# Post COVID-19 Respiratory Perspective

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BC ECHO for **Post-COVID-19 Recovery**

# Disclosure statement

- No conflict of interest to disclose

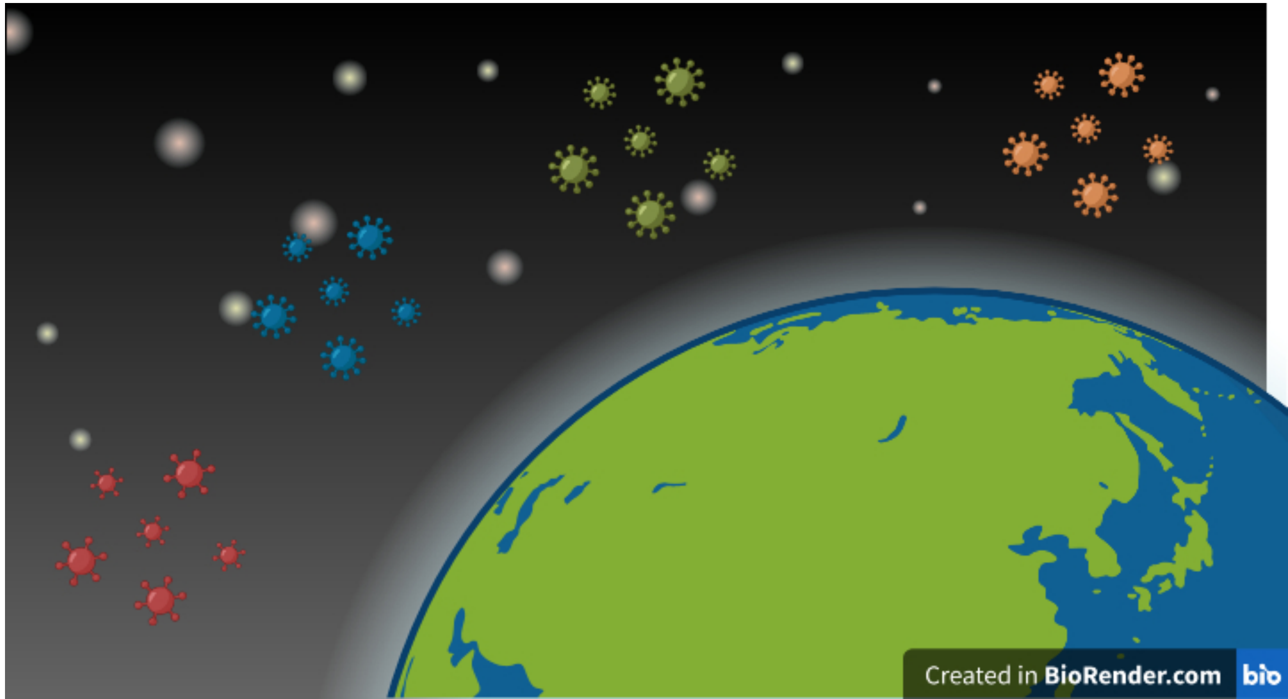
# Learning Objectives

- *Understand the long-term respiratory complications of COVID-19*
- *How to apply pulmonary rehabilitation strategies to clinical practice*
- *How to support and improve functional status and quality of life for patients living with long term respiratory consequences of COVID-19*
- *Locating respiratory tools and resources*

# Introduction

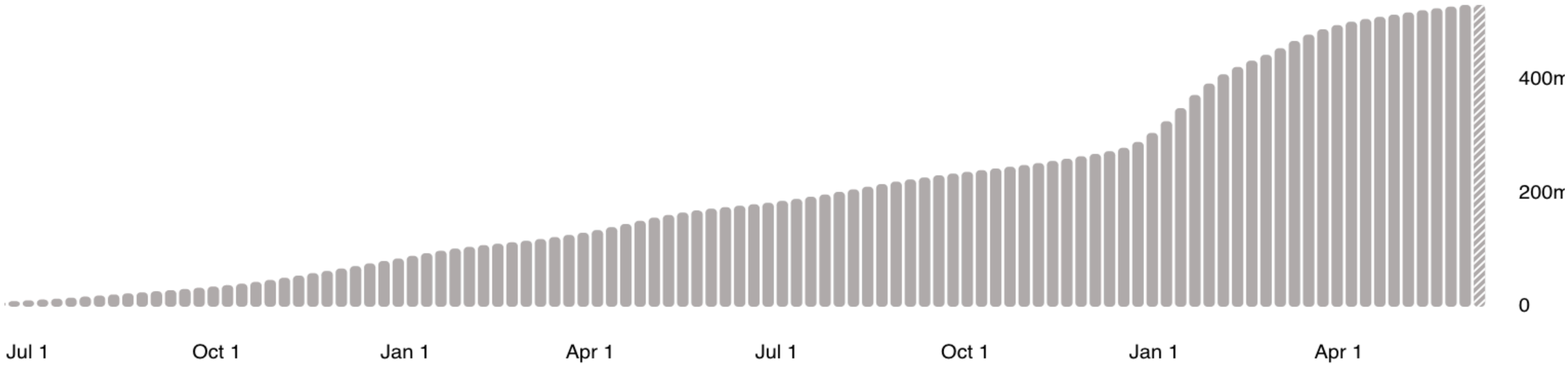
Fatal coronavirus outbreaks in last 20 years

1. SARS (severe acute respiratory syndrome, 2002 and 2003)
2. MERS (Middle East respiratory syndrome, since 2012), and
3. Covid-19 (since 2019)

