COVID-19 Natural History of Severe Disease

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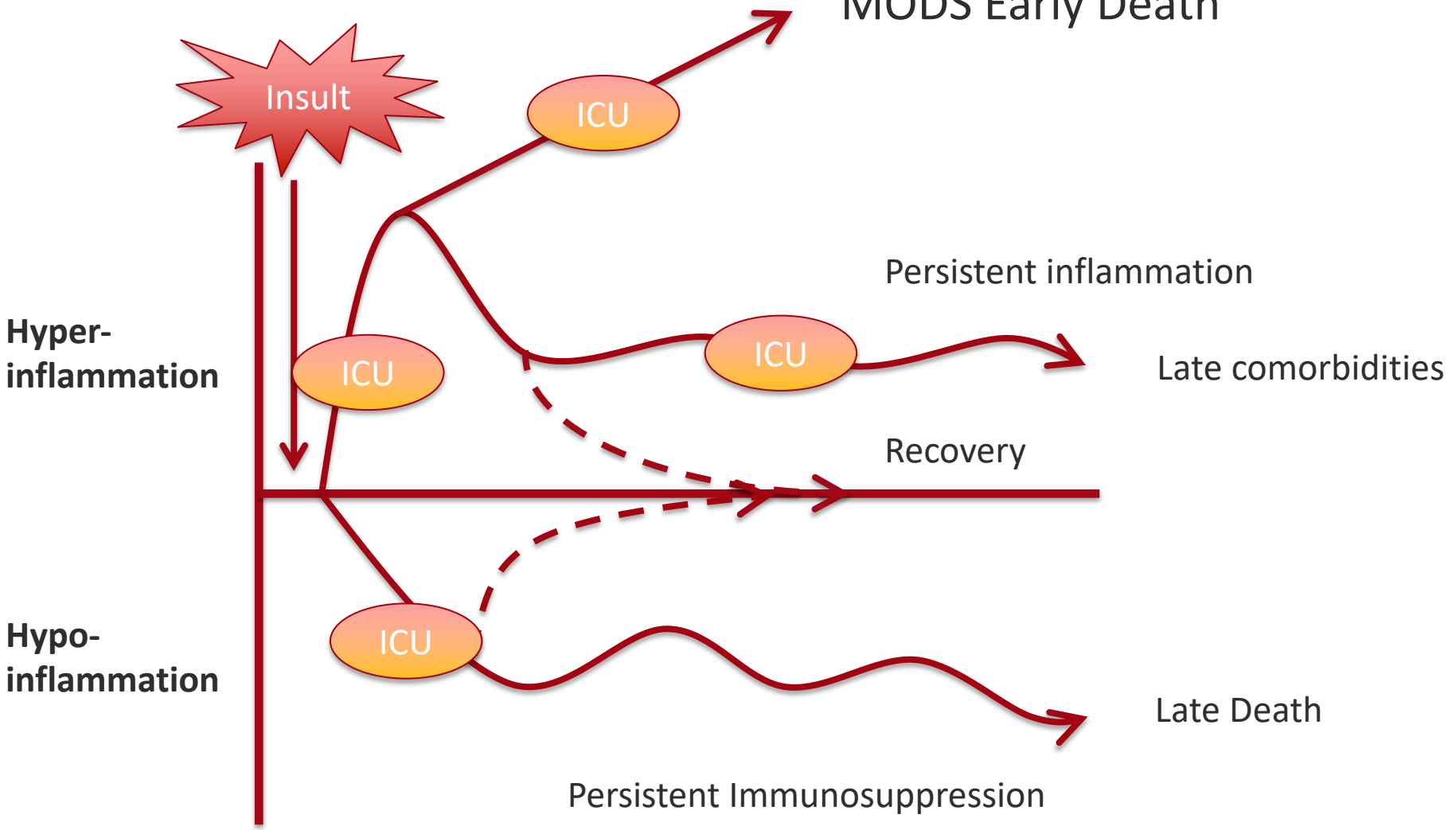
Central questions in severe COVID-19

Modern critical care involves supporting failing organs to allow for recovery.

