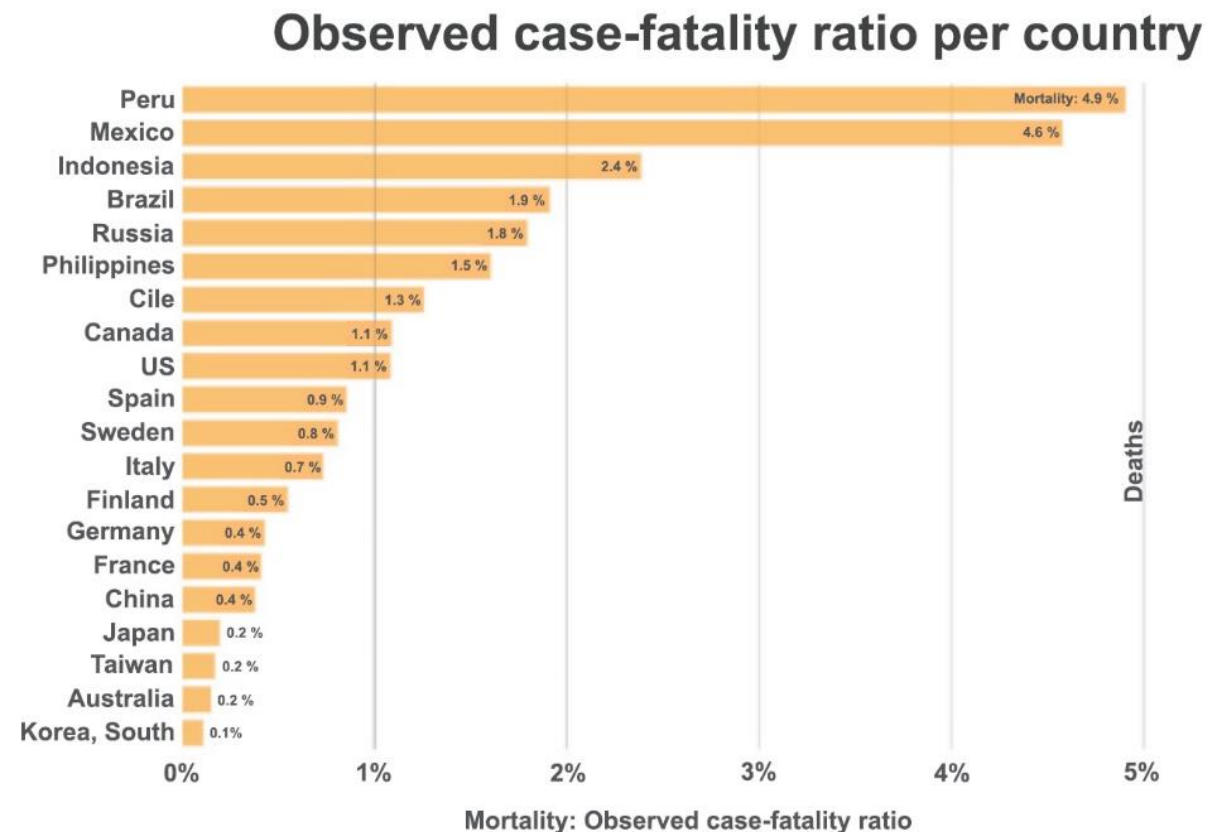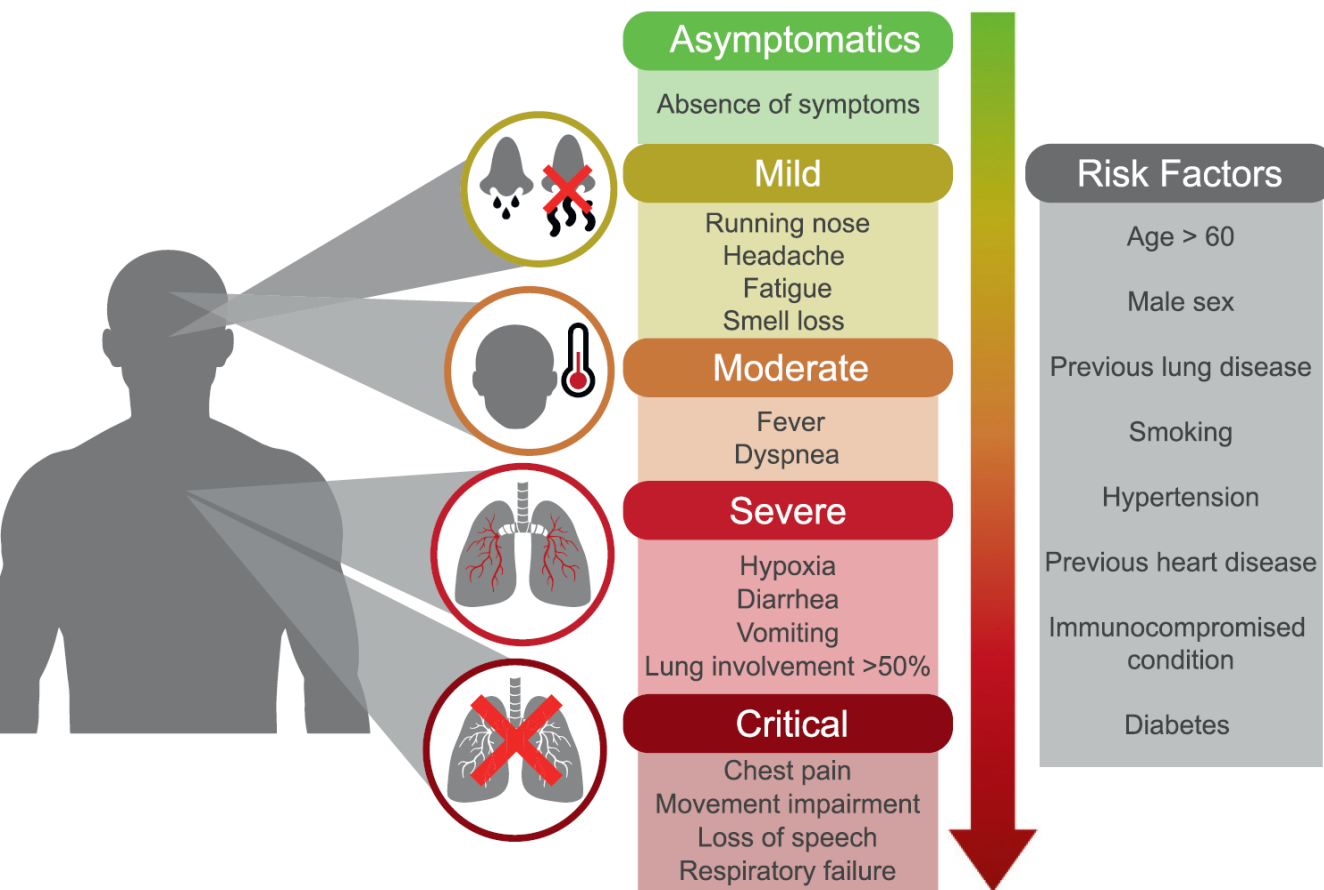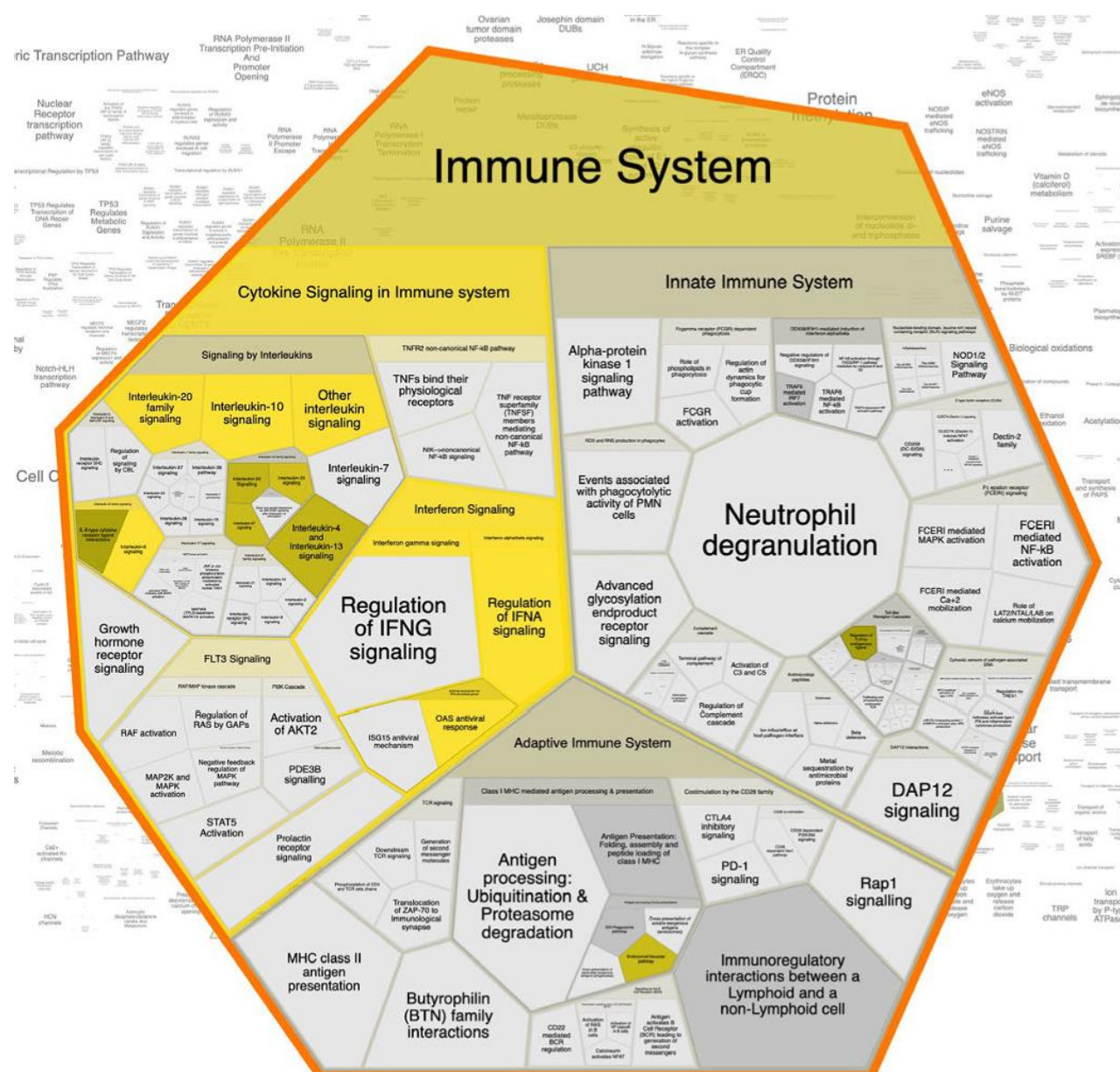# COVID-19 and the Lungs:
Risks and Outcomes