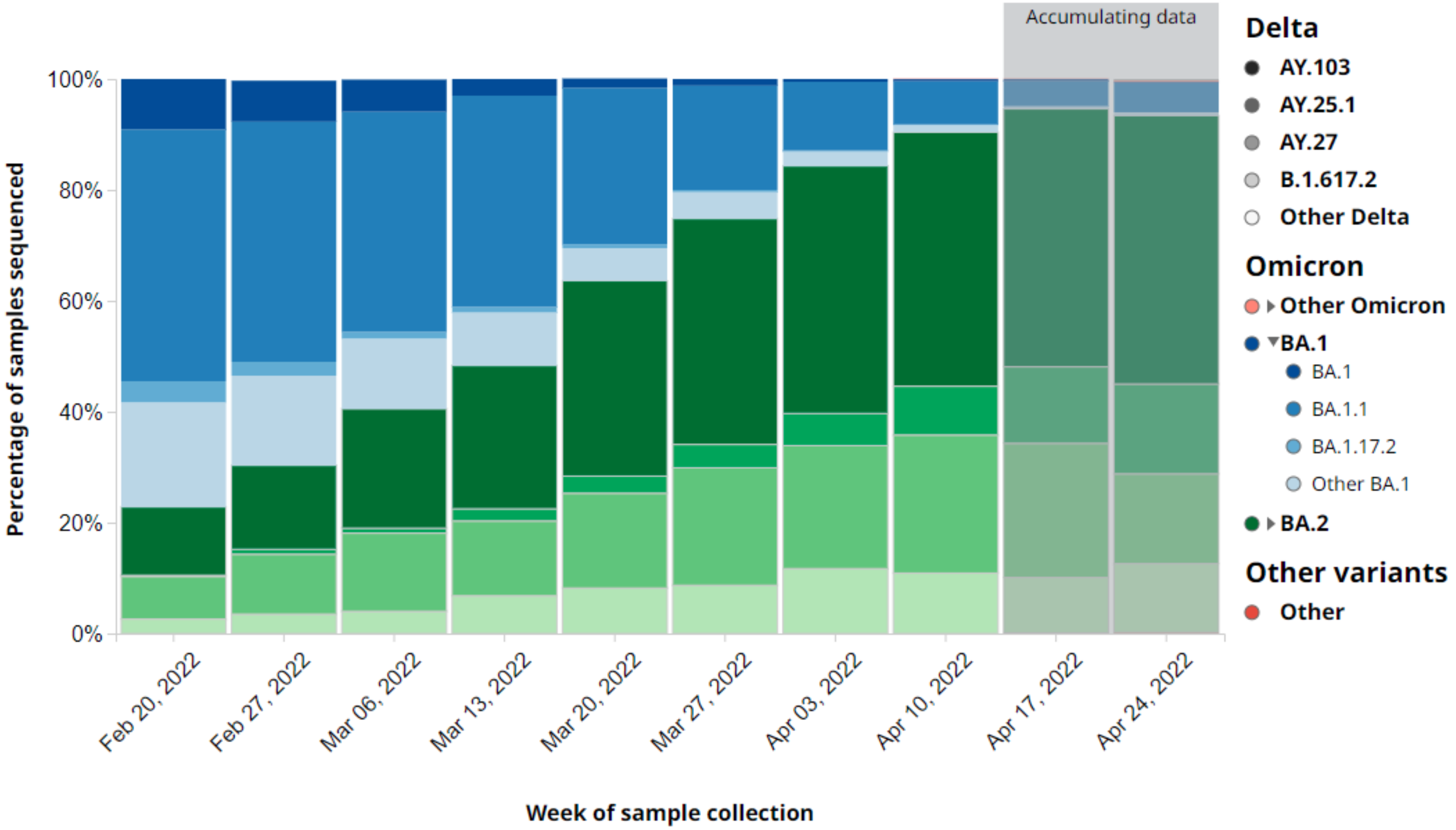


# Introduction

- Globally, more than 100 million confirmed cases of COVID-19 caused by SARS-CoV-2 infection reported.
- Pulmonary, cardiovascular, neurologic, hematologic, and GI systems involved in the acute COVID-19 illness

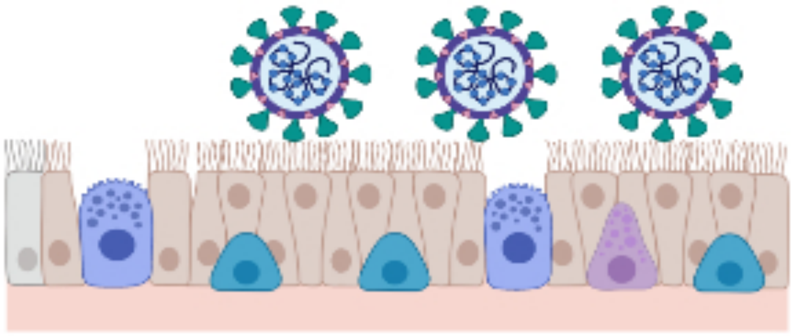



https://covid19.who.int/. Updated June 30, 2022. Accessed June 30, 2022.

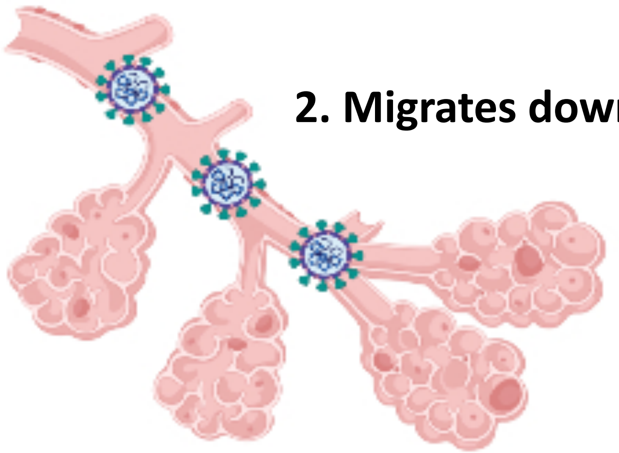



http://www.bccdc.ca/health-info/diseases-conditions/covid-19/about-covid-19/variants. Updated July 3, 2022. Accessed July 3, 2022.

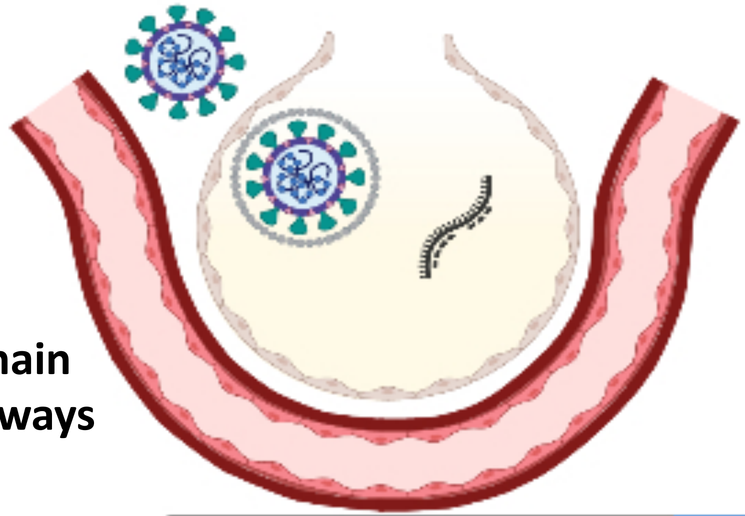
# What are the initial steps of infection?



