

# **Post-acute Sequelae of COVID-19 (PASC):**

## **Organizing Pneumonia and Fibrosis**

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# Disclosures

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## Clinical Research:

RNAi-investigational drug in patients with IPF; Nitto Denko Corporation

Starscape: Evaluation of Safety and Efficacy of Recombinant Human Pentraxin-2 in IPF; Roche

RECOVER: Researching Covid and Recovery; NIH



# Overview of COVID-19 Cases

## “The Hidden Pandemic”

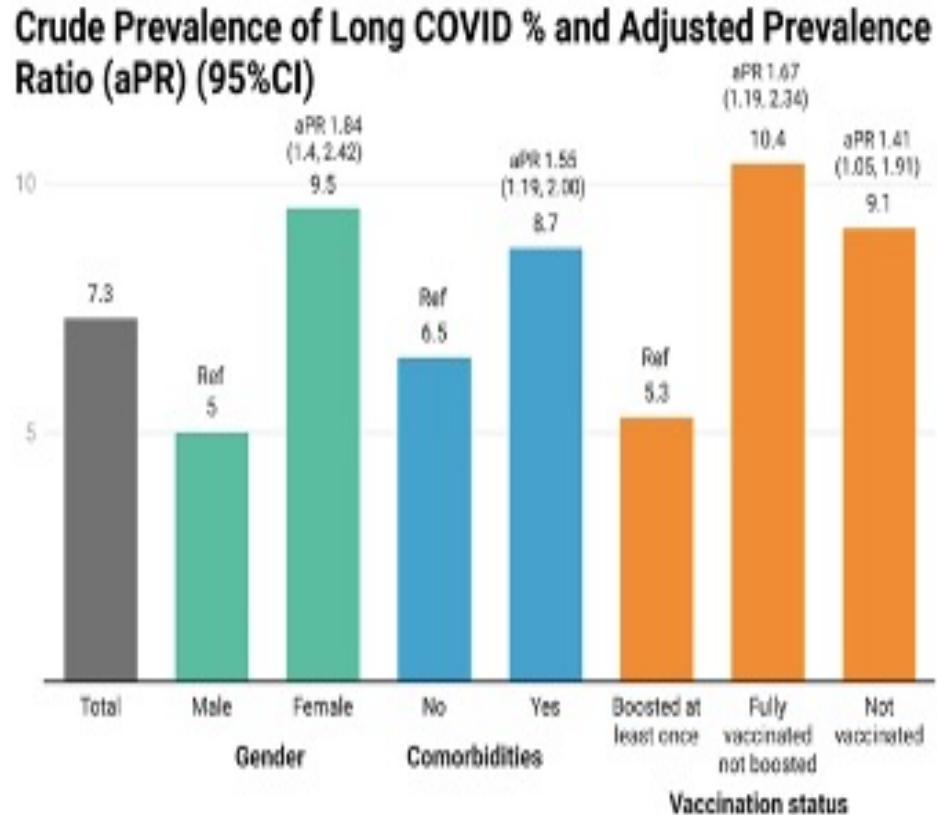
	Total Cases	Deaths
World-wide	668 M	6.7 M
United States	101.8 M	1.1 M

January, 2023



# Epidemiology of long COVID in US adults

In a population-representative sample, we estimated **7.3%** of US adults, approximately **18 million adults**, had symptoms of long COVID during the two-week study period ending July 2, 2022.



- 25% reported day-to-day activities impacted “a lot”
- >28.9% had SARS-CoV-2 > 12 months ago