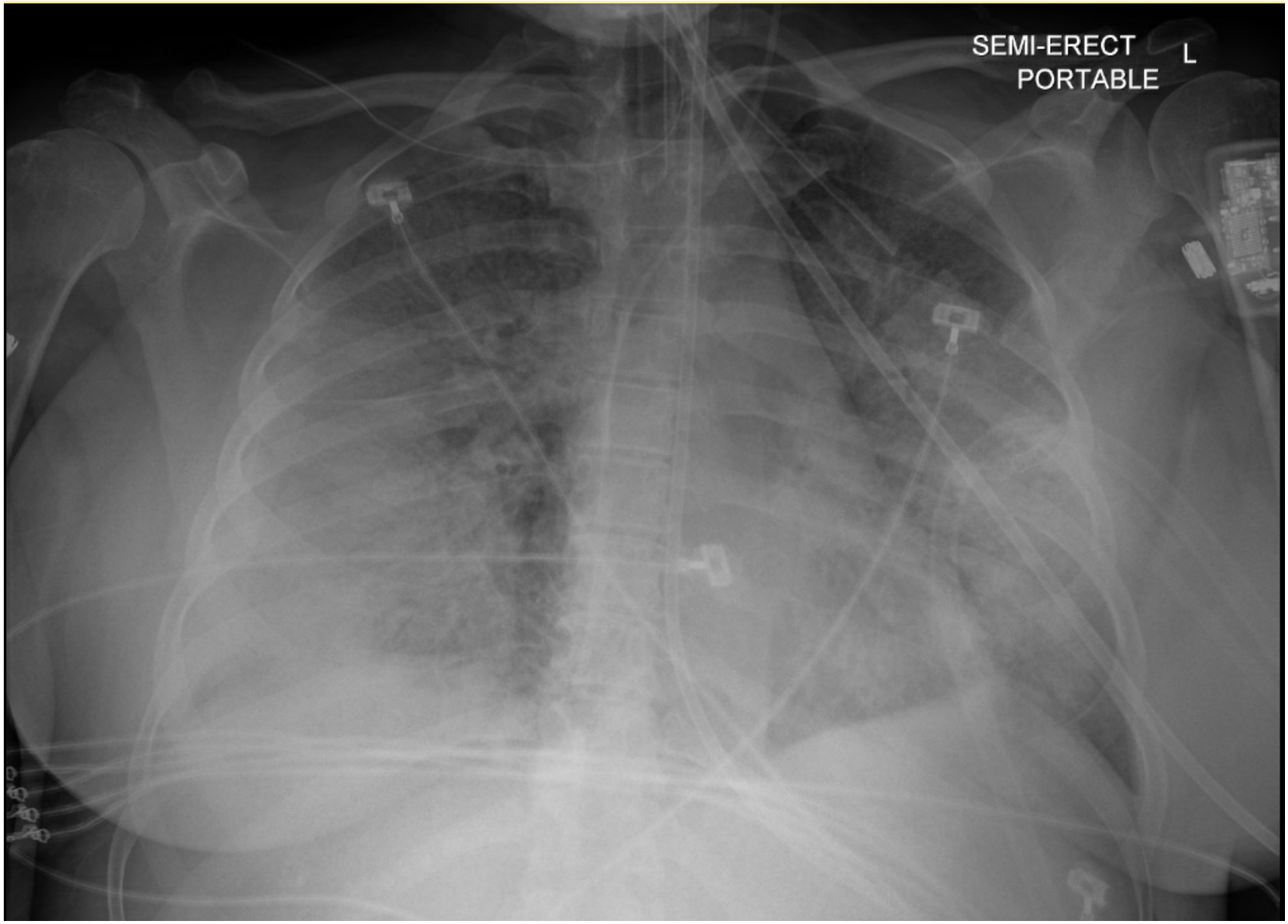
Therapy also targets specific pathogens and the non-specific inflammatory response (steroids).

Can we better understand the natural history of severe COVID-19?

State and Phase



Hotchkiss et al **Nat Rev Dis Primers** 2016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Does baseline severity of COVID-19 respiratory failure predict outcomes?

Summary of ventilator data of 260 patients admitted to WCM with respiratory failure treated with mechanical ventilation