Joe Zein, MD, PhD, MBA

*The **2023** Annual Meeting of the Lebanese Pulmonary Society*

Severe COVID-19 has been associated with age, male sex, and comorbidities. Disease heterogeneity is caused by host-related risk factors, genetic factors and intrinsic characteristics of the virus.

Cappadona C. Infect Genet Evol. 2023

Genetic susceptibility to severe COVID-19

Genetic association studies are fundamental to identify biological mechanisms underlying disease susceptibility and severity.

Impact of Vaccination, Prior Infection, and Therapy on Omicron Infection and Mortality

Impact of Vaccination, Prior Infection, and Therapy on Omicron Infection and Mortality

	Patients, No.	Positive, No. (%)	Odds Ratio (95% CI)
Delta Period			
Unvaccinated	75 579	17 481 (23)	
Dose 2			
≥ 180 days	46 741	7292 (16)	0.45 (.44–.47)
< 180 days	19 590	1810 (9)	0.28 (.26–.29)
Dose 3			
≥ 180 days	3676	380 (10)	0.31 (.28–.34)
< 180 days	16 008	585 (4)	0.10 (.09–.11)
Other vaccination	9655	1450 (15)	0.48 (.45–.51)
Prior Infection	11 456	479 (4)	0.17 (.16–.19)
Omicron Period			
Unvaccinated	40 800	18 089 (44)	
Dose 2			
≥ 180 days	28 804	13 755 (48)	1.03 (1.00–1.06)
< 180 days	8271	3300 (40)	0.77 (.74–.81)
Dose 3			
≥ 180 days	3158	894 (28)	0.52 (.48–.56)
< 180 days	35 471	8329 (23)	0.37 (.35–.38)
Other vaccination	7938	2985 (38)	0.71 (.68–.75)
Prior Infection	11 476	3450 (30)	0.57 (.55–.60)
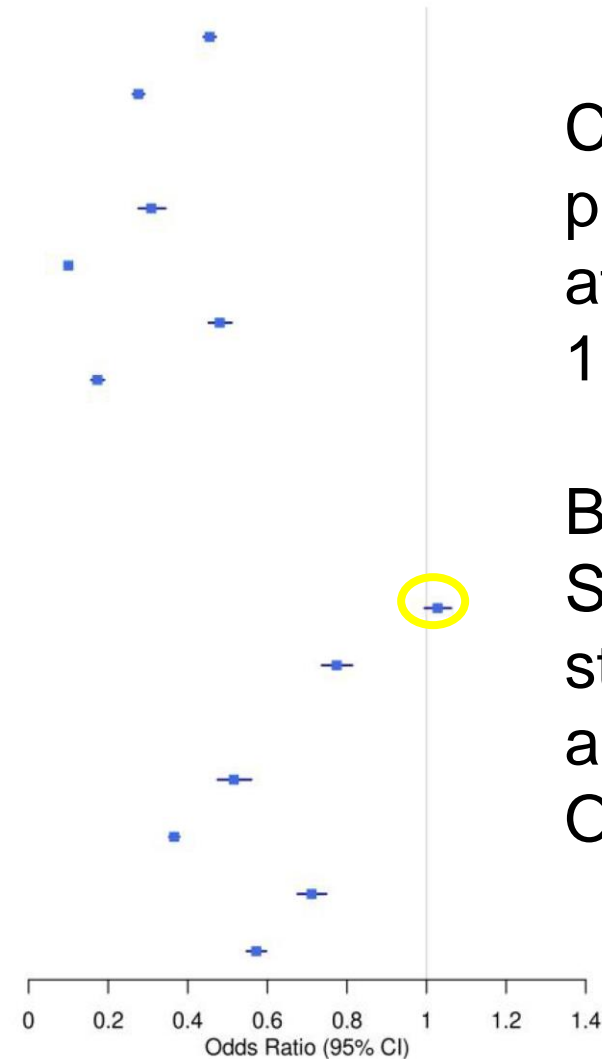
Cross-sectional study of 295 691 patients tested for SARS-CoV-2 at Cleveland Clinic between 10/1/2021 and 1/31/ 2022.

Booster vaccination and prior SARS-CoV-2 infection provide strong protection against ICU admission and death from Omicron infection.

Zein J. J Infect Dis. 2023

The relatively low mortality of the Omicron variant is due to both reduced lethality of this variant and increased population immunity acquired from booster vaccination and previous infection.