Robertson et al Clin Infect Dis 2022 Dec 21



# WHO Definition of PASC

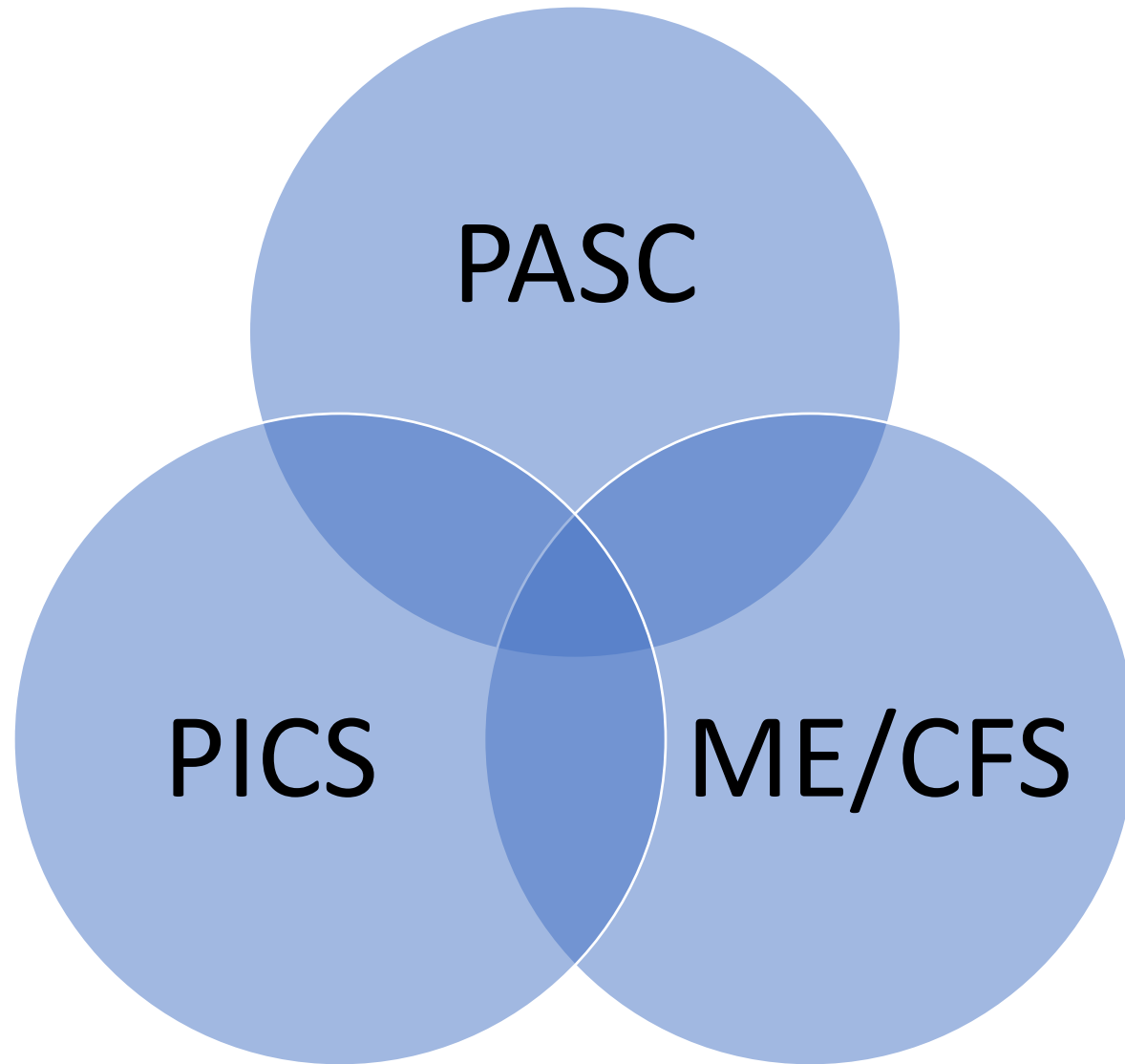
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The continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation.

December 7, 2022



Overlap:



