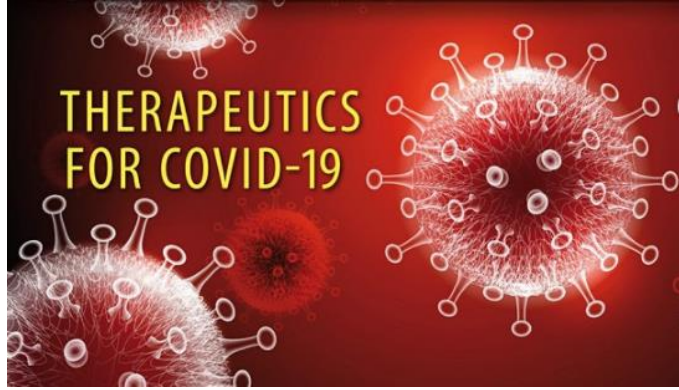

Pathogenesis and Management of ARDS

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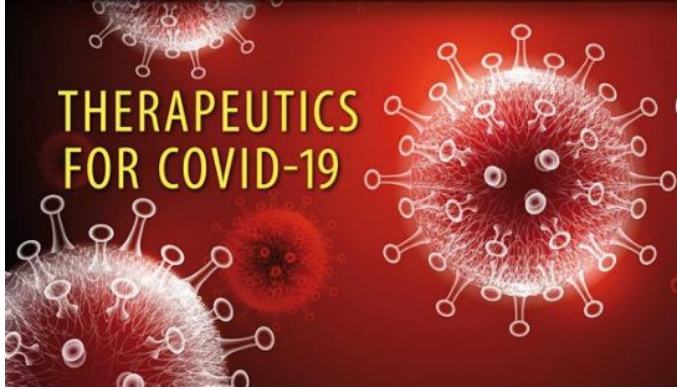
Conflicts of Interest:



bioMerieux/Biofire

Curetis

Pathogenesis and Management of COVID-19 ARDS

- The most common and most lethal complication of SARS-CoV-2 infection is acute hypoxemic respiratory failure
  - Acute cardiomyopathy much less than early reports
  - AKI common but not as lethal
  - Multiple effects on long term morbidity
- Management of COVID-19 pneumonia/ARDS has a major impact on outcomes independent of pharmacologic manipulations
- **Data collection for interventions in hospitalized patients with COVID-19 should include non-pharmacologic management**
  - Precedent set with ARDS studies – mandate or record whether following LTVV strategy