Zein J. J Infect Dis. 2023
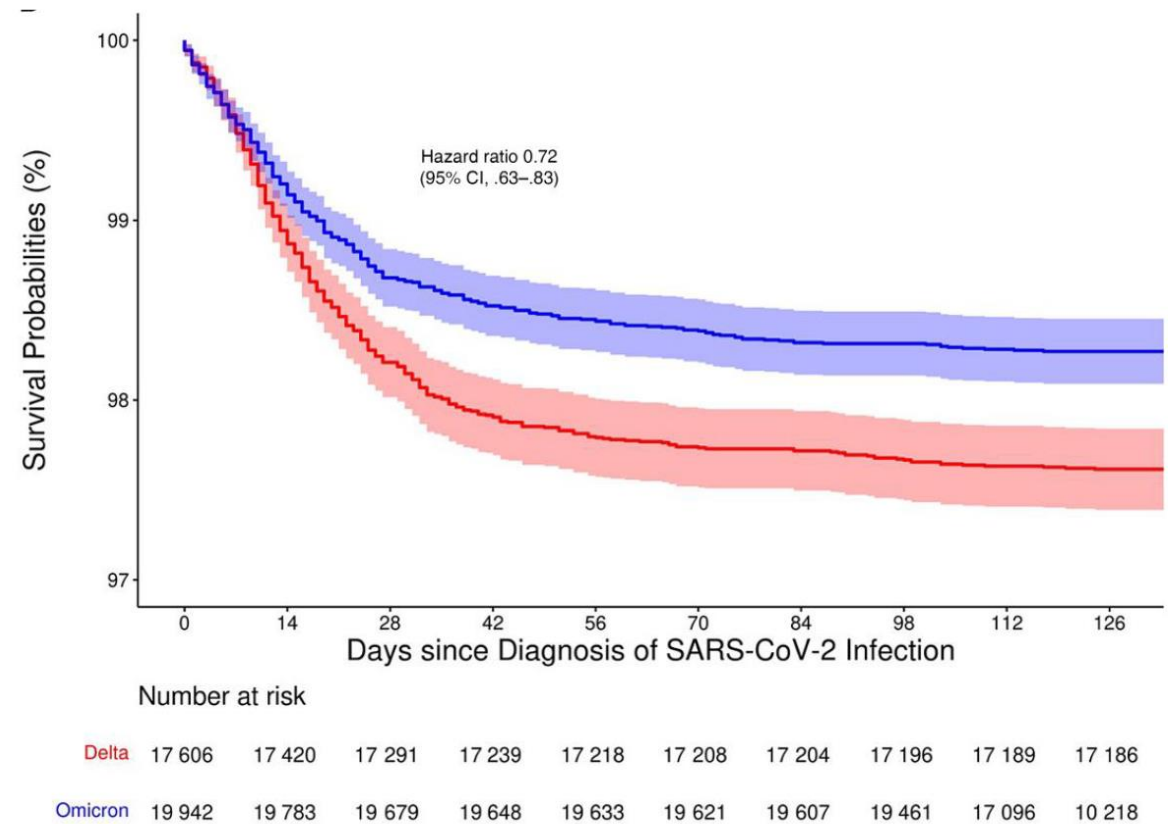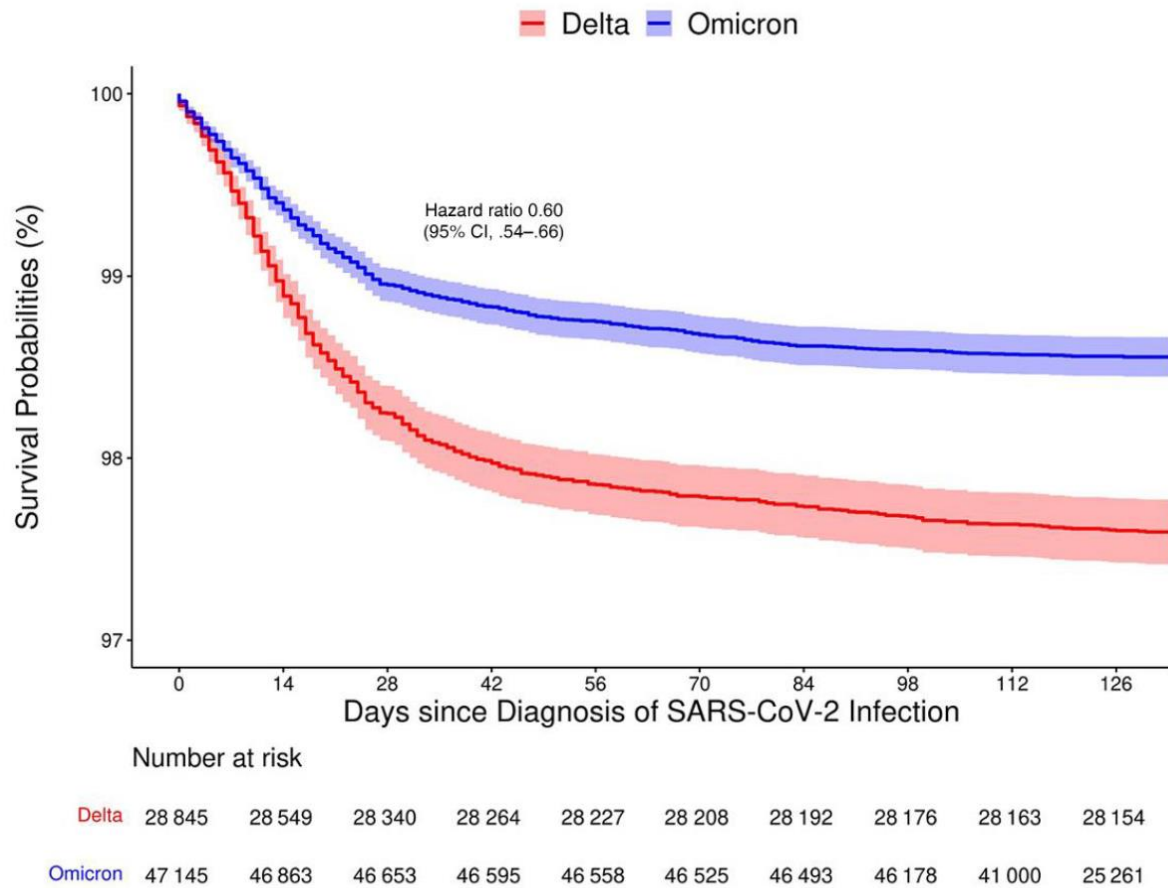
COVID-19 and the Lungs

Chronology of events during SARS-CoV-2 infection.

SARS- CoV-2 infects cells with ACE2 and TMPRSS2

Active replication and virus release → cell death

Cell death → Damage Associated Molecular Patterns

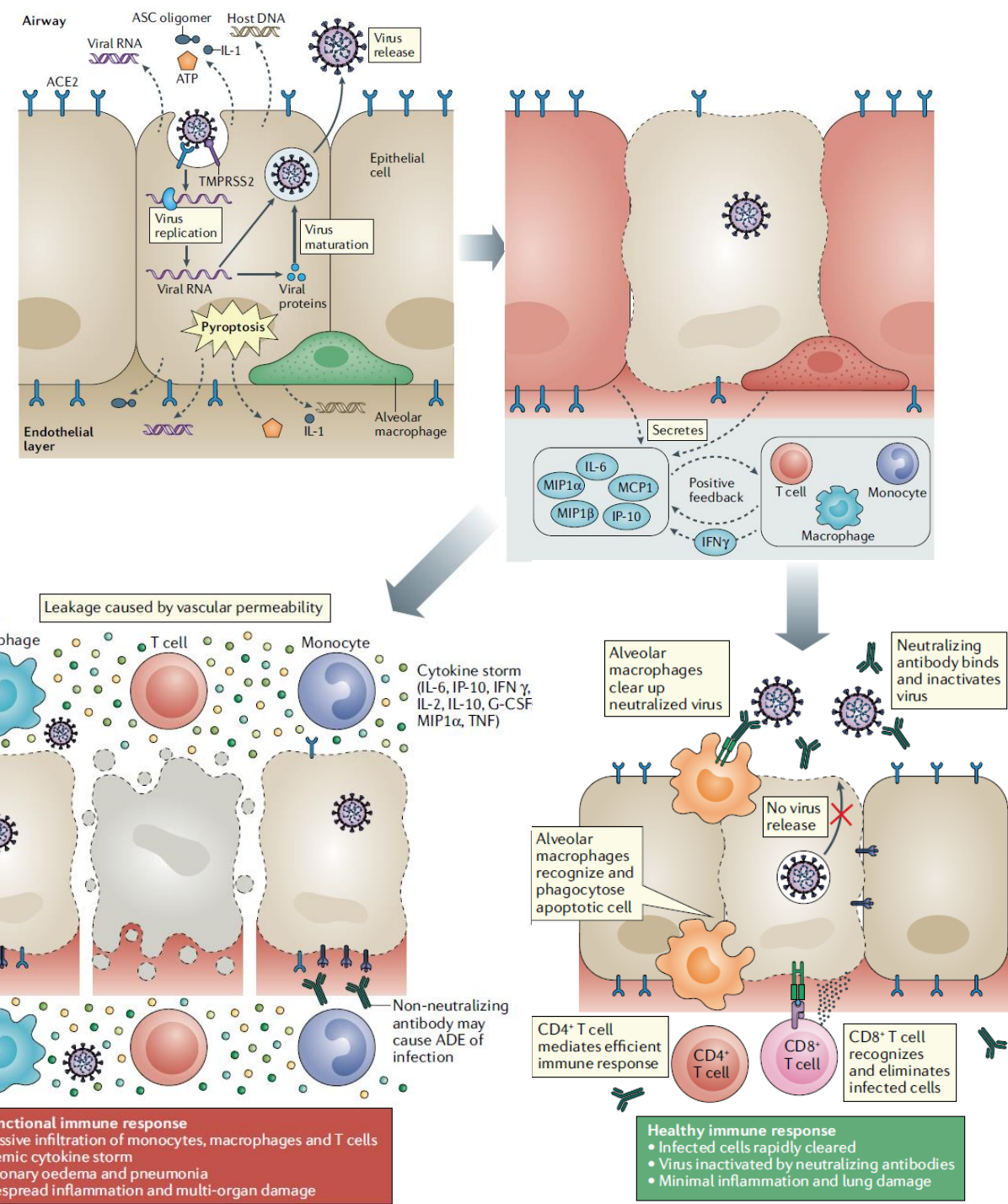DAMP → proi-nflammatory cytokines and chemokines → attract monocytes, macrophages and T cells