Schenck et al **Ann Am Thorac Soc** 2020

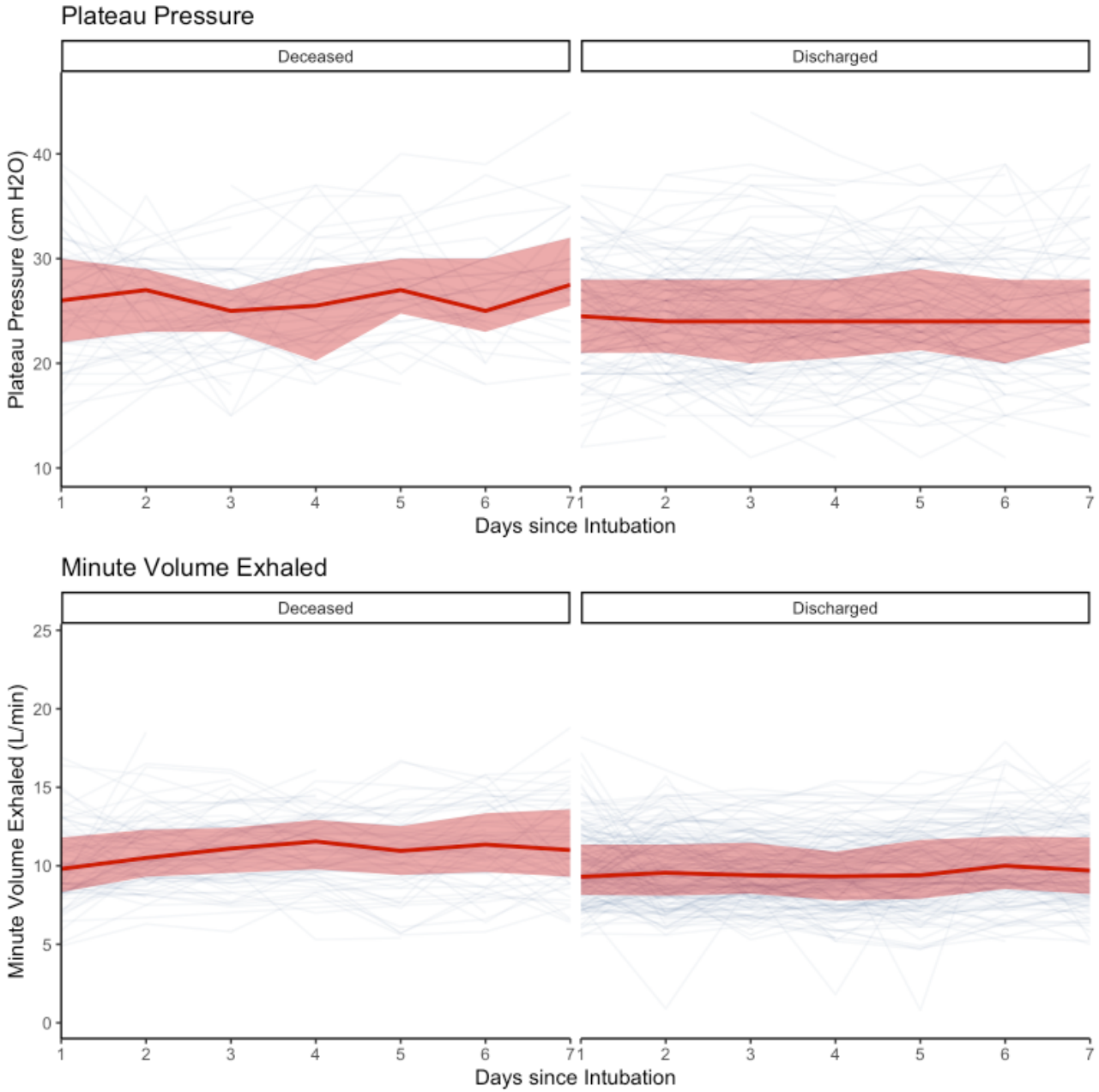
Summary

Day 1 Comparisons

Ventilator Parameters by Status, Day 1

Characteristic	Deceased, N = 90[1]	Discharged, N = 170[1]	p-value[2]	q-value[3]
PCO2 Arterial	46 (38, 52)	44 (38, 52)	0.5	0.8
PO2 Arterial	92 (75, 121)	93 (74, 130)	>0.9	>0.9
Minute Volume Exhaled	9.80 (8.33, 11.80)	9.30 (8.15, 11.35)	0.4	0.7
PEEP	10.0 (9.0, 12.0)	10.0 (8.5, 12.0)	0.3	0.6
Tidal Volume	450 (400, 500)	450 (400, 500)	0.8	>0.9
Peak Inspiratory Pressure	31.0 (25.0, 35.0)	30.0 (26.0, 34.8)	0.6	0.8
Plateau Pressure	26.0 (22.0, 30.0)	24.5 (21.0, 28.0)	0.2	0.6
PF Ratio	105 (84, 137)	117 (86, 160)	0.086	0.5
Tidal Volume / PBW	6.92 (6.24, 7.70)	7.06 (6.36, 8.31)	0.2	0.6
Static Compliance	28 (23, 36)	29 (22, 40)	0.4	0.7
Driving Pressure	15.0 (12.0, 18.2)	14.0 (11.0, 16.5)	0.065	0.5
Ventilatory Ratio	1.93 (1.51, 2.32)	1.80 (1.47, 2.30)	0.6	0.8

Schenck et al **Ann Am Thorac Soc** 2020



Schenck et al **Ann Am Thorac Soc** 2020

Non-pulmonary severe COVID-19

Intubation → ARDS (26.3%)

Myocardial infarction (4.7%)

Stroke (2.3%)

Thromboembolic events (7%)

Renal failure (7%)