# Sequelae of COVID-19

## Etiology and Pathophysiology

Organ damage from acute infection phase

Persistent inflammatory state

Endothelial damage/clotting

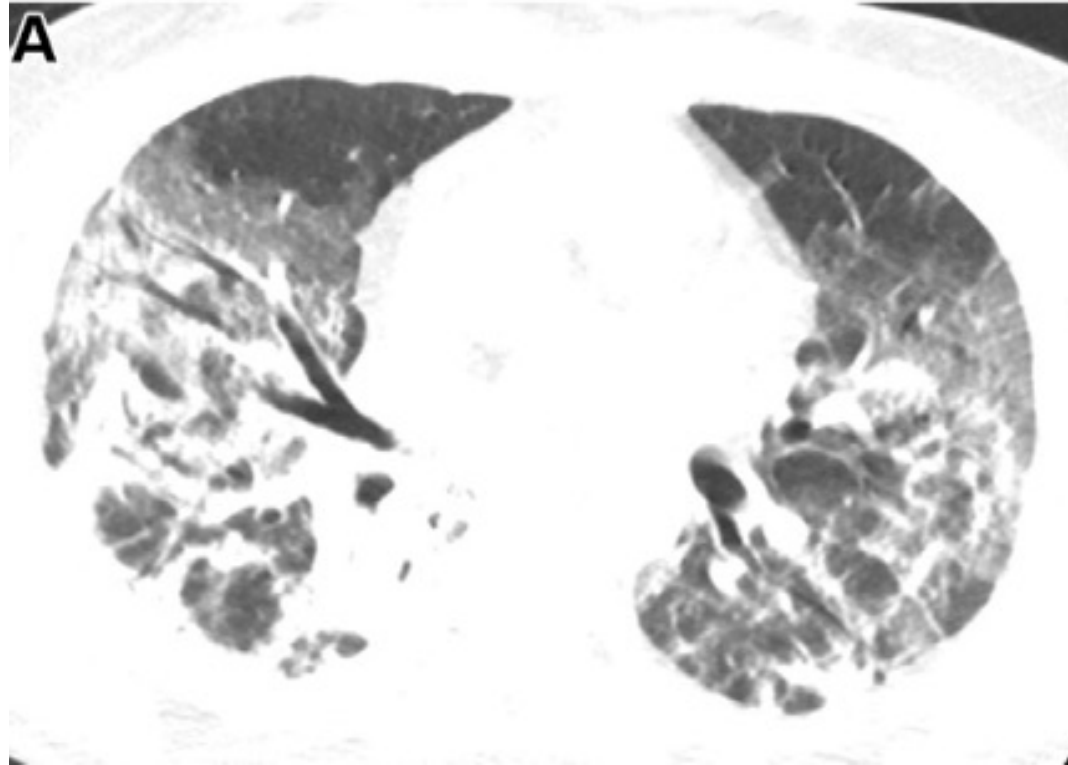
Ongoing viral activity associated with a host viral reservoir