2 Different Immune Responses:
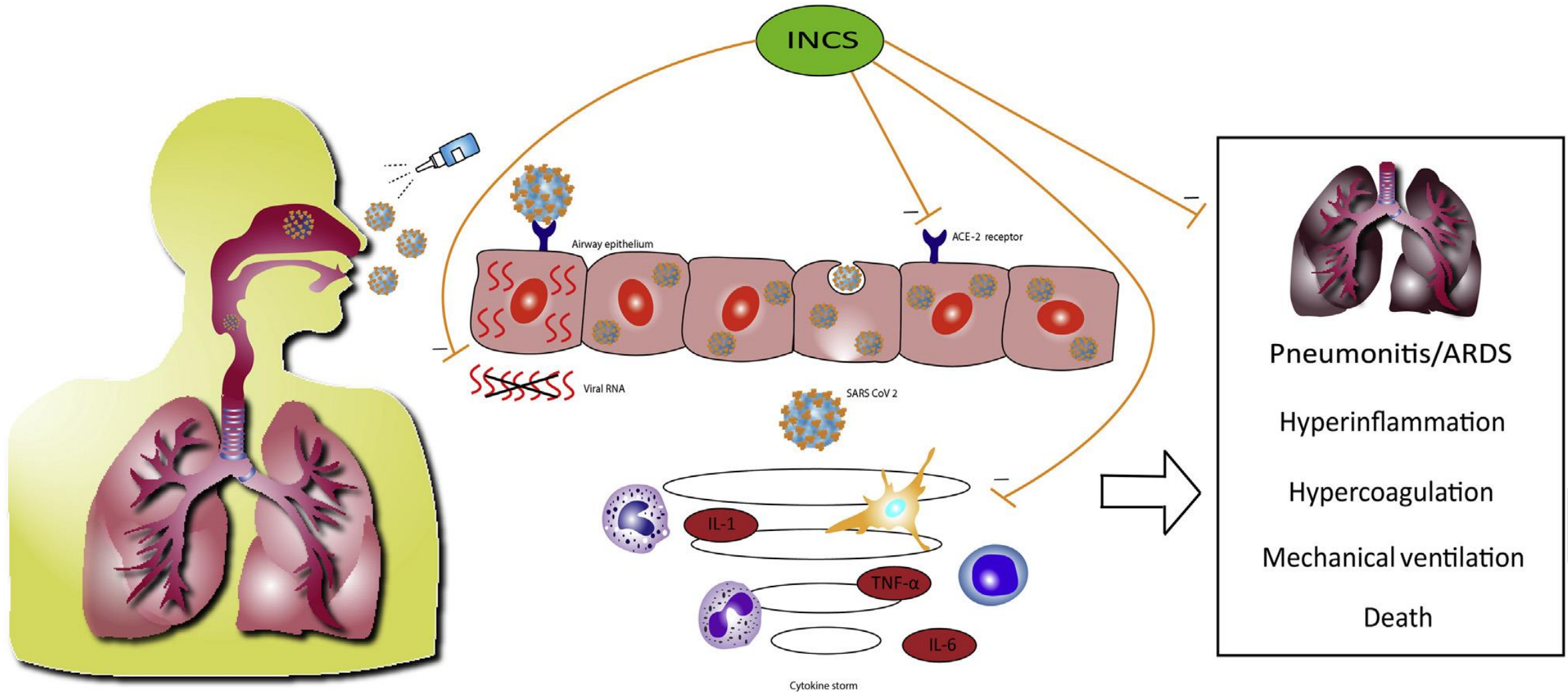1. Healthy immune response.
   • Neutralizing Ab (RBD: receptor binding domain)

2. Dysfunctional immune response.
   • ADE: Ab dependent enhancement (MIS-C).

Zirui Tay M, *Nature Review,* 2020

COVID-19: Start with the Nose

Lipworth B, *JACI-IP*, 2021

Intranasal Corticosteroids are Associated with Better Outcomes in COVID-19

All Patients (n = 72,147)

| Outcome	OR [95%CI]
Hospital Admission	
Unadjusted	0·92 [0·87; 0·97]
Adjusted	0·78 [0·72; 0·85]
ICU Admission	
Unadjusted	0·89 [0·80; 0·99]
Adjusted	0·77 [0·65; 0·92]
Hospital Mortality	
Unadjusted	0·85 [0·74; 0·97]
Adjusted	0·76 [0·61; 0·94]
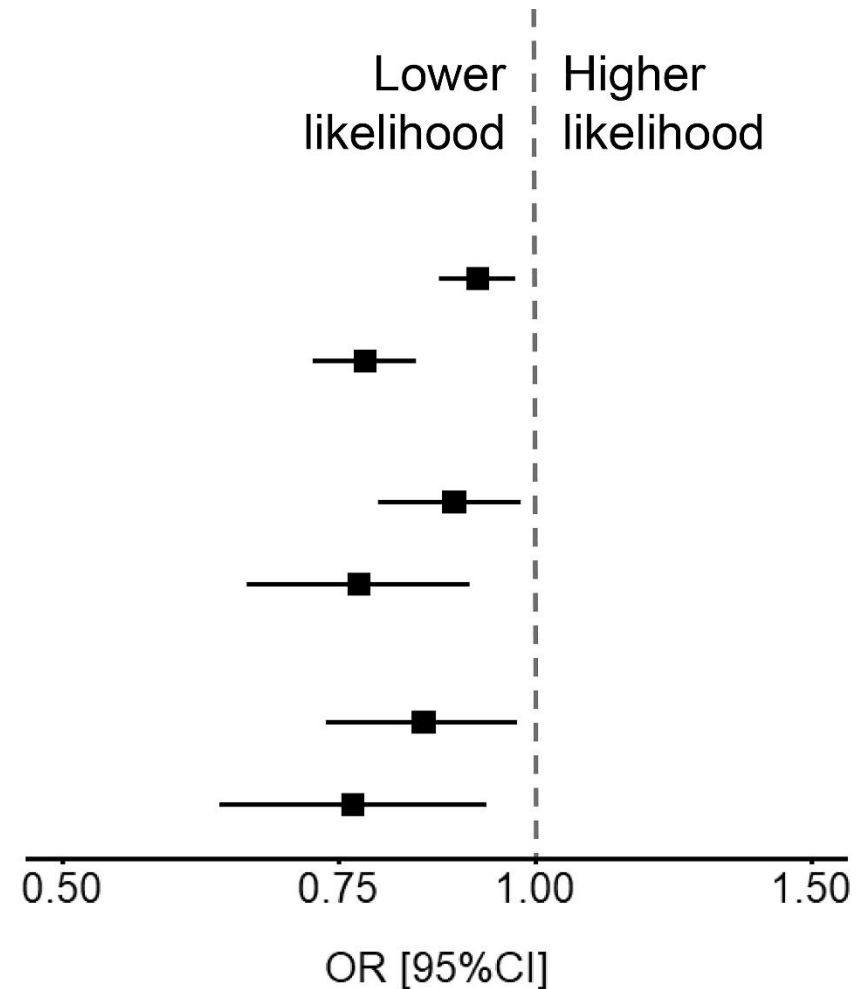
The risk of COVID-19-related hospitalizations is higher in severe asthma.