1. Binds to epithelial cells in the respiratory tract



2. Migrates down to the lower airways

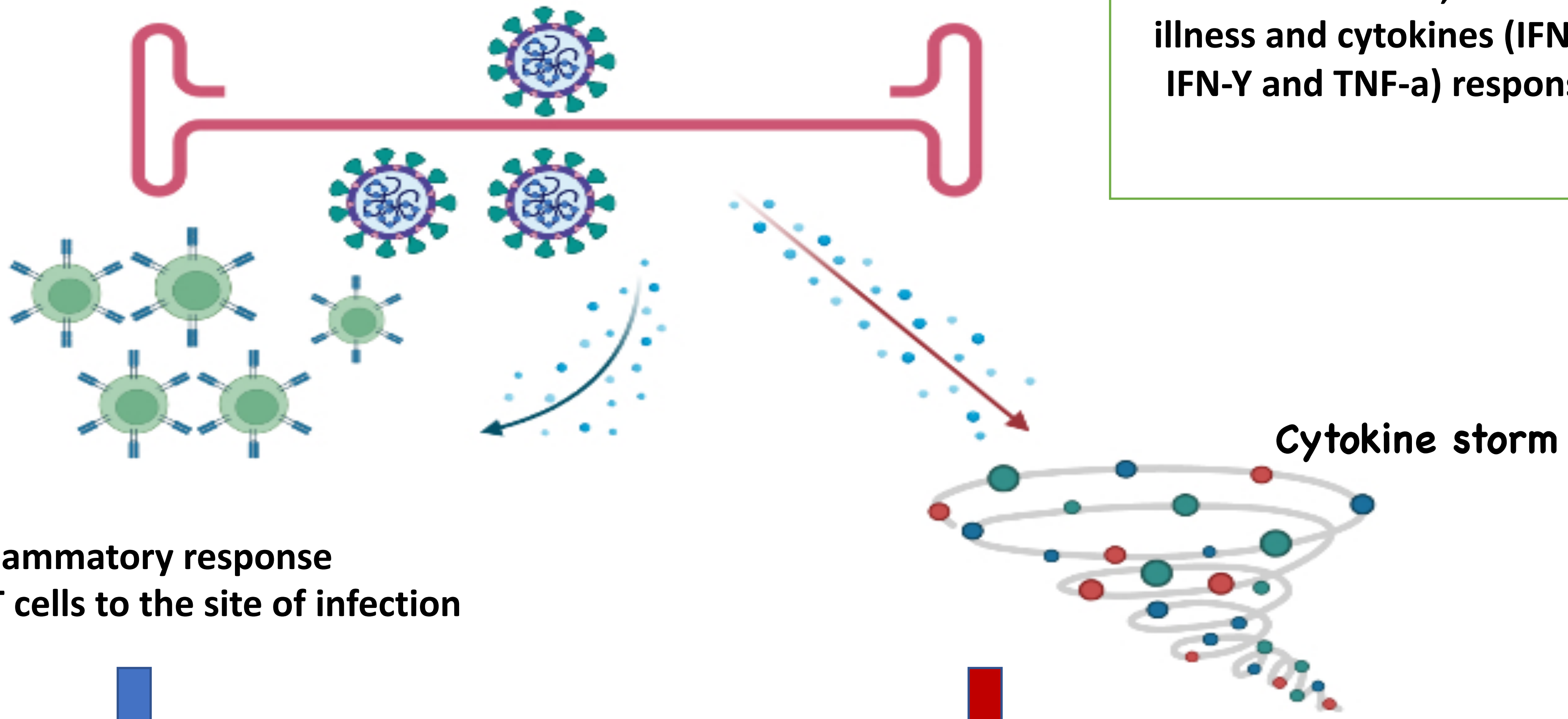


3. S1 subunit of the S protein binds to the peptidase domain of the angiotensin-converting enzyme 2 (ACE2) in the airways epithelial cells and vascular endothelial cells

Gubernatorova EO. Cytokine Growth Factor Rev. 2020

# What next?

**Evidence suggests correlation between viral load, severity of illness and cytokines (IFN-a, IFN-Y and TNF-a) response**