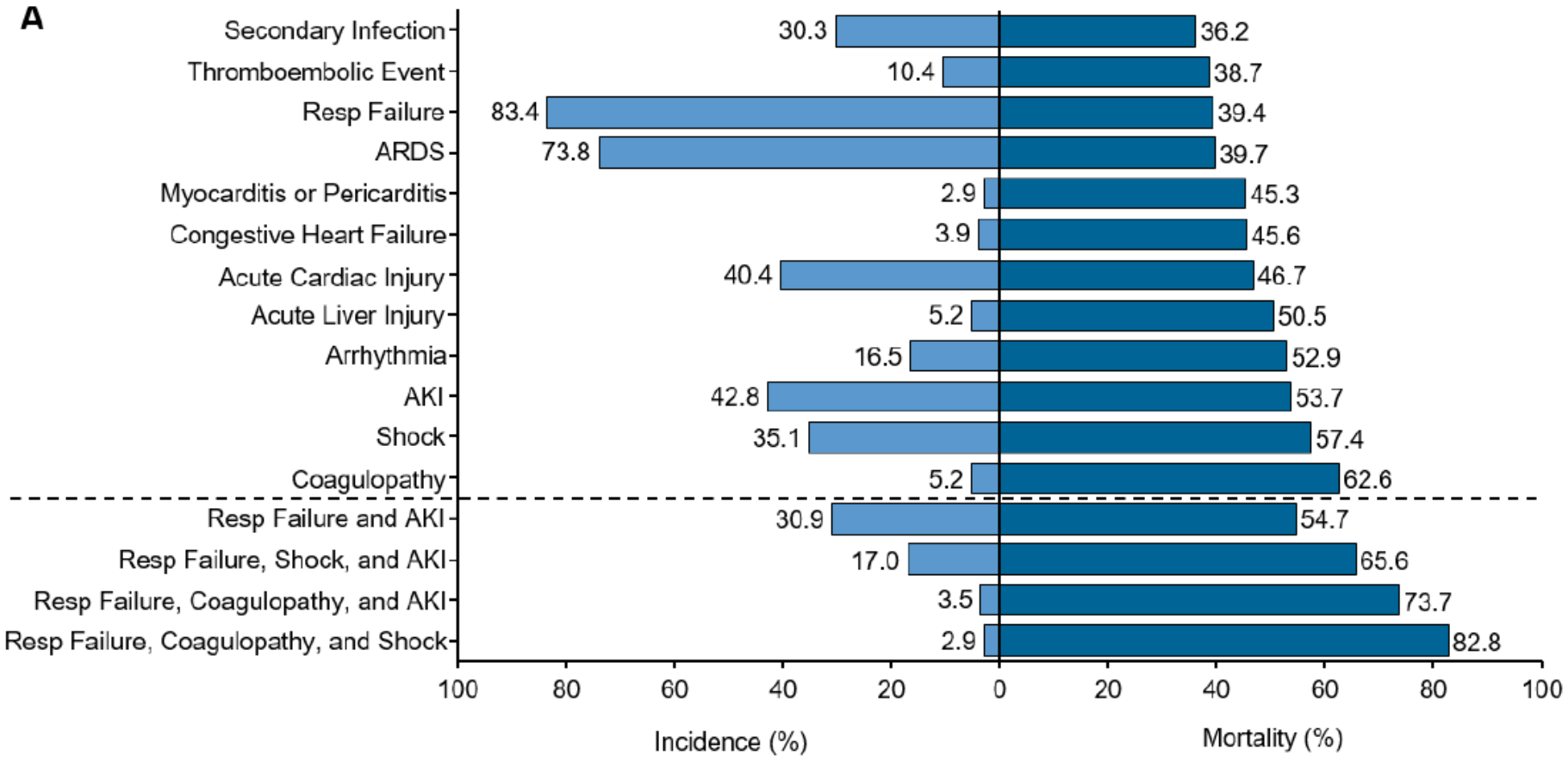
Merkler et al **JAMA Neurology** 2020

Goyal et al **Ann Intern Med** 2020

Goyal et al **NEJM** 2020

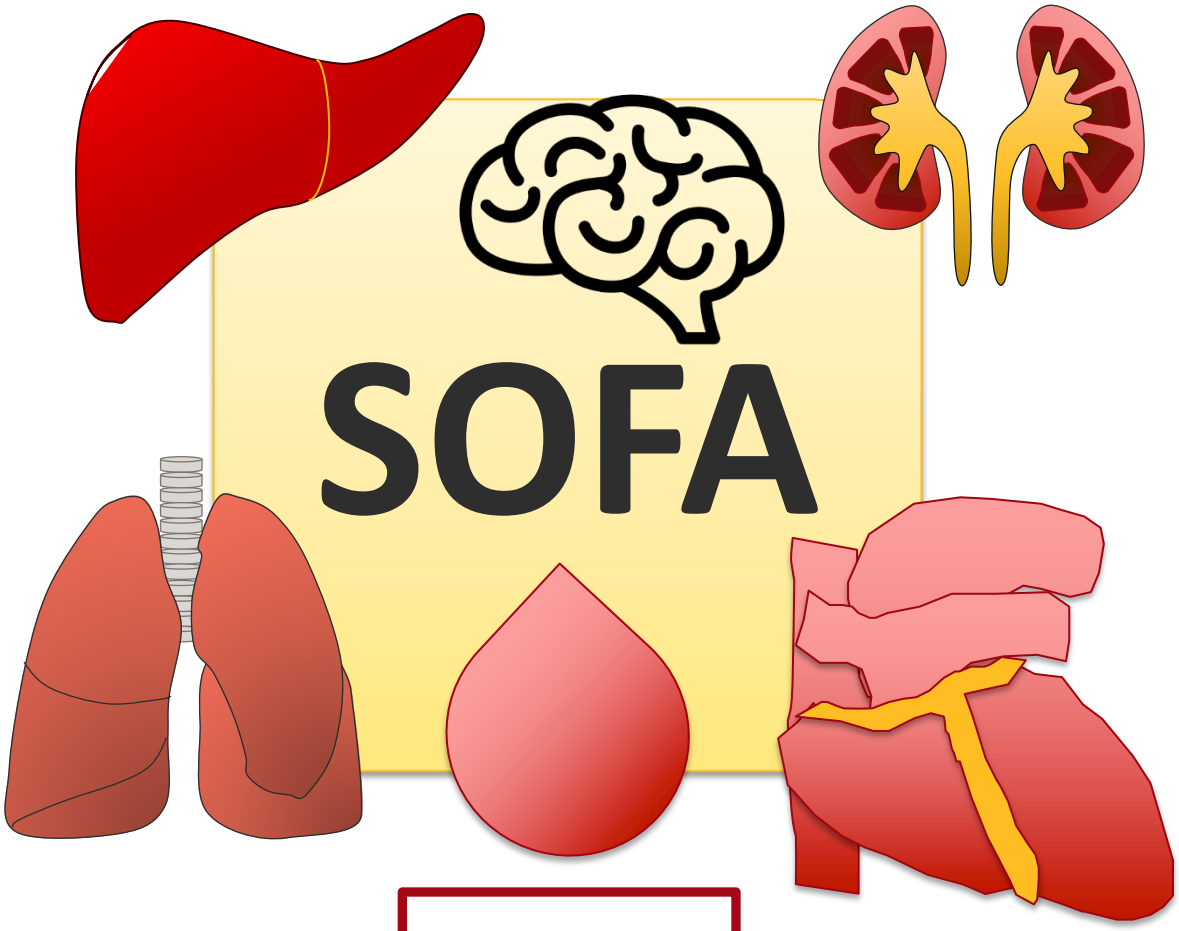
