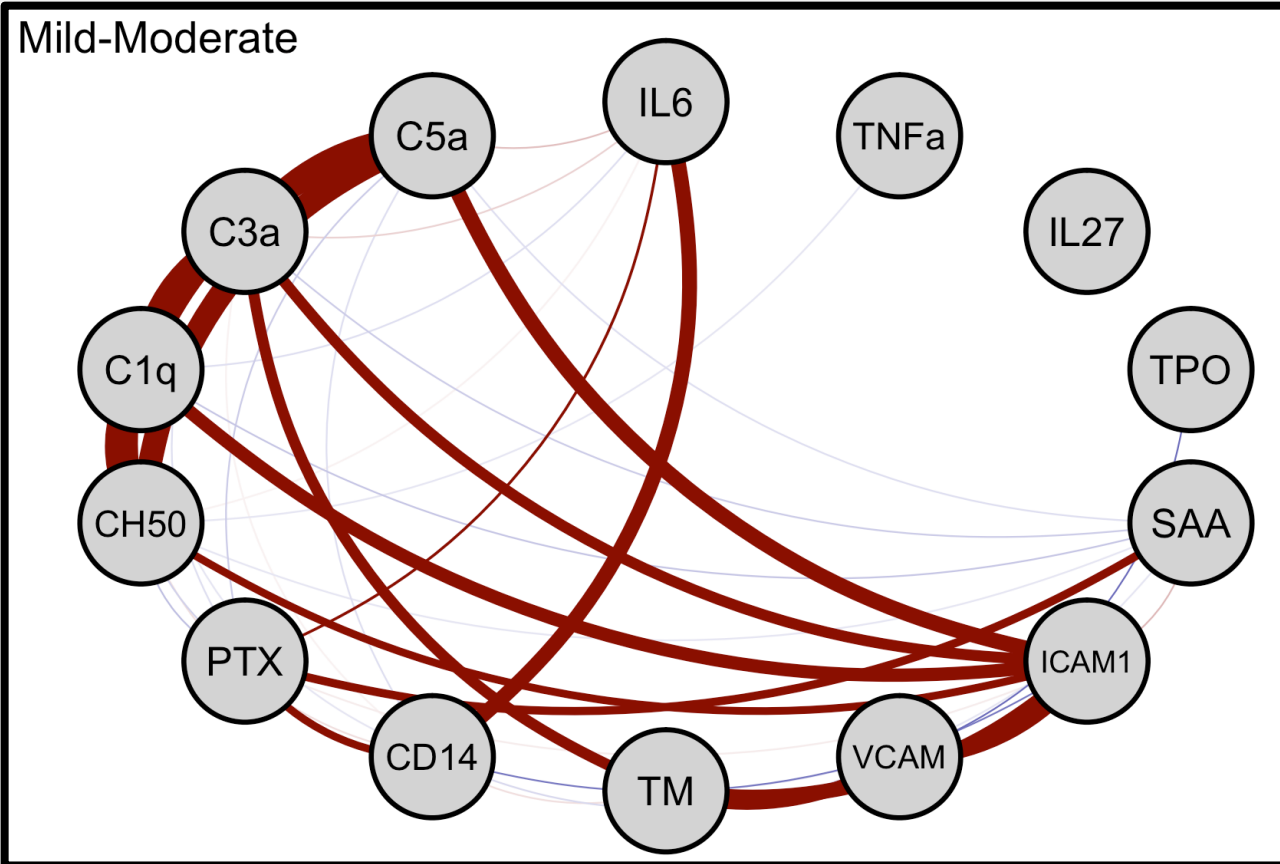
- Significant:**
- Pentraxin-3
  - D-dimer
  - IL-6
  - CRP

# Leptin → associates with protection from COVID-19 mortality

## In-Hospital Mortality



# Correlation Networks



# Conclusions

- **Innate immune/myeloid activation (sCD14, IL27)**
- **Endothelial damage markers:**
  - Tied to pathogenesis; potential prognostic markers
- **Metabolic biomarkers (irisin, leptin)**
  - Associate with protection from severe disease
- **PTX-3 predictive marker of severe COVID-19**
- **Comparison to current hosts/newer variants**



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