**Virus entry & initial inflammatory response attracts virus-specific T cells to the site of infection**

Recovery or mild illness in most people

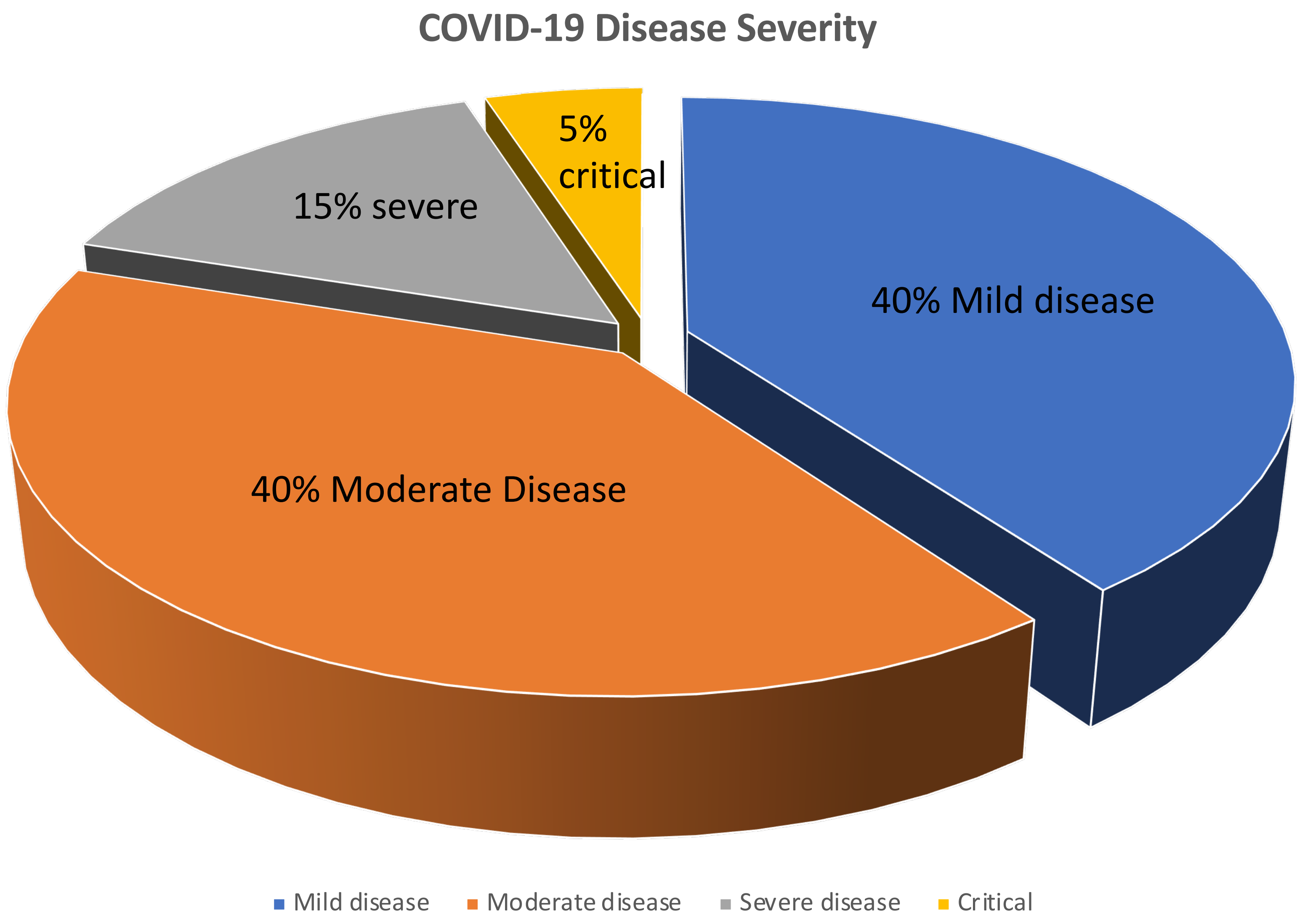
Severe disease



Gubernatorova EO. Cytokine Growth Factor Rev. 2020

Ref 3

# Majority of COVID-19 patients have mild to moderate disease

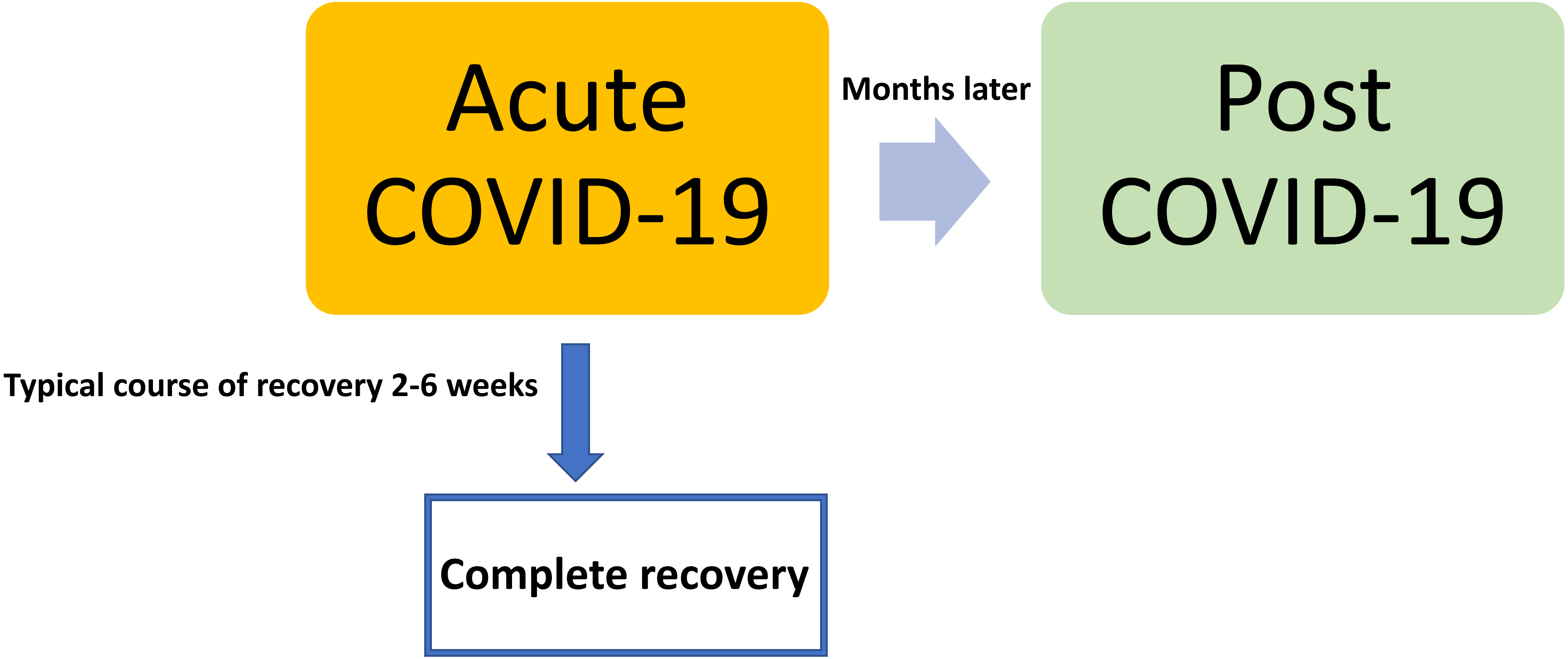



**Incubation period 1-14 days**

Wu Z, McGoogan JM. JAMA. 2020

# Impact of COVID-19

- **Post COVID-19 complications may lead to a major long-term impact on communities and health care systems**



What proportion of patients experience persistent symptoms after acute illness?

# What are the long-term sequelae of COVID-19?

**A large UK study of over 1 million people with self-reported long COVID**

**Of people with self-reported long COVID:**

**40% first had (or suspected they had) COVID-19 at least one year previously.**

https://www.ons.gov.uk

# What are the long-term sequelae of COVID-19?

**A large UK study of over 1 million people with self-reported long COVID**
**As of December 6, 2021**

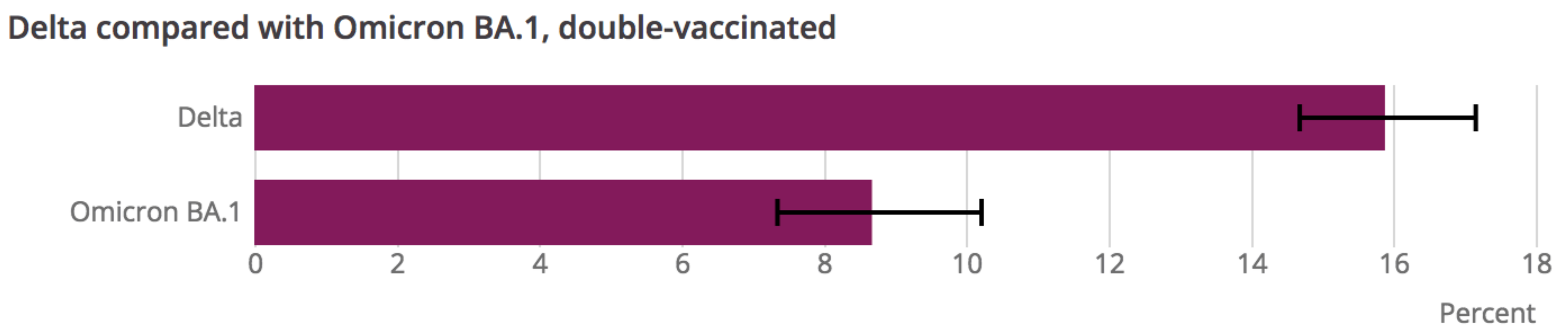
**Of people with self-reported long COVID:**