Gupta et al **JAMA Intern Med** 2020

Additive organ dysfunction predicts poor outcomes



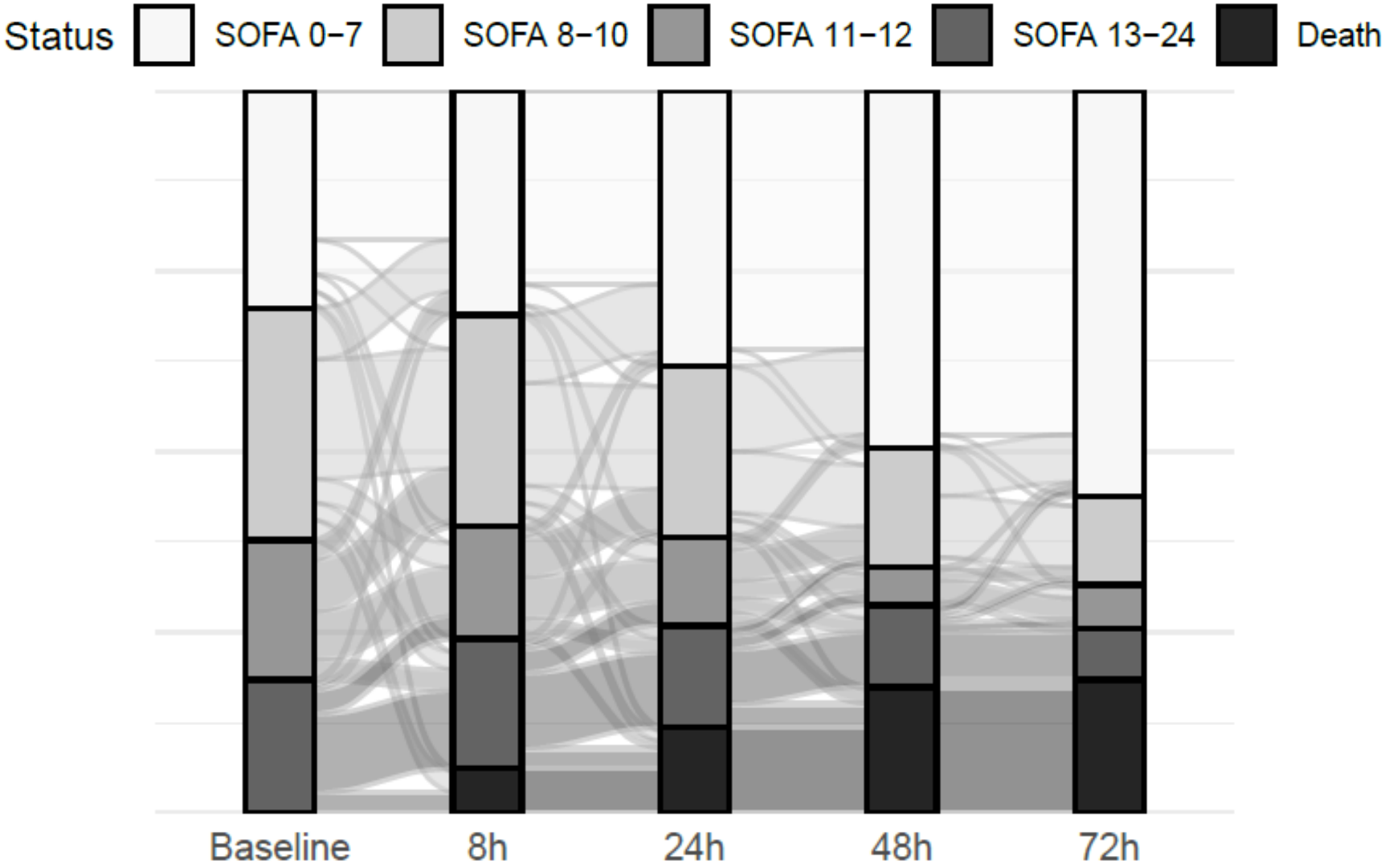
Gupta et al **JAMA Intern Med** 2020

Organ Failure Subphenotyping