Pathogenesis and Management of COVID-19 ARDS

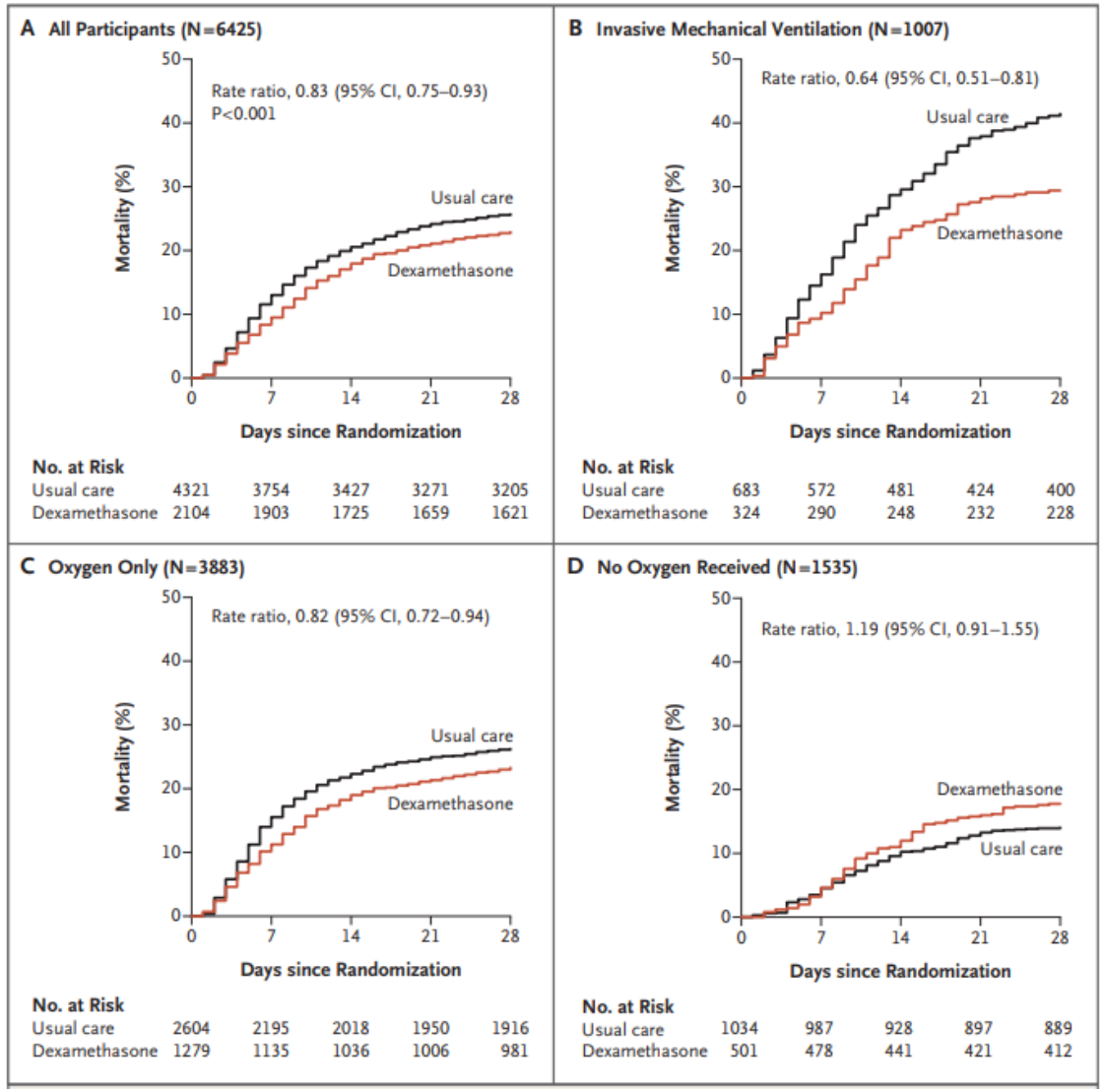
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

- Controlled, open-label trial
- Dexamethasone 6mg PO/IV daily x10
- Randomized to other active treatments as well