**Most commonly seen in females, age 35-69 years, another health condition**

https://www.ons.gov.uk

# What are the long-term sequelae of COVID-19? Differences between variants

**For double-vaccinated participants, self-reported long COVID was less common after infections compatible with the Omicron BA.1 variant than the Delta variant**

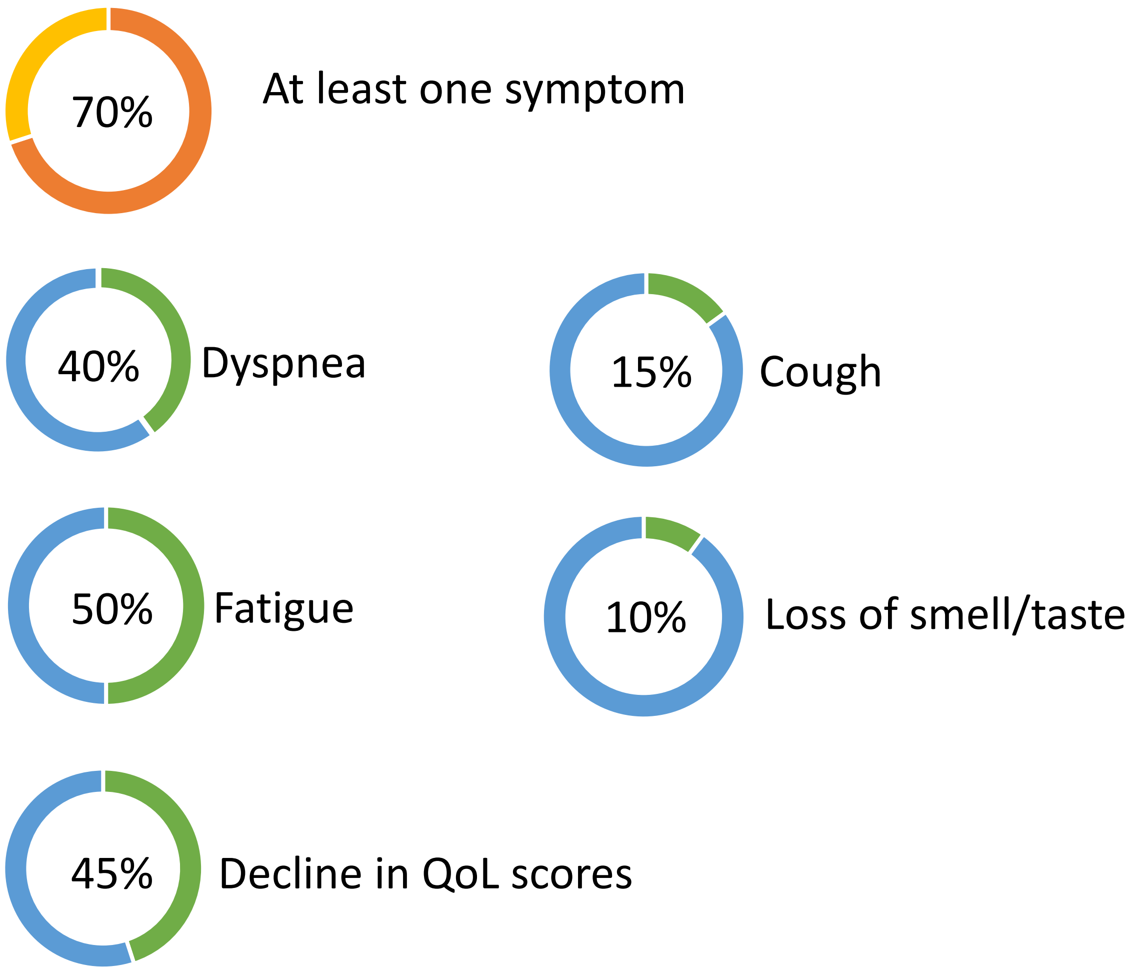



https://www.ons.gov.uk

# What are the long-term sequelae of COVID-19?

**60- day follow-up**, hospitalized patients

- United states - 488 patients
- Italy – 143 patients
- France – 150 patients




> 50 long-term effects

Chopra V. et al.Ann Intern Med. 2021
Carfi, A.et.al. JAMA. 2020
Carvalho-Schneider, C. et al. *Clin. Microbiol. Infect. 2021*

# What range of symptoms occur in COVID-19 survivors? Not hospitalized – 6 months

**A prospective study from Norway:**

**247 home-isolated patients**

- 55% (136/247) experienced persistent symptoms at 6 months

**most common:**

- **fatigue (30%)**
- **disturbed taste and/or smell (27%)**
- **concentration impairment (19%)**
- **memory loss (18%)**
- **dyspnea (15%)**

**55% had at 1 symptom**

**Most of these patients Included young adults (16 – 30) !**

Blomberg, B. et al. nature med. 2021

# Respiratory complications after COVID-19

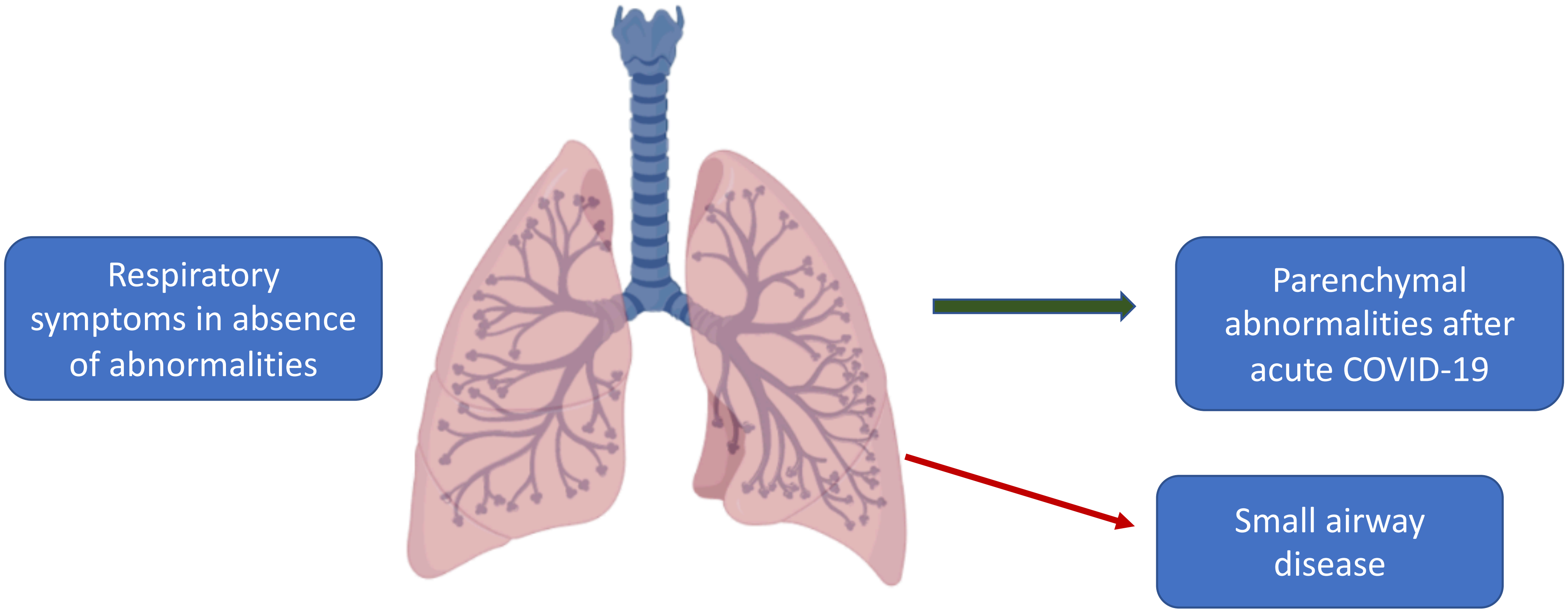
- Dyspnea is one of the common symptoms that persist after COVID-19