A - Analyses Stratified by Asthma Therapy		Hospitalization n=11,221	ICU Admission n=2470	Mortality n=2158
	n	OR [95% CI]	OR [95% CI]	OR [95% CI]
No Asthma	62,042	1	1	1
Inactive Asthma	3890	1.05 [0.95; 1.17]	0.89 [0.72; 1.11]	0.78 [0.60; 1.01]
Active Asthma				
Short Acting Beta Agonist Alone	3828	1.37 [1.24; 1.51]	1.26 [1.04; 1.52]	0.80 [0.60; 1.05]
Low-dose iCS	877	1.23 [1.00; 1.50]	0.98 [0.64; 1.50]	0.63 [0.34; 1.18]
Low-dose iCS - LABA	761	1.13 [0.91; 1.41]	1.10 [0.72; 1.70]	0.70 [0.38; 1.27]
High-dose iCS - LABA	363	1.54 [1.16; 2.06]	1.21 [0.70; 2.10]	1.13 [0.57; 2.23]
Triple therapy	93	2.61 [1.16; 4.26]	1.65 [0.73; 5.00]	1.37 [0.52; 3.60]
Chronic Oral Corticosteroids	115	3.00 [1.60; 4.70]	2.09 [0.87; 6.10]	1.62 [0.54; 4.85]
Anti IgE Biologic Therapy	42	1.60 [0.66; 3.87]	NA	NA
Anti IL5(Rα), IL4Rα Biologic Therapies§	54	3.31 [1.75; 6.24]	NA	NA

| B - Analyses Stratified by Asthma Exacerbations		Hospitalization n=1069	ICU Admission n=214	Mortality n=104
Number of Exacerbations	n	OR [95% CI]	OR [95% CI]	OR [95% CI]
0	4194	1	1	1
1	1562	0.87 [0.73; 1.04]	0.74 [0.51; 1.06]	1.27 [0.79; 2.06]
≥ 2	362	1.09 [0.80; 1.47]	0.84 [0.46; 1.54]	1.96 [0.93; 4.17]

Asthma Biologic Therapy During COVID-19 Infection

- In the abscence of any data to suggest any potential harm, the current recommendations is to continue biologic therapy during the COVID-19 pandemic in patients with severe asthma for whom biologic therapies have been shown to be effective.

- In the presence of conflicting data, the recommendation to continue, postpone or withold biologic therapy during acute COVID-19 infection in patients with severe asthma should be made on a case-by-case basis.

- For patients using biologic therapies for asthma, the dose should not be administered on the same day as a COVID-19 vaccine to better identify side effects.