Pathogenesis and Management of COVID-19 ARDS

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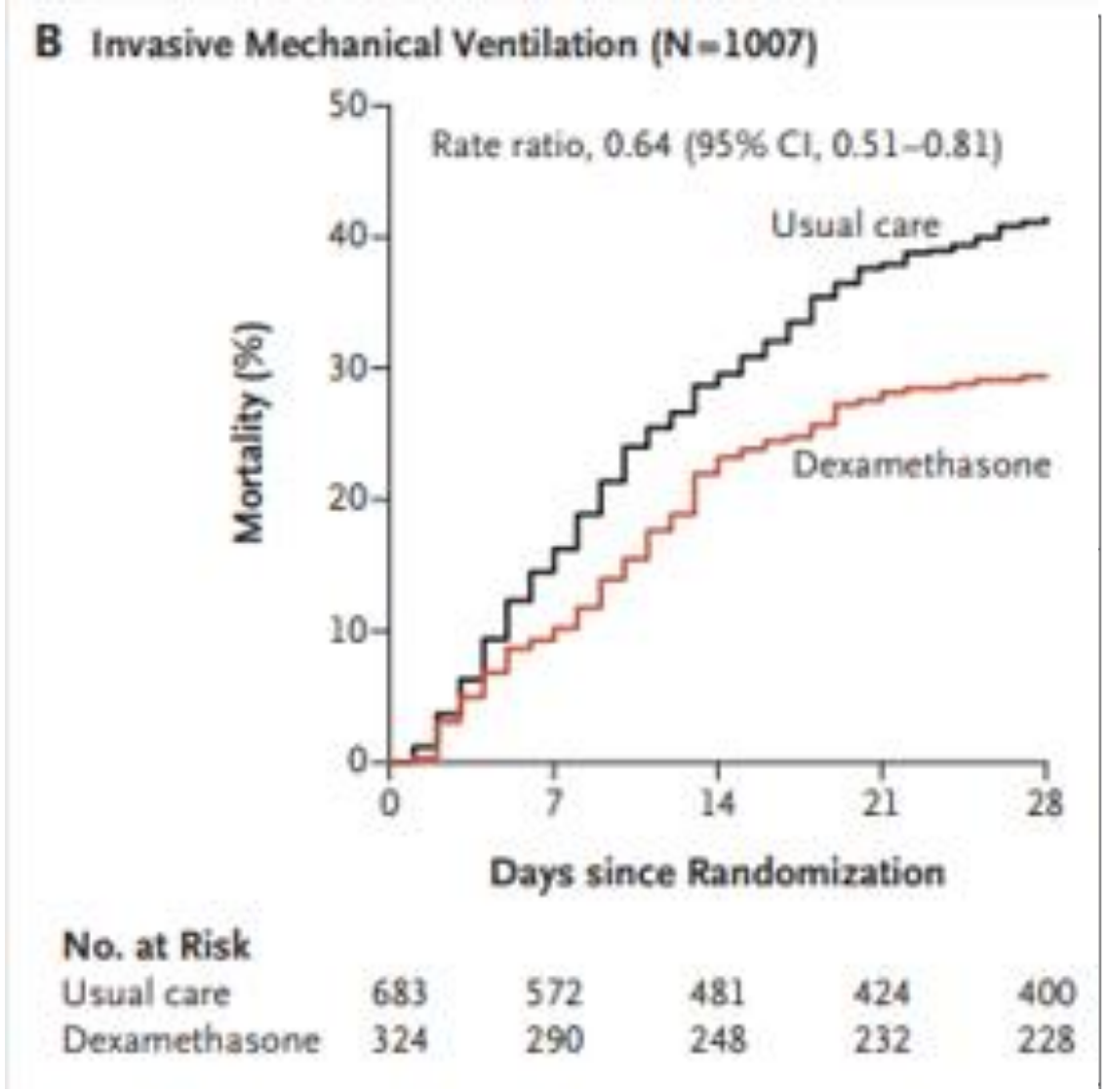
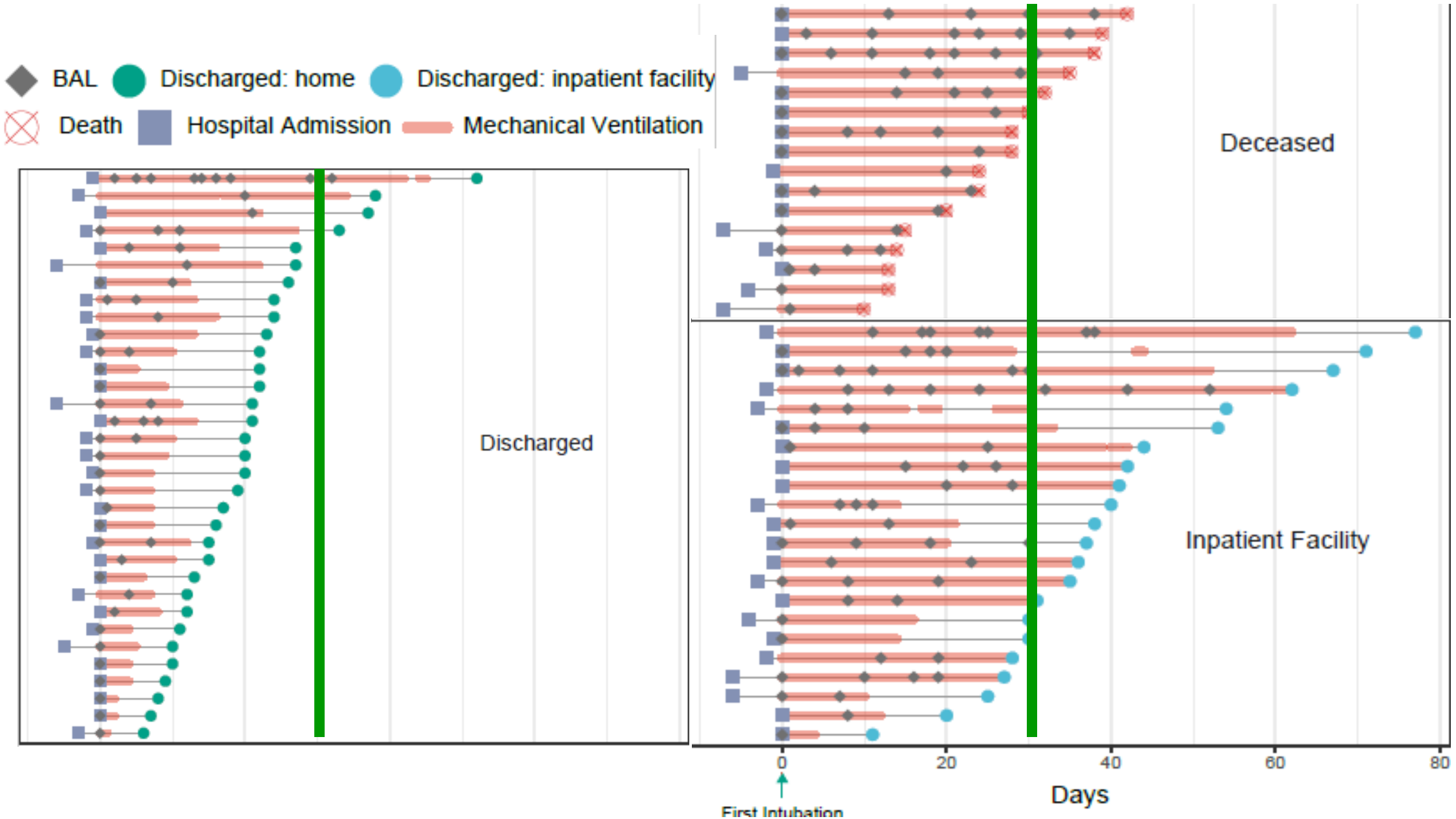