23% and 66%

w/ significant shortness of breath weeks after acute illness

Al-Jahdhami I. Oman med. J. 2022

# Long-term respiratory complications



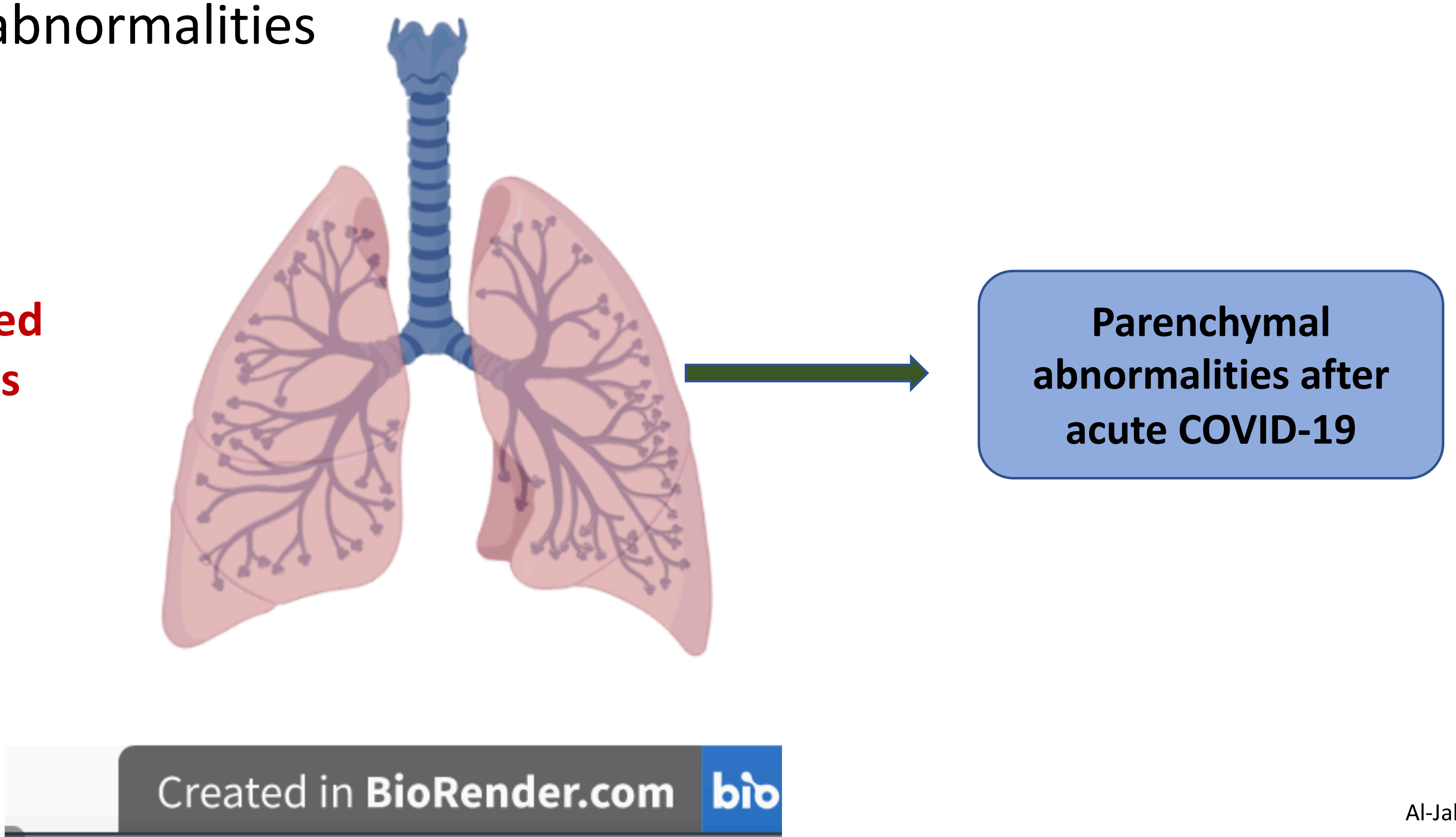
# Long-term respiratory complications

**<u>Post COVID Interstitial lung changes:</u>**

Persistent parenchymal abnormalities

**Proportion varies widely:**

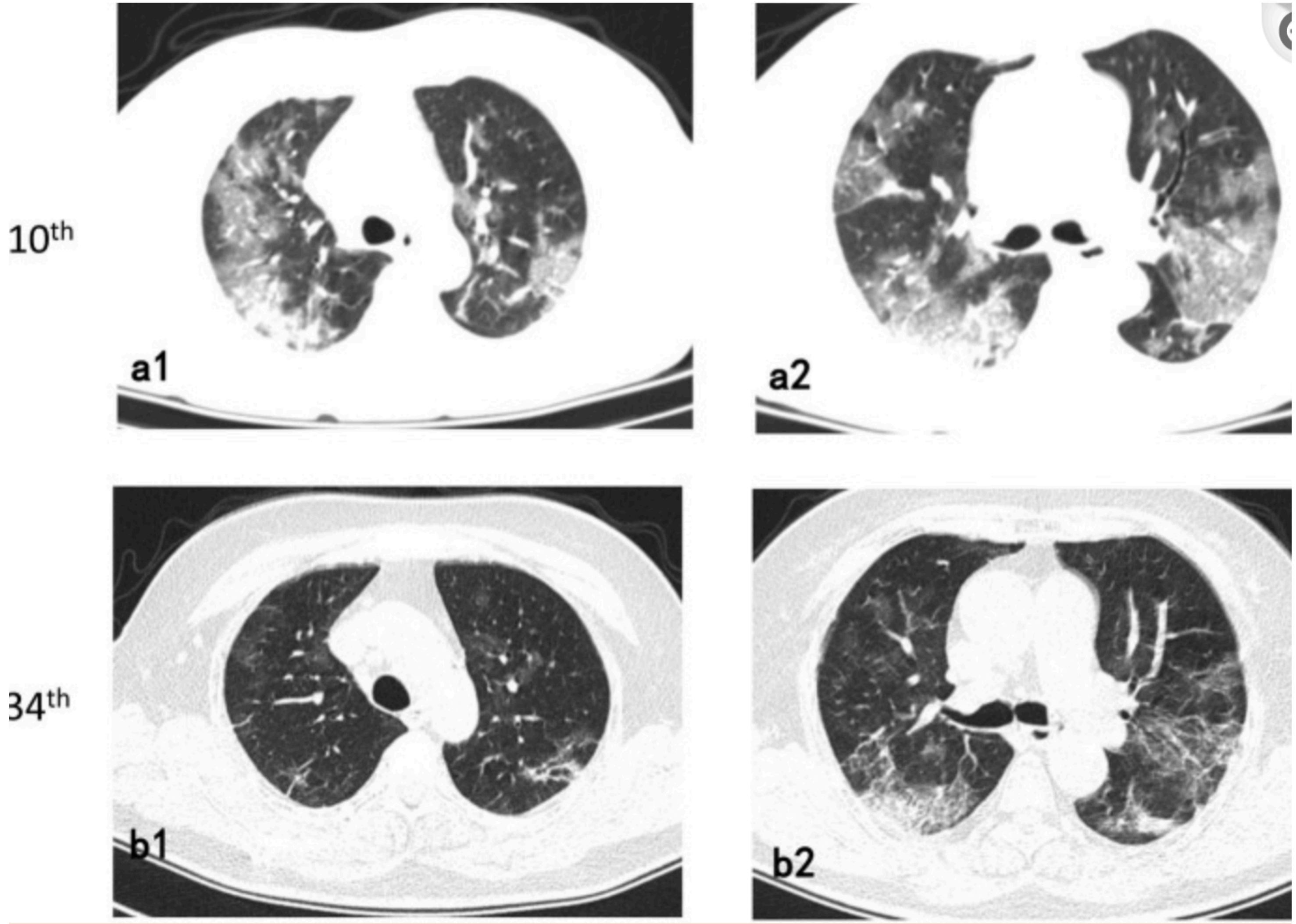
**72% of mechanically ventilated**
**4.8% of all hospital discharges**




Al-Jahdhami I. Oman med. J. 2022

# Post COVID ILD – evolution of radiology

Case example of Severe COVID-19 acute illness




Ground glass opacities, consolidation predominate

↓

Absorption of ground glass opacities
In early recovery phase

↓

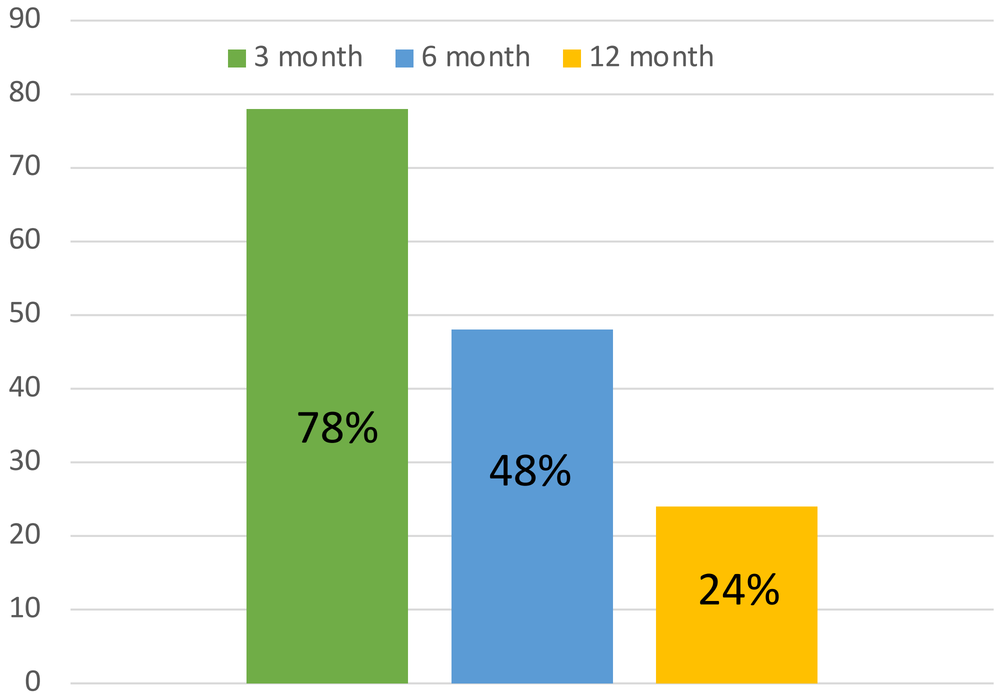
Reticulation, interlobular thickening

↓

Slow absorption of pulmonary fibrosis

Fang Y. Am J Emerg med. 2020

# How do CT findings change over time?




Proportion of patients with at least one abnormal finding on CT

**The most common abnormal radiologic features in patients demonstrating residual disease were:**

1. **GGO**
2. **Interlobular septal thickening**