Inadequate immune response



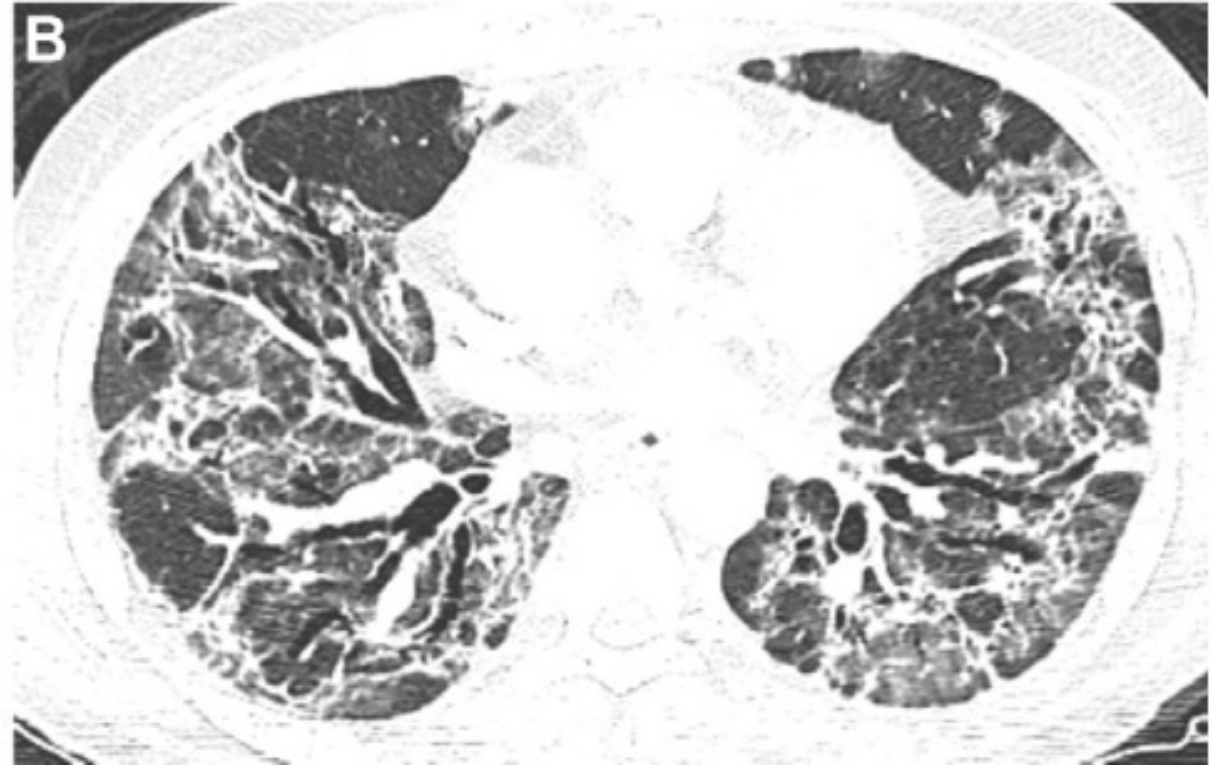
# PASC-CT chest- Fibrosis

2 weeks p admission



Diffuse GGO; Retic

6 months p admission



GGO; traction bronchiectasis; architectural distortion; air trapping (?? Honey-comb)



# Who gets Post-COVID Pulmonary Fibrosis (PCPF)?

- Meta-analysis to investigate prevalence of PCPF
- 13 studies: 2,018 pts; prev 44.9%
- Sx: dyspnea, cough, chest pain, fatigue
- Assoc. Factors: COVID severity; mech vent; Rx with steroids, antibiotics, immunoglobulin; COPD

Amin et al. Ann Med Surg (Lond) 2022, May 7



# Natural history of PCPF

- Prospective cohort study-76 pts-4.4 mos p hosp
- Fibrotic patterns-chest ct: mech vent; male; more severely ill; ↑↑LDH; shorter telomere length
- Fibrosis: cough, DLCO, fragility
- Dyspnea: frailty score, ↓ grip strength

McGroder et al Thorax 2021 Dec



# Management of PCPF

- Observe: patients improving on their own
- Anti-fibrotics
  - **Pirfenidone**—blocks fibroblast prolifer, myofibroblast differentiation, collagen deposition; anti-inflammatory; ↓ expression ACE-2 receptor
  - short term course → with improvement in uncontrolled reports



# Clinical Trials for PCPF

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- Pirfenidone; Deupirfenidone
- Nintedanib
- Fuzheng Huayu
- Sirolimus
- Canrenoate potassium
- Longidaze
- Collagen-polyvinylpyrrolidone
- Antifibrotic monocyte
- Treamid
- Tetrandrine
- Genistein nanoparticles