- The initiation of new monoclonal antibody therapies should be avoided for 1 to 2 weeks following the COVID-19.
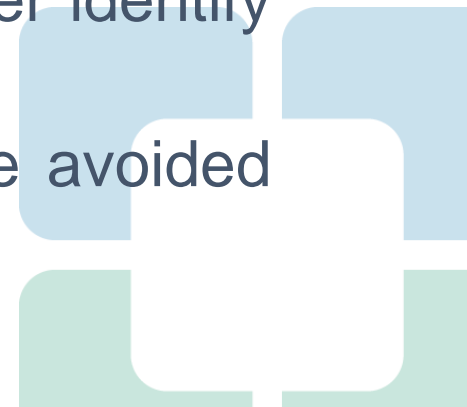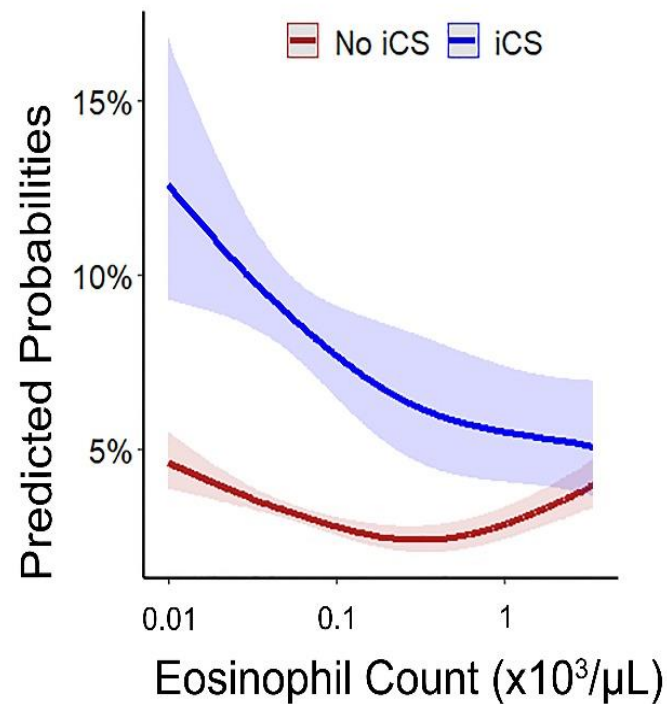
Eosinophilia is associated with improved COVID-19 outcomes in inhaled corticosteroids-treated patients.
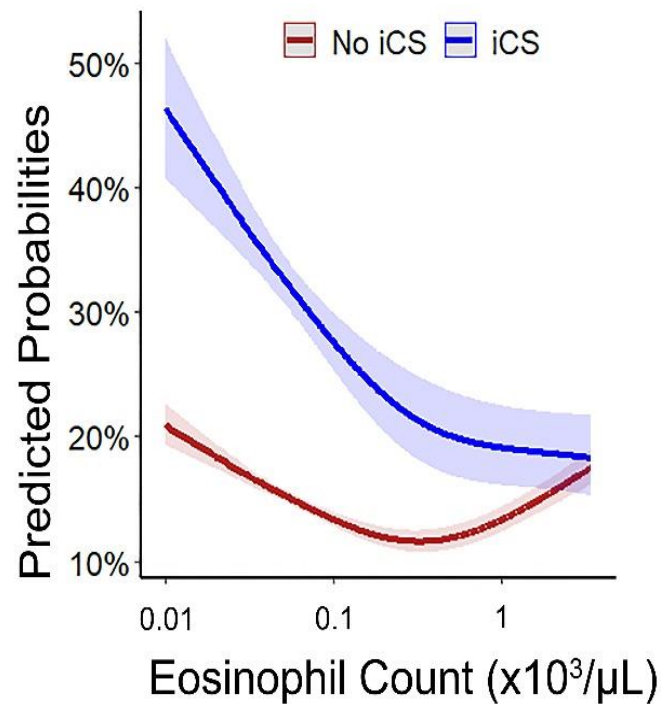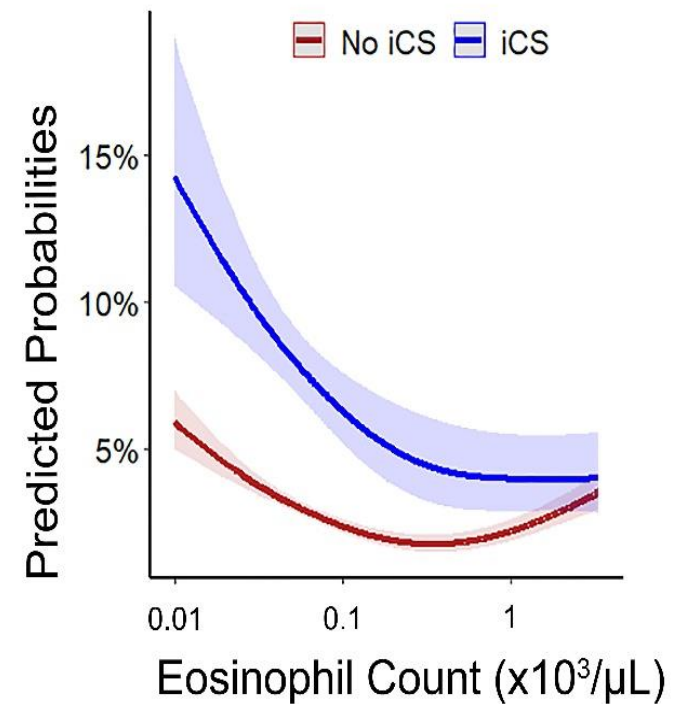
SARS-CoV-2 infection in the COPD population is associated with increased healthcare utilization
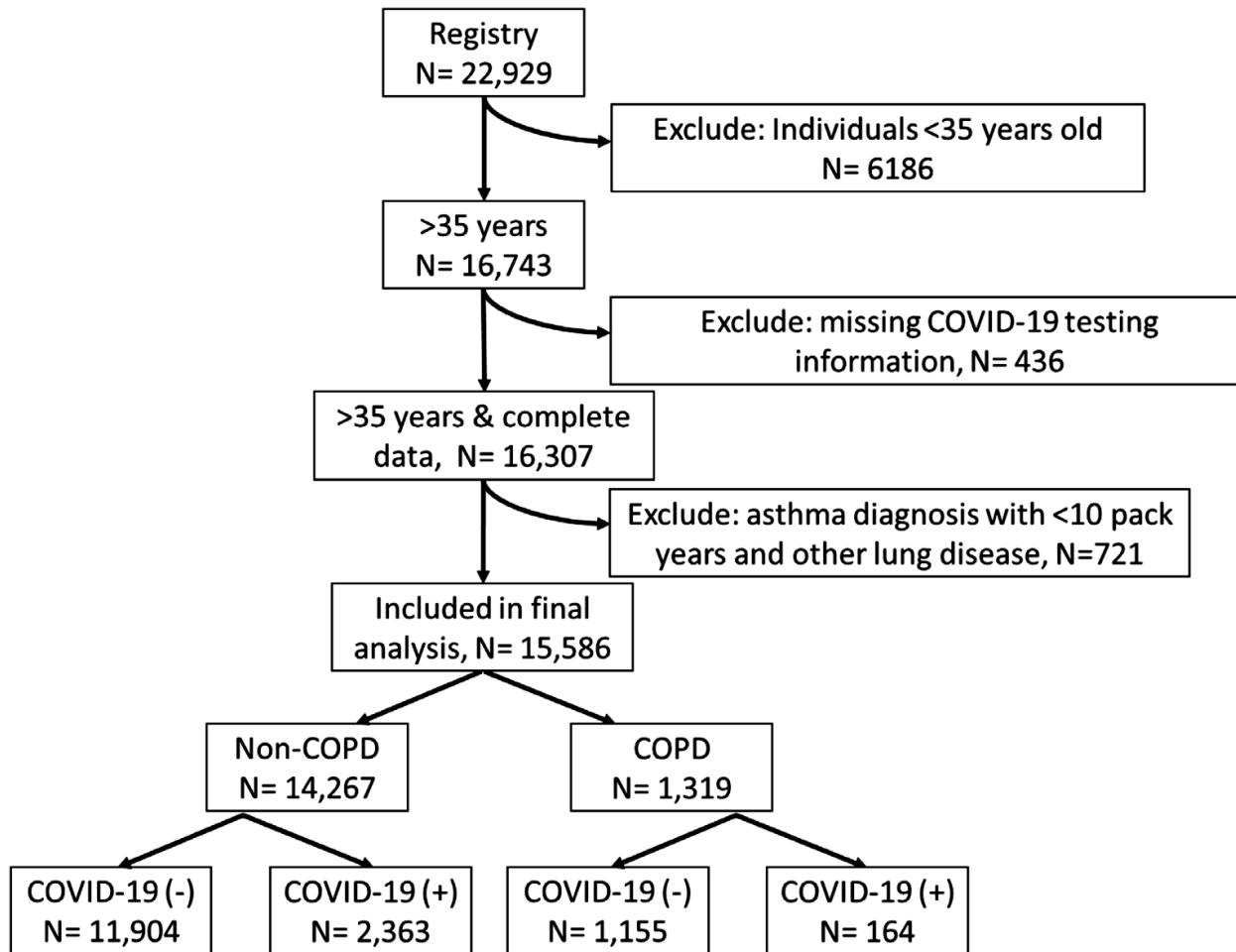
Outcome	OR (95% CI)
Positive CV-19 test	
Unadjusted	0.72 (0.66-0.77)
Adjusted	0.97 (0.89-1.05)
Risk for hospitalization	
Unadjusted	2.57 (2.22-2.96)
Adjusted	1.36 (1.15-1.60)
ICU admission	
Unadjusted	1.23 (1.06-1.43)
Adjusted	1.20 (1.02-1.40)
Noninvasive ventilation	
Unadjusted	0.99 (0.86-1.14)
Adjusted	1.13 (0.97-1.32)
Invasive mechanical ventilation	
Unadjusted	1.47 (1.27-1.70)
Adjusted	1.49 (1.28-1.73)
In-hospital mortality	
Unadjusted	1.51 (1.14-1.96)
Adjusted	1.08 (0.81-1.42)
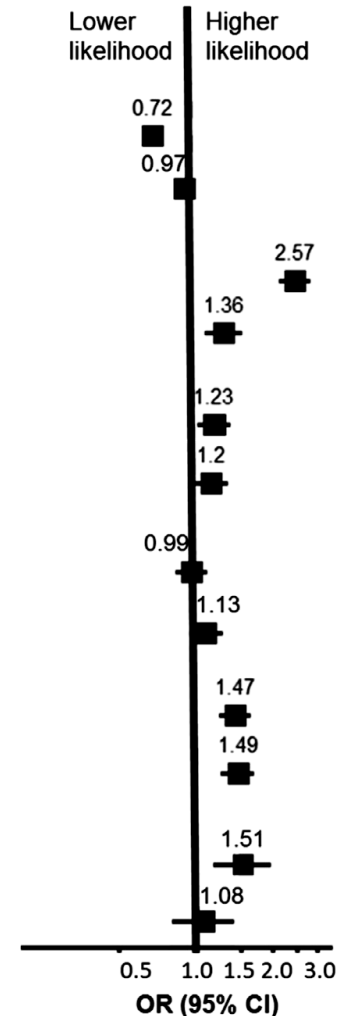
Cumulative exposure to cigarette smoke is an independent risk factor for hospital admission and death from COVID-19.

Table 2. Logistic Regression Models for COVID-19 Outcomes by Smoking Status Among the Cohort

Outcome	Odds ratio (95% CI)		
	Unadjusted	Adjusted for age, race, and gender	Adjusted for age, race, gender, medication,[a] and comorbidity[b]
Hospitalization given a positive COVID-19 test			
Never smoker	1 [Reference]	1 [Reference]	1 [Reference]
0-10 Pack-years	1.41 (1.10-1.81)	0.99 (0.76-1.30)	0.96 (0.70-1.30)
10-30 Pack-years	2.48 (2.01-3.07)	1.41 (1.12-1.78)	1.16 (0.85-1.58)
>30 Pack-years	4.65 (3.72-5.82)	2.25 (1.76-2.88)	2.19 (1.52-3.14)
ICU admission given a positive COVID-19 test and hospitalization			
Never smoker	1 [Reference]	1 [Reference]	1 [Reference]
0-10 Pack-years	1.33 (0.84-2.08)	1.19 (0.75-1.89)	1.08 (0.65-1.79)
10-30 Pack-years	1.74 (1.23-2.45)	1.55 (1.09-2.21)	1.34 (0.86-2.13)
>30 Pack-years	2.11 (1.54-2.89)	1.69 (1.23-2.35)	1.34 (0.86-2.10)
Death given a positive COVID-19 test			
Never smoker	1 [Reference]	1 [Reference]	1 [Reference]
0-10 Pack-years	2.38 (1.50-3.80)	1.66 (0.98-2.83)	1.07 (0.59-1.94)
10-30 Pack-years	3.40 (2.31-5.02)	1.47 (0.96-2.27)	0.88 (0.51-1.52)
>30 Pack-years	6.11 (4.33-8.61)	1.89 (1.29-2.76)	1.26 (0.75-2.10)
Per pack-year			
Hospitalization	1.030 (1.026-1.034)	1.015 (1.011-1.019)	1.013 (1.007-1.019)
ICU admission	1.012 (1.007-1.016)	1.008 (1.003-1.013)	1.005 (0.999-1.012)
Death	1.026 (1.020-1.031)	1.007 (1.002-1.013)	1.003 (0.995-1.010)

Inhaled corticosteroids do not adversely impact outcomes in COVID-19 positive patients with COPD

Table 4. Multivariate logistic regression analysis of COPD patients comparing those on ICS versus those not on ICS.