BAL
Discharged: home
Discharged: inpatient facility
Death
Hospital Admission
Mechanical Ventilation
Deceased
Discharged
Inpatient Facility
0
20
40
60
80
Days
First Intubation

Pathogenesis and Management of COVID-19 ARDS

- While ordinal, the COVID-19 scale is not proportional
- Correctly get the important transition for inpatients at the need for more than low flow nasal cannula
  - Previously required ICU transfer
  - Subjective decisions
  - HFNC not available everywhere; shortages
  - Benefit/risk of noninvasive ventilation unknown, especially early in pandemic
- **Critical issue is threshold for intubation**
  - Early – concern for rapid deterioration
  - Late – concern for high mortality with ventilation
    - Limited ventilator availability
    - Excessive mortality in overwhelmed healthcare systems thought to be baseline – promulgated by social media

Late breached standard critical care teaching – is COVID-19 really different or not?

COVID-19 Therapeutic Trial Synopsis
Draft February 18, 2020

R&DBlueprint
Powering research to prevent epidemics

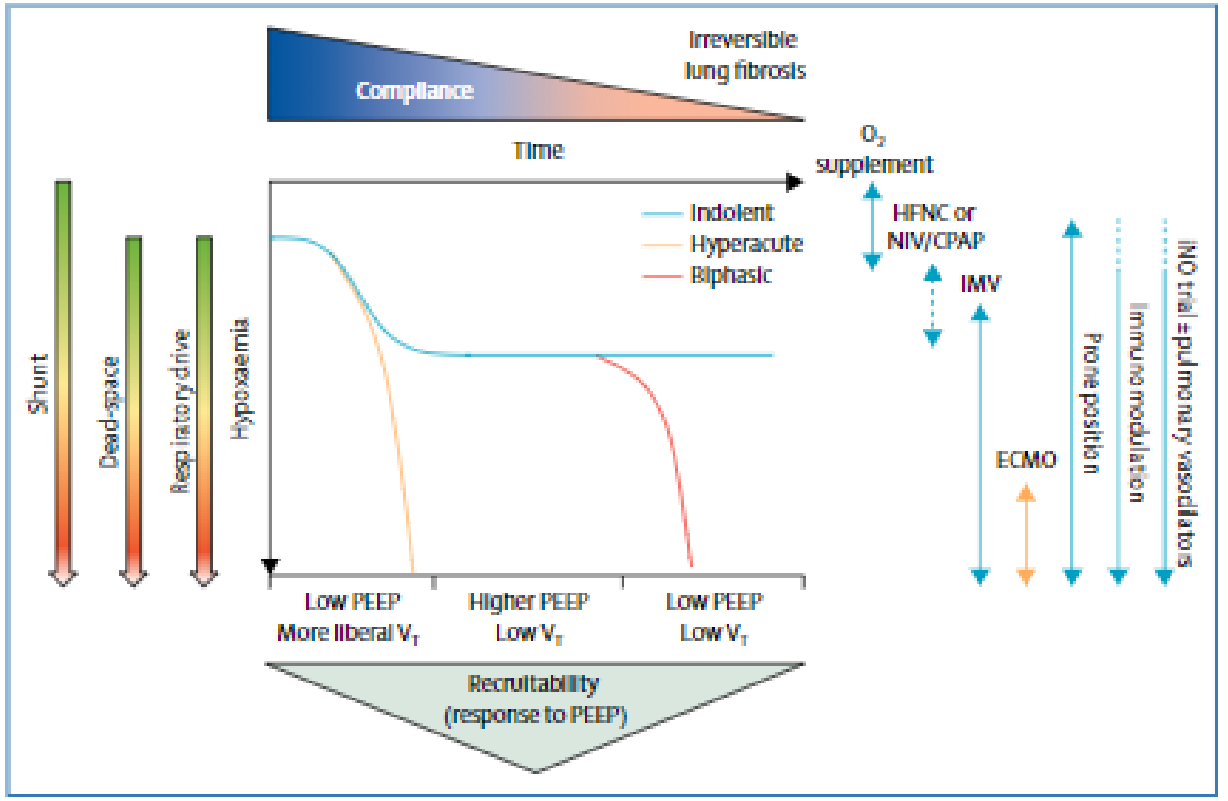
Ordinal Scale for Clinical Improvement

Patient State	Descriptor	Score
Uninfected	No clinical or virological evidence of infection	0
Ambulatory	No limitation of activities	1
	Limitation of activities	2
Hospitalized Mild disease	Hospitalized, no oxygen therapy	3
	Oxygen by mask or nasal prongs	4
Hospitalized Severe Disease	Non-invasive ventilation or high-flow oxygen	5
	Intubation and mechanical ventilation	6
	Ventilation + additional organ support – pressors, RRT, ECMO	7
Dead	Death	8

Pathogenesis and Management of COVID-19 ARDS

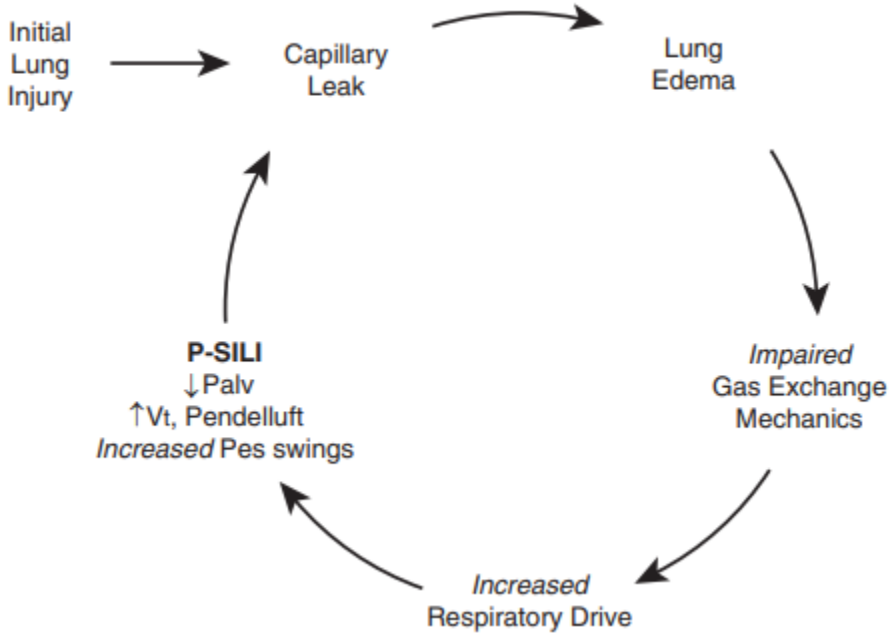
Is COVID-19 ARDS or not?