3. **Reticular opacities**

At least 20% of patients
have residual CT abnormalities
at 1 year

Wu X. et al. Lancet Resp med. 2021

Longitudinal study
Vancouver cohort
N = 40

| PFT (%-predicted) | 3 months | 6 months | 12 months | p-value |
|---|---|---|---|---|
| $FEV_1$ | 90 ± 17 | 91 ± 16 | 91 ± 17 | 0.39 |
| FVC | 90 ± 17 | 93 ± 17 | 94 ± 18 | **0.001** |
| $FEV_1$/FVC | 79 ± 7 | 77 ± 7 | 76 ± 8 | **<0.001** |
| TLC | 83 ± 14 | 87 ± 13 | 88 ± 13 | **<0.001** |
| DLCO | 76 ± 16 | 80 ± 17 | 80 ± 16 | **<0.001** |
| **PROMs** | | | | |
| Dyspnea (UCSD) | 10 (3-25) | 9 (3-30) | 9 (2-22) | 0.26 |
| Cough (VAS) | 30 (10-60) | 24 (10-35) | 15 (8-50) | 0.62 |
| Frailty (Frailty Index) | 0.07 (0.02-0.14) | 0.07 (0.02-0.17) | 0.07 (0.02-0.14) | 0.99 |
| Mood (PHQ-9) | 2 (1-6) | 1 (0-5) | 2 (0-4) | 0.10 |
| Sleep (PSQI) | 5 (3-9) | 6 (3-9) | 5 (3-8) | 0.73 |
| QoL (EQ5D VAS) | 75 (68-90) | 80 (75-90) | 80 (70-90) | **<0.001** |
| **CT features (% of lung volume)** | | | | |
| GGO | 11.3 (5.6-19.6) | - | 0 (0-3.3) | **<0.001** |
| Reticulation | 4.4 (1.6-7.9) | - | 1.7 (0-3.3) | **0.004** |