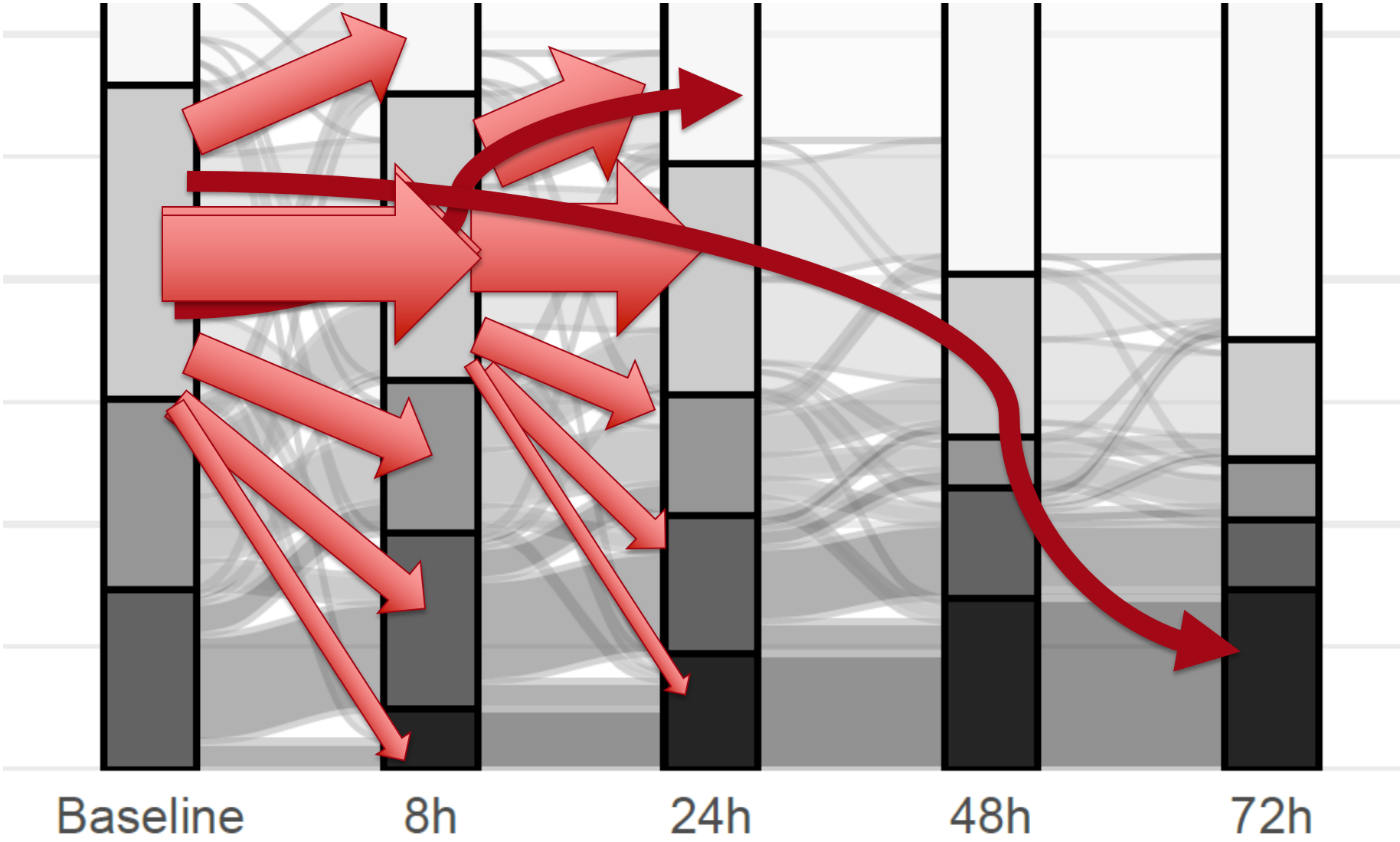


Su et al **medrxiv** 2020

Organ dysfunction trajectory

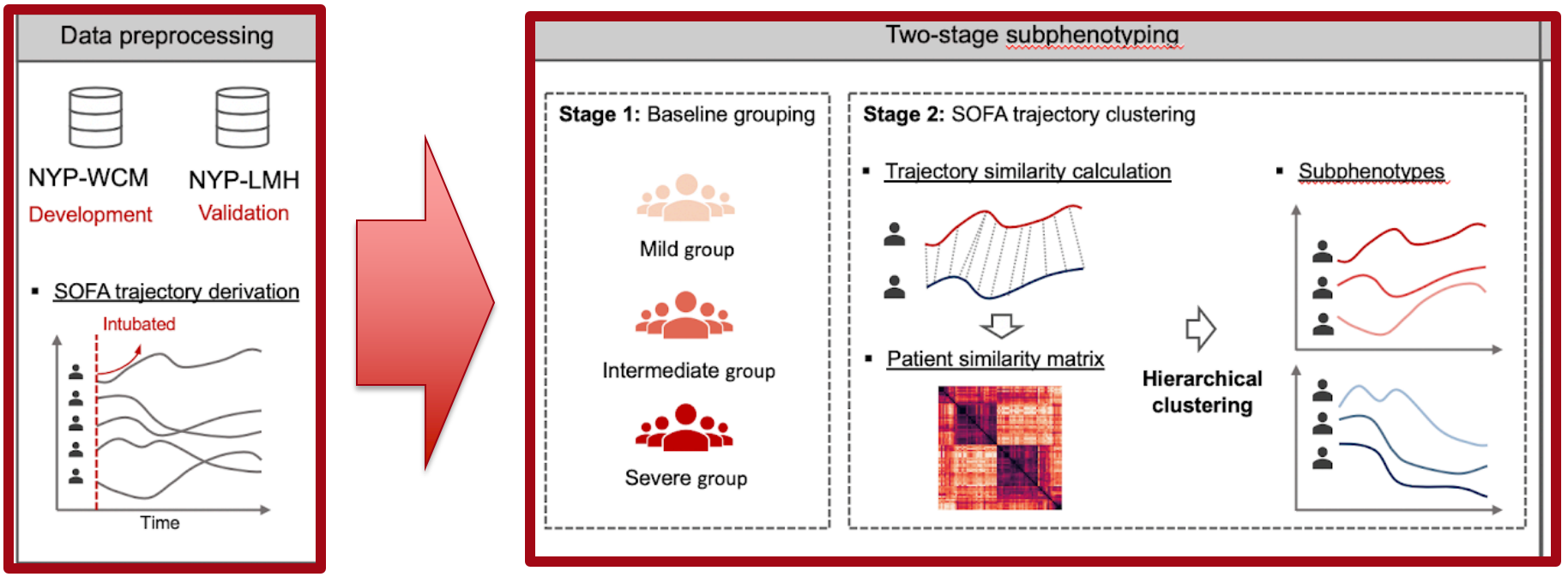


Zampieri et al **AJRCCM** 2019



Zampieri et al **AJRCCM** 2019