- Obvious answer is yes: meets all components or most recent syndrome definition (Berlin criteria)
  - Earliest versions included a compliance measurement = "stiff" lungs
- Early noted many patients with COVID-19 pneumonia had normally compliant lungs despite severe hypoxemia
- Recruitability – very beneficial effect of proning which is often not practiced outside of academic centers in US



Camporota et al, Lancet Respir Med, 2020

Prevention of Self-Induced Lung Injury (S-ILI) in COVID-19 Pneumonia/ARDS



- Early intubation – many have significant role in preventing low compliance phenotype
- Avoiding noninvasive ventilation
- Optimizing ventilator settings
- Neuromuscular blockade
- High levels of sedation

- Not clear what stimulates excessive respiratory drive and what limits protective reflexes
- Appears unique to some types of viral pneumonia

Seem to correlate with pro-inflammatory biomarkers

Brochard et al, AJRCCM, 2017

Pathogenesis and Management of COVID-19 ARDS

CRITICAL CARE PERSPECTIVE

Lung- and Diaphragm-Protective Ventilation

Ewan C. Goligher[1,2,3], Martin Dres[4,5], Bhakti K. Patel[6], Sarina K. Sahetya[7], Jeremy R. Beitler[8], Irene Telias[1,2,9], Takeshi Yoshida[10], Katerina Vaporidi[11], Domenico Luca Grieco[12,13], Tom Schepens[14], Giacomo Grasselli[15,16], Savino Spadaro[17], Jose Dianti[1,2,18], Marcelo Amato[19], Giacomo Bellani[20], Alexandre Demoule[4,5], Eddy Fan[1,2,3,21], Niall D. Ferguson[1,2,3,21,22], Dimitrios Georgopoulos[11], Claude Guérin[23], Robinder G. Khemani[24,25], Franco Laghi[26,27], Alain Mercat[28], Francesco Mojoli[29], Coen A. C. Ottenheijm[30], Samir Jaber[31], Leo Heunks[32]*, Jordi Mancebo[33]*, Tommaso Mauri[13,14], Antonio Pesenti[13,14], and Laurent Brochard[1,9]*; for the Pleural Pressure Working Group, Acute Respiratory Failure Section of the European Society of Intensive Care Medicine

- Steroids benefited ARDS for high tidal volume-induced lung injury
- Maybe benefit of steroids has nothing to do with anti-inflammatory, anti-cytokine strategy
  - Worse outcomes in NMH cohort but baseline mortality in 15-20% range
  - Failure of anti-IL6r strategies would be explained

Bacterial Co-infection in Initial BALs of COVID-19 Pneumonia/ARDS Patients

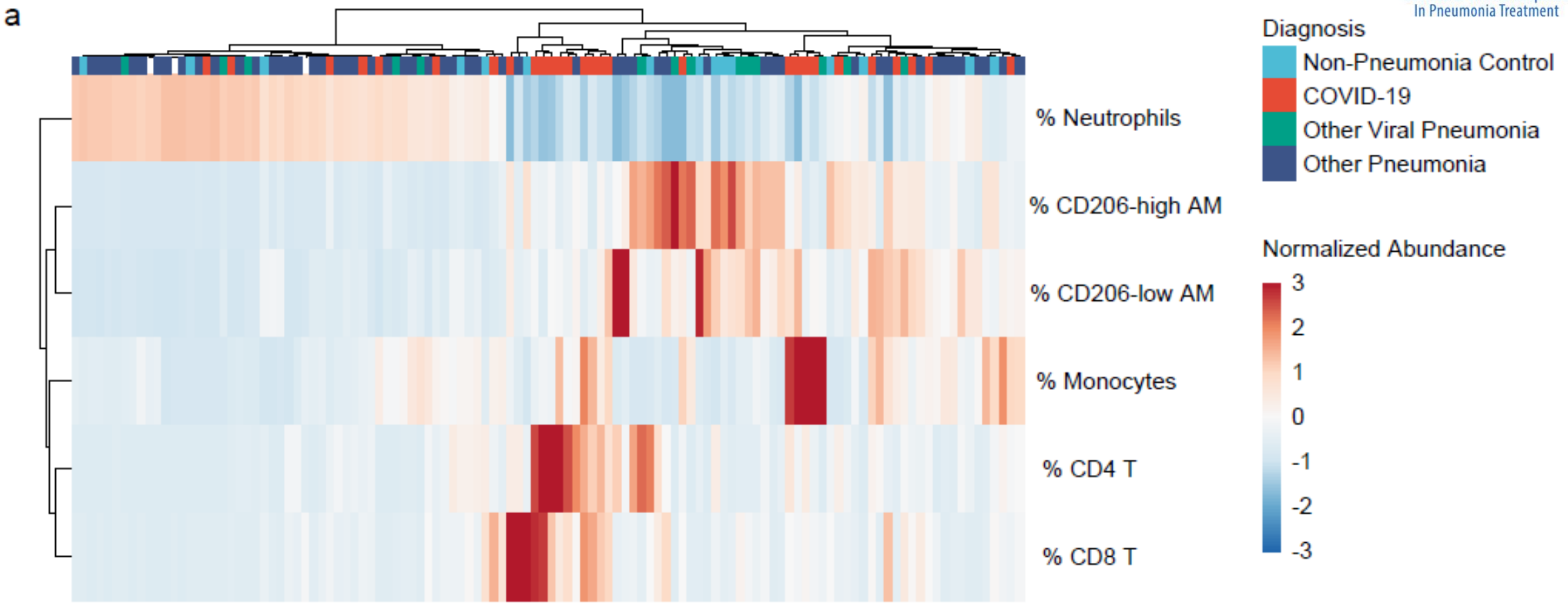
- Roughly 20% of COVID-19 patients have bacterial pneumonia at the time of intubation
- Usual Cap pathogens are the most common etiologies of bacterial superinfection in COVID-19