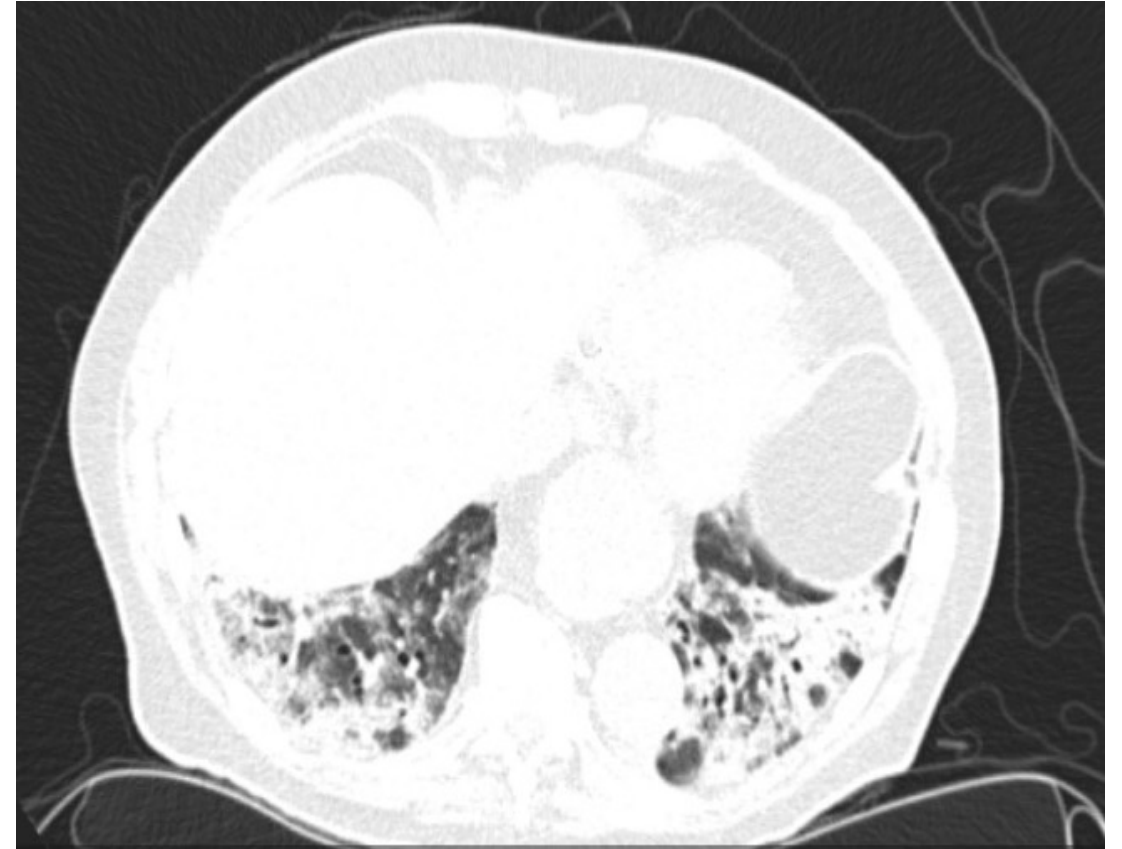


# Current treatment for Post COVID OP (PCOP)

- No approved treatments
- Most pts with PCOP recover within 1 yr
- 5-25% need specialized Rx
- Steroids → response in majority
  - Limited by high relapse frequency
  - Adverse Side effects
- “Steroid-sparing” agents – limited data



# 79 yo man, 4 weeks after COVID pneumonia with persistent hypoxemia



Peripheral predominant mixed ground glass and consolidative opacities bilaterally, some with a perilobular morphology, seen in all lung lobes. Associated mild bronchial dilation, particularly in the lower lobes. There is also associated architectural distortion and cicatricial atelectasis.

# Organizing Pneumonia

- Common with many infections
- Viral-induced damage to alveolar epithelial cells and endothelial cells, associated with inflammation, intra-alveolar edema
- Fibroproliferative process
  - without major disruption of lung architecture
  - reversible



# Persistent Post COVID-19 Inflammatory ILD: An Observational Study of Steroid Treatment

- 837 pts screened by phone for sequelae of Covid-19 pneumonia @ 4 weeks post discharge
  - Pts with sx had out-pt eval @ 6weeks
  - 39% reported ongoing sx
  - 4.8% - dx with ILD, predominantly org. pneumonia
  - Objective: to prevent fibrosis with permanent deficit
  - 30 pts received steroid treatment
  - Result: ↑ in transfer factor of 32%; ↑ in FVC of 10%
- Improvement in sx and imaging

**Caveats:** small group; not RCT; ? Spontaneous recovery; ?

Long-term

Annals ATS Jan 12, 2021





# CORE Clinic & Lessons Learned

- Avoid cognitive bias
- Consider differential diagnosis as usual
- Do not assume that sx that occur post-COVID-19 are necessarily secondary to COVID -19
- Speculation: Auto-immune (and other) disorders may become more apparent following the immune/inflammatory disorder associated with acute COVID



# New Diagnoses – MGH Pulmonary CORE Clinic

- Auto- immune disorders
- ANCA+ disease
- Asthma
- Bronchiectasis
- Bronchiolitis
- Organizing pneumonia
- Pulmonary fibrosis
- + ANA
- Small fiber neuropathy
- Dysautonomia
- Fibromyalgia
- Sleep-related breathing problem
- Laryngeal abnormalities
- Malignancy



# RECOVER

- REsearching COVID to Enhance Recovery
- NIH-sponsored initiative seeking to understand, prevent, and treat PASC
- Award of nearly \$470 million
- More than 30 institutions utilizing a set of main protocols
- Build a study population of tens of thousands
- Big Data