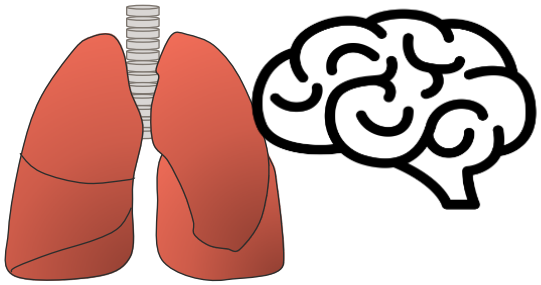
Two staged evaluation of organ dysfunction trajectory



Su et al **medrxiv** 2020

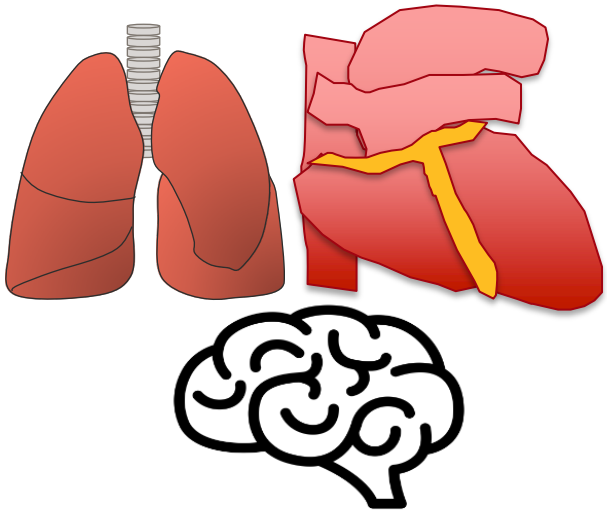
SOFA based grouping by number of failing organs