	COPD taking ICS versus COPD not taking ICS		
	Unadjusted OR (95% CI)	Adjusted (model1) * OR (95% CI)	Adjusted (model 2) * OR (95% CI)
COVID positive	0.89 (0.79–0.99)	0.85 (0.76–0.96)	0.85 (0.76–0.96)
Hospital admission	1.34 (1.09–1.65)	1.26 (1.02–1.55)	1.12 (0.90–1.38)
ICU admission[1]	1.29 (0.84–1.99)	1.38 (0.89–2.17)	1.31 (0.82–2.10)
Ventilator[2]	1.61 (0.79–3.32)	1.37 (0.64–2.98)	1.65 (0.69–4.02)
Mortality[1]	0.90 (0.54–1.52)	0.94 (0.54–1.64)	0.80 (0.43–1.49)

OR: Odds ratio, CI: Confidence interval, ICS: inhaled corticosteroid.

* Model 1 = Adjusted for gender, race, age.

* Model 2 = Adjusted for gender, race, age, smoking status (current versus former), comorbidities (asthma, obesity, diabetes mellitus, congestive heart failure, hypertension), and month of COVID positivity.

[1] Cohort includes only hospitalized patients.

[2] Cohort includes only ICU patients.

Post-Acute COVID-19 Syndrome

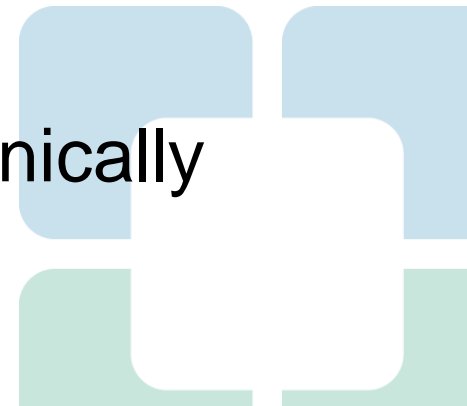Nalbandian A. *Nature Medicine*. 2021
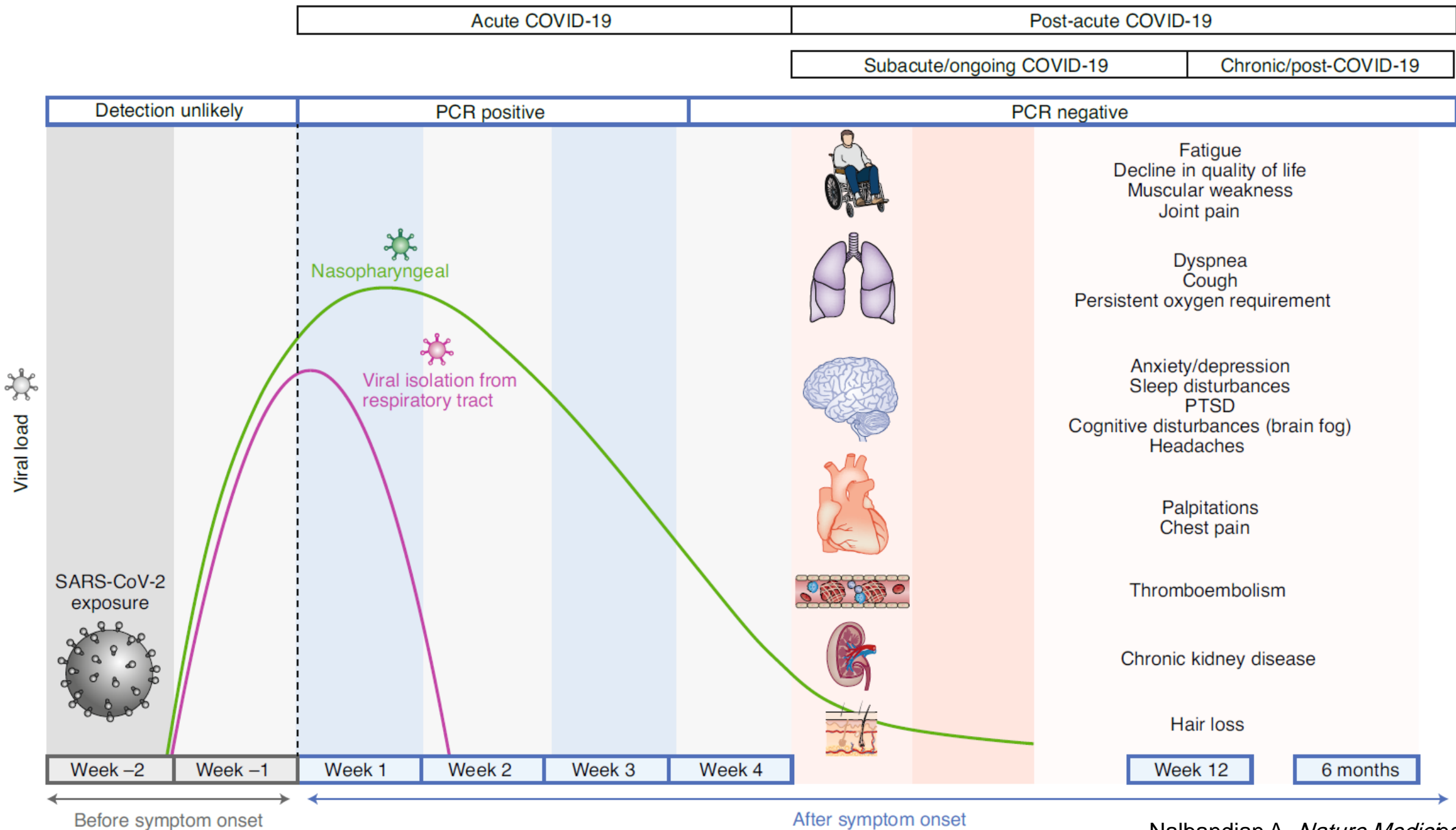
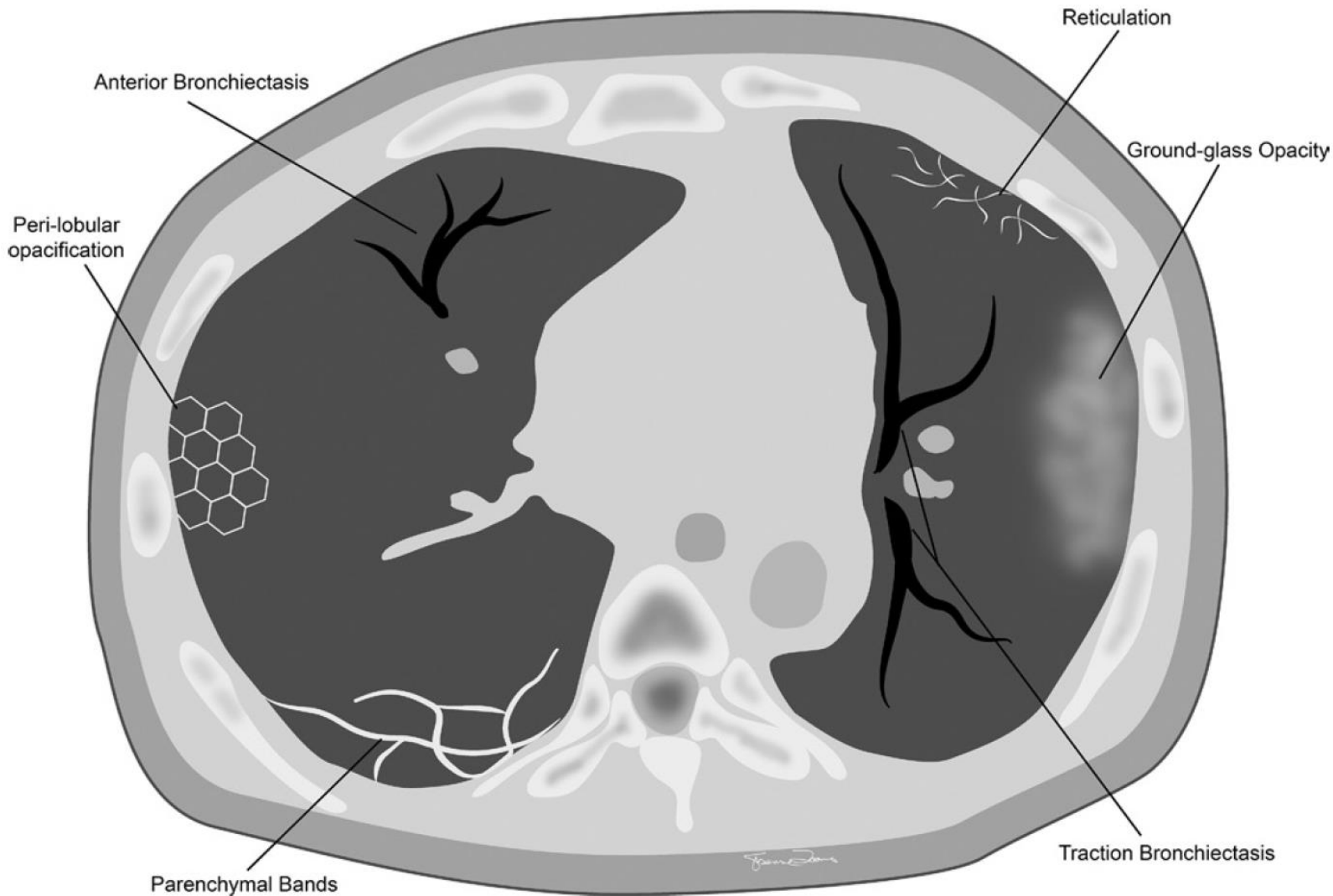# Post-acute COVID-19 Syndrome.