Proportion of Cell Types in Early COVID-19 BALs

Within 48 hours of Intubation

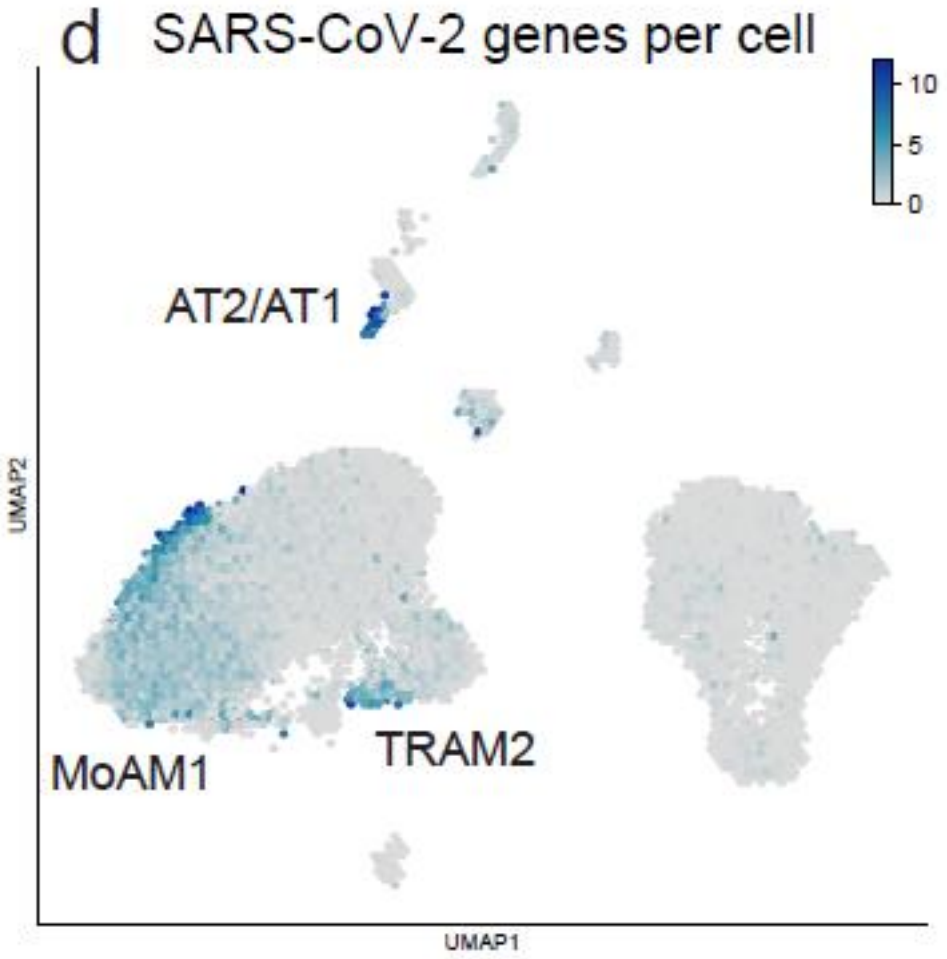
- SARS-CoV-2 has a disproportionate enrichment of lymphocytes in BAL