Mild



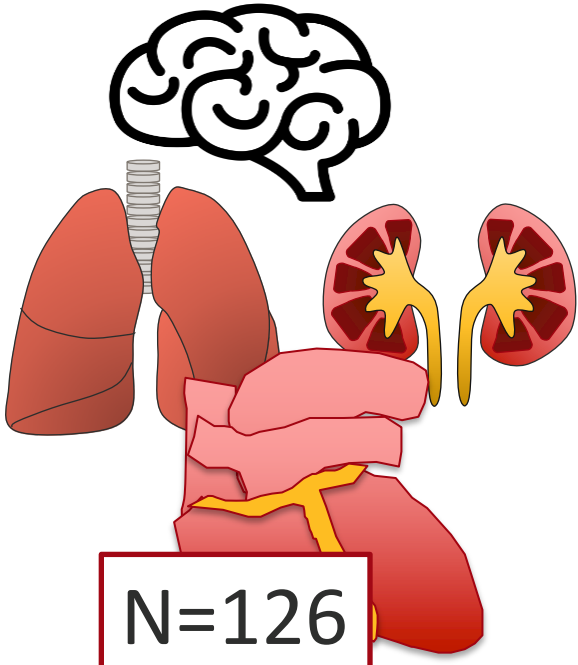
N=76

Intermediate



N=116

Severe



N=126

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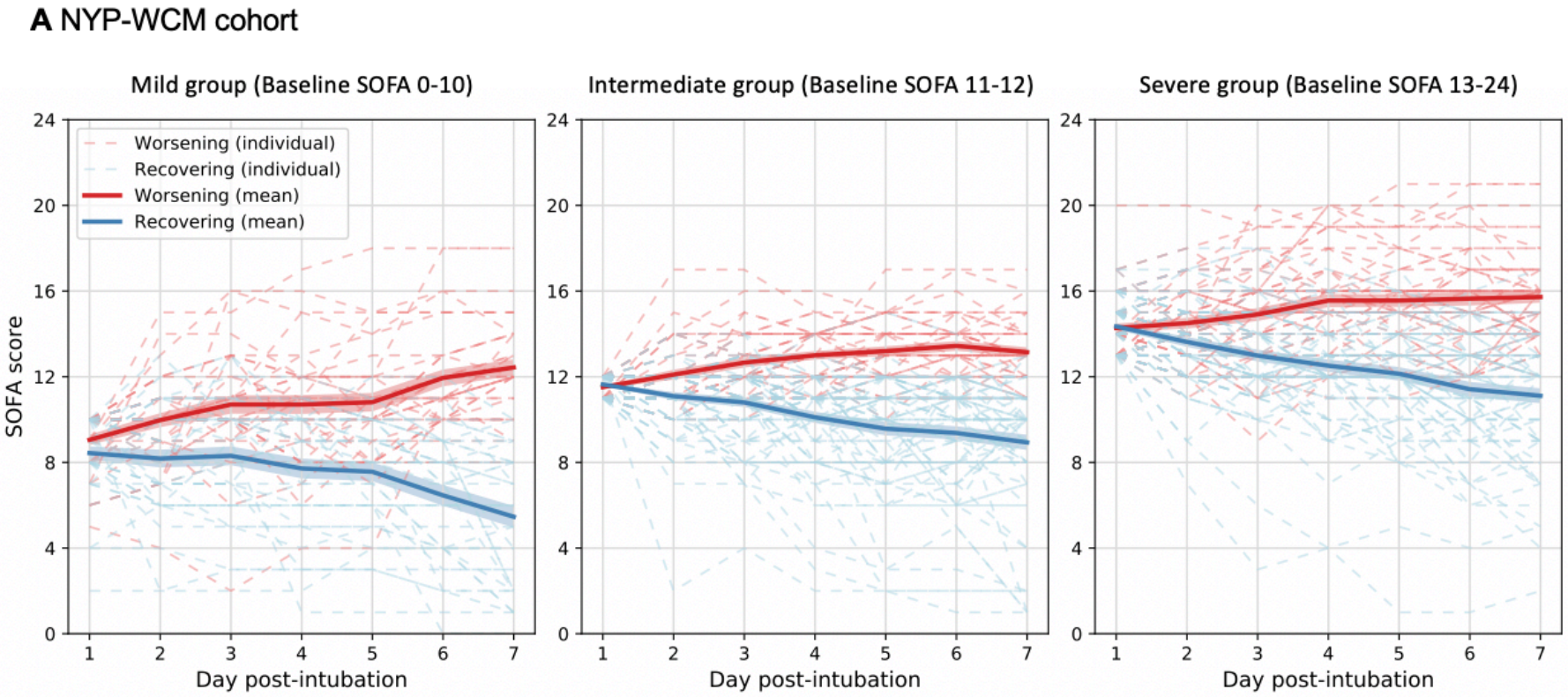
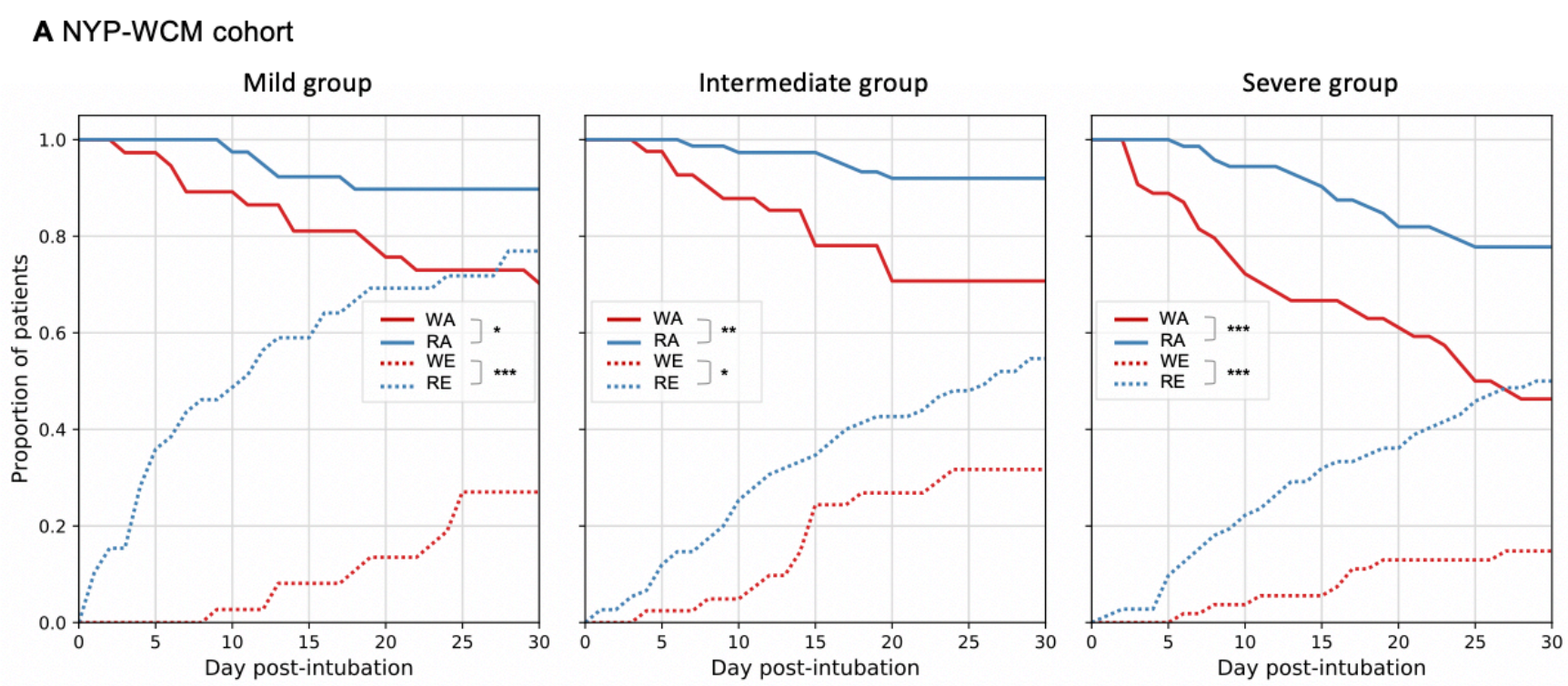
There are distinct worsening and recovering subphenotypes



Su et al **medrxiv** 2020

Trajectory predicts outcomes



Su et al **medrxiv** 2020

Summary and questions

Pulmonary and non-pulmonary organ dysfunction is important in COVID-19 critical illness.

Additive non-improving organ failure drives outcomes.

Are there specific treatments for pulmonary and non-pulmonary organ dysfunction in COVID-19 to prevent progression?

Can we identify and modulate dynamic COVID-19 inflammatory states in real time?

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