Pulmonary Sequelae:

- Symptoms:
  - Dyspnea, decreased exercise capacity and hypoxia
- Physiological changes:
  - ↓ DLCO, restrictive defect
- Radiological changes:
  - GGO, fibrotic changes

Follow-up

- Home pulse oximetry, 6MWTs, PFTs, HRCT/CTA as clinically appropriate

Commonly seen chronic CT findings after COVID-19 infection.

Anterior Bronchiectasis

Peri-lobular opacification

Parenchymal Bands

Reticulation

Ground-glass Opacity

Traction Bronchiectasis
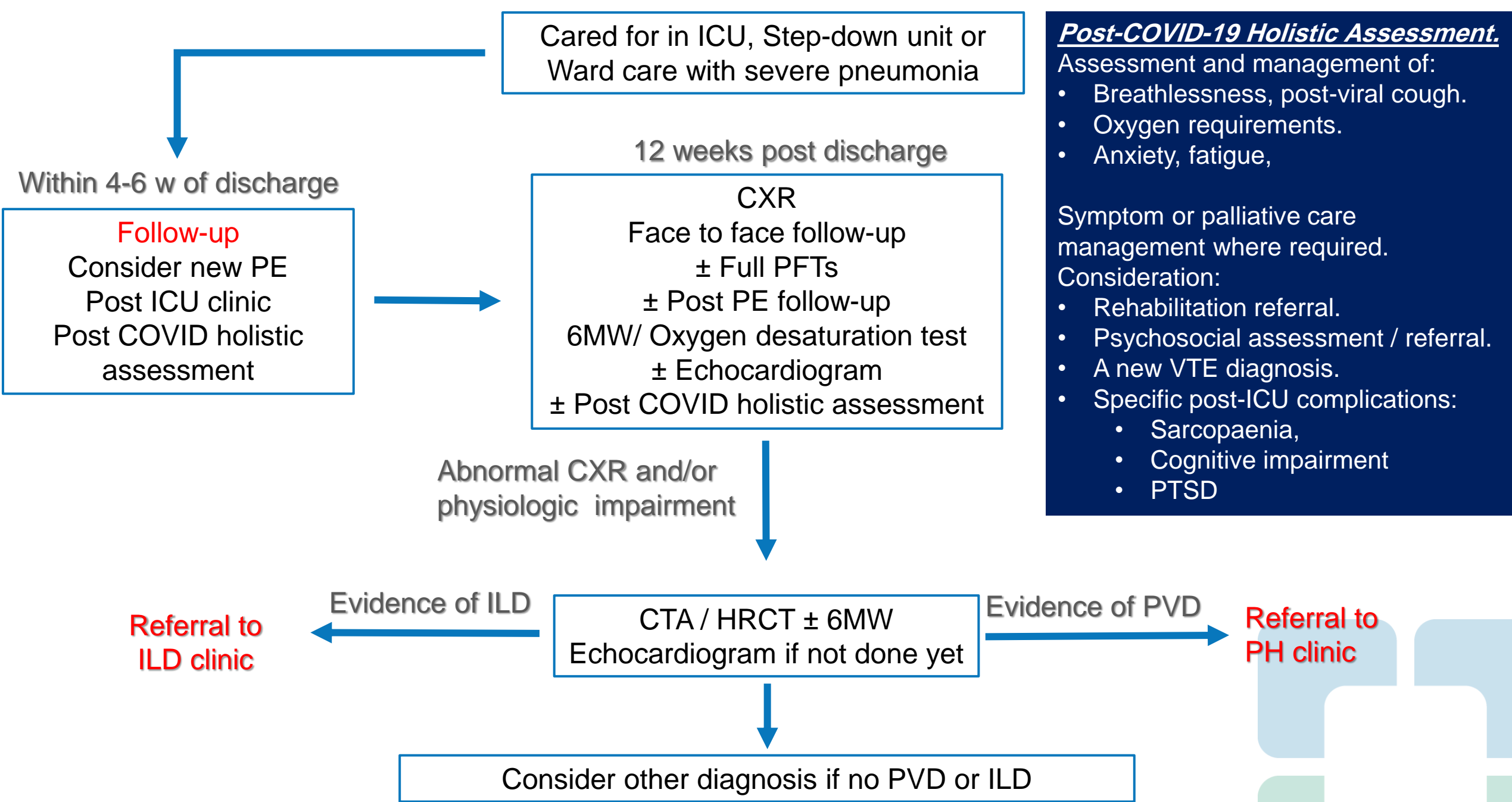
Many patients demonstrate persistent lung abnormalities after COVID-19 infection.

CT appearance can usually continue to improve for up to 1 year.

Fibrosis is uncommon except in severe disease.

Murphy MC, Radiology 2023

Specific aims of COVID-19 pneumonia follow-up

- To identify the early, medium and long-term respiratory complications of COVID-19

- To appropriately follow affected patients.

- Early identification of patients with PVD and pulmonary fibrosis:
  - The most serious and potentially life-limiting complications of COVID-19.

- Assess and manage acute patients needs:
  - Breathlessness, oxygen requirements, rehabilitation, palliative care/symptom management and psychosocial needs.

- To confirm that CXR changes from COVID-19 pneumonia and reassure patients who made full recovery.

- To coordinate and optimize the use of respiratory, radiology and physiology resources.

- To identify and treat patients with undiagnosed pre-existing respiratory disease.

Cared for in ICU, Step-down unit or Ward care with severe pneumonia

Post-COVID-19 Holistic Assessment.
Assessment and management of:
- Breathlessness, post-viral cough.
- Oxygen requirements.
- Anxiety, fatigue,

Symptom or palliative care management where required.
Consideration:
- Rehabilitation referral.
- Psychosocial assessment / referral.
- A new VTE diagnosis.
- Specific post-ICU complications:
  - Sarcopaenia,
  - Cognitive impairment
  - PTSD

Within 4-6 w of discharge

Follow-up
Consider new PE
Post ICU clinic
Post COVID holistic assessment

12 weeks post discharge

CXR
Face to face follow-up
± Full PFTs
± Post PE follow-up
6MW/ Oxygen desaturation test
± Echocardiogram
± Post COVID holistic assessment

Abnormal CXR and/or physiologic impairment

Evidence of ILD

Referral to ILD clinic

CTA / HRCT ± 6MW
Echocardiogram if not done yet

Evidence of PVD

Referral to PH clinic

Consider other diagnosis if no PVD or ILD

George PM. *Thorax* 2020

George PM. *Thorax* 2020

Thank you