BAL cell types by flow cytometry

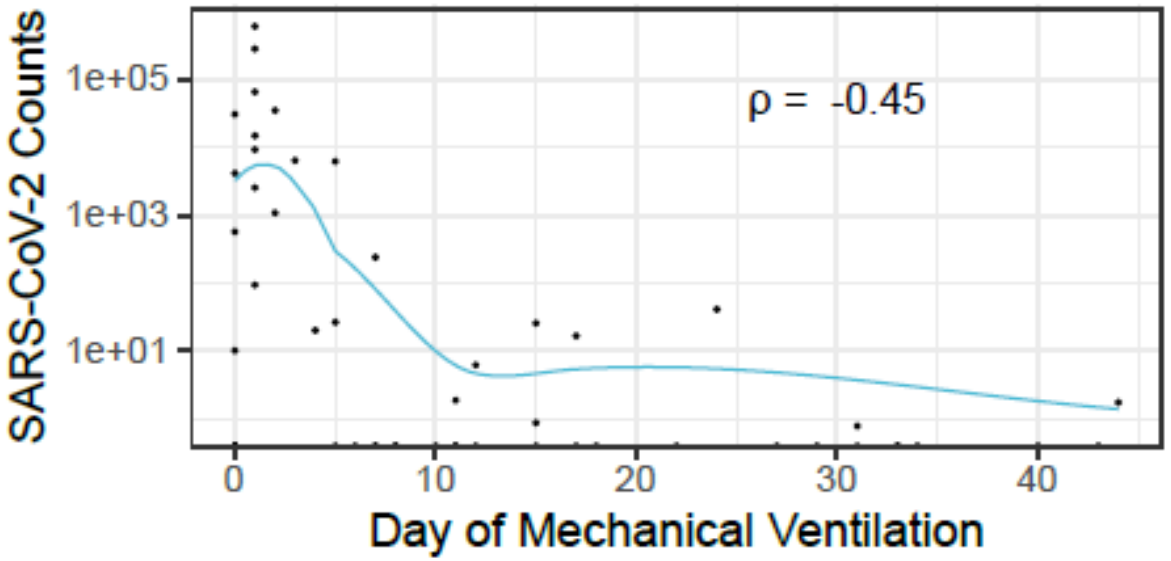


https://www.biorxiv.org/content/10.1101/2020.08.05.238188v1

SARS-CoV-2 CAN infect macrophages and monocytes



SARS-CoV-2 antisense RNA as well as sense

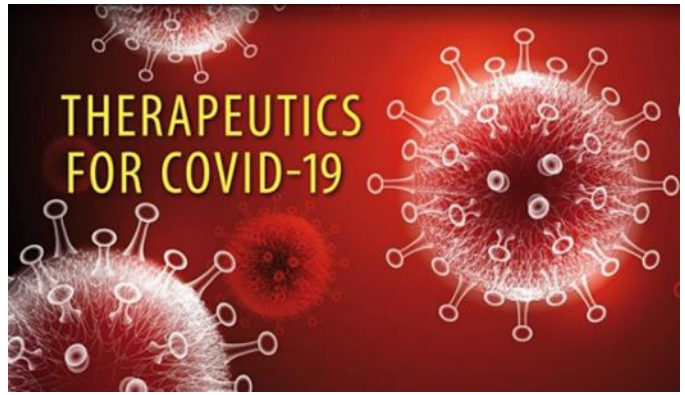


https://www.biorxiv.org/content/10.1101/2020.08.05.238188v1

Northwestern Medicine
Feinberg School of Medicine

Pathogenesis and Management of COVID-19 ARDS

- Mortality and changes in the ordinal scale are dependent on non-pharmacologic management of severe COVID-19 pneumonia
- Interventional trials that seek to specifically impact the severe end of the COVID-19 pneumonia spectrum face significant challenges to dissect signal from noise
  - Effect of these non-randomized issues are more likely in smaller studies and in those from very heterogeneous centers
  - If unable to be standardized, data on management should at least be recorded
- Examples of strategies:
  - Time from need for more than simple nasal cannula to intubation
  - Tidal volume/PEEP/FiO_2



“An expert is a person who has made all the mistakes that can be made in a very narrow field”

Niels Bohr