**The natural history of COVID-19 recovery: changes in physiologic, radiologic, and patient-reported outcomes 12 months after symptom onset**

Alyson W. Wong MD,[1,2*] Aditi S. Shah MD,[1*] Cameron J. Hague MD,[3] James C. Johnston MD,[4,5] Christopher J. Ryerson MD[1,2], Christopher Carlsten MD[1,4]

# Which individuals are more likely to develop irreversible fibrotic changes?

- Not well defined, but some evidence suggests..

Age older than 50 years

Severe disease

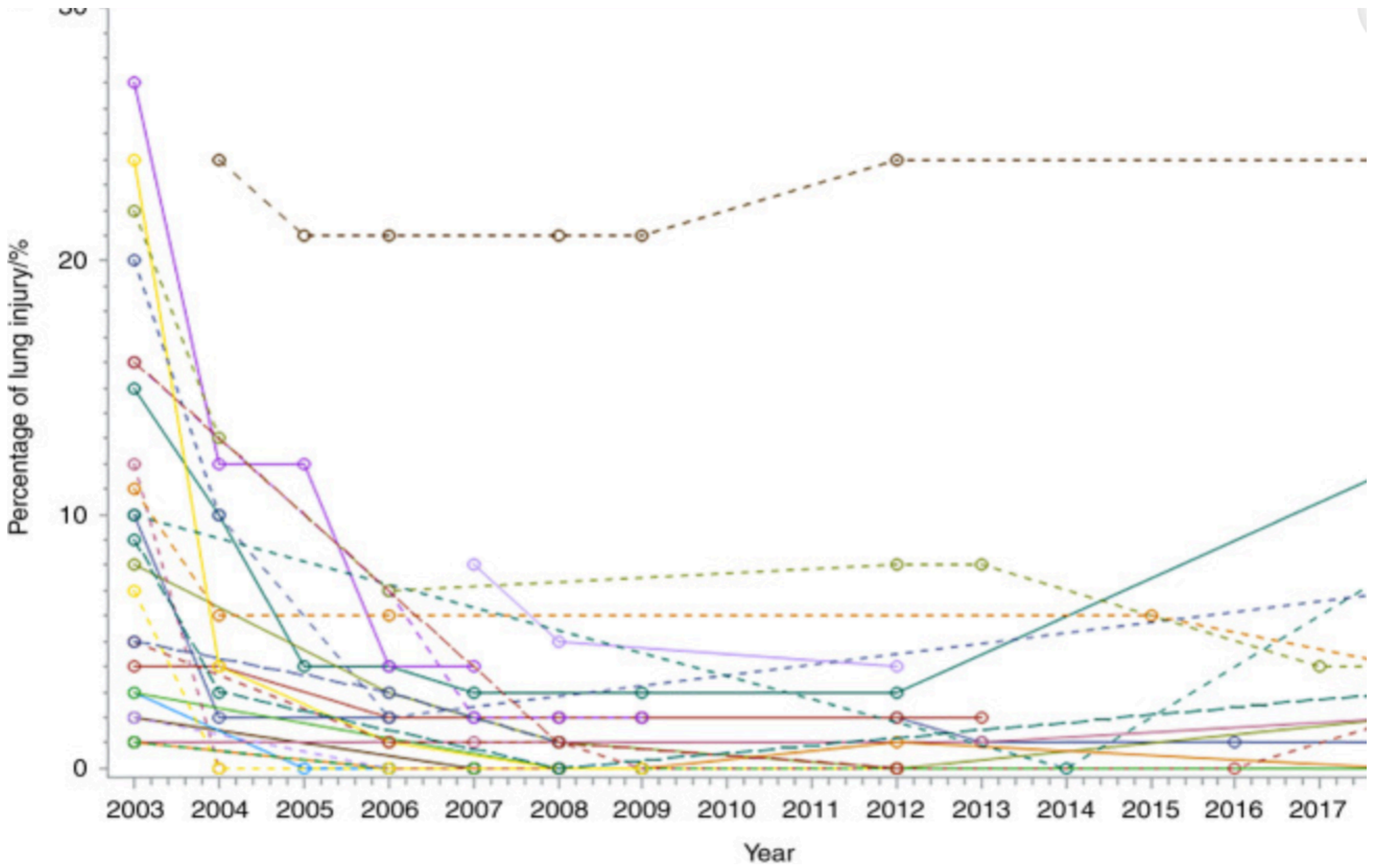
Development of ARDS or need for mechanical ventilation.

Han X. radiology. 2021

# Questions that remain unanswered

- Will this trigger a pathway of progressive fibrosis?
- Glucocorticoids are used for managing organizing pneumonia, which leads to physiologic and radiologic improvement. However, the natural progression of the parenchymal abnormalities is unclear
- Will the persistent fibrotic changes seen at 12 months eventually recover or will they remain fixed?

# Lessons from other coronavirus outbreaks




**71 patients with SARS**

**15-year follow up study**

- **% of lung injury reduced by 1 year, then plateaued over following 14 years**
- **Same trend noticed with pulmonary function**

Zhang P. et al. Bone Res. 2020

# Post COVID Interstitial lung Changes management

**Post COVID Interstitial Lung Changes**

- Management is not well established

**Clinical practice:** corticosteroids used in select cases, such as post COVID organizing pneumonia

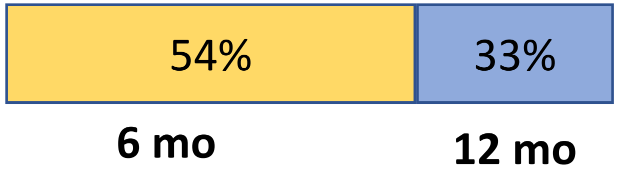
# What findings can we expect in pulmonary investigations?

**Data from prospective cohort study, China**

## Pulmonary function test

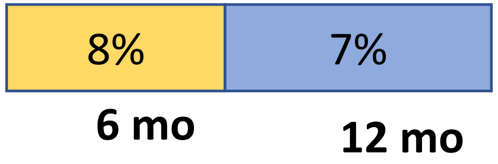
**Proportion of people with abnormal PFTs reduces over time.**

- DLCO impairment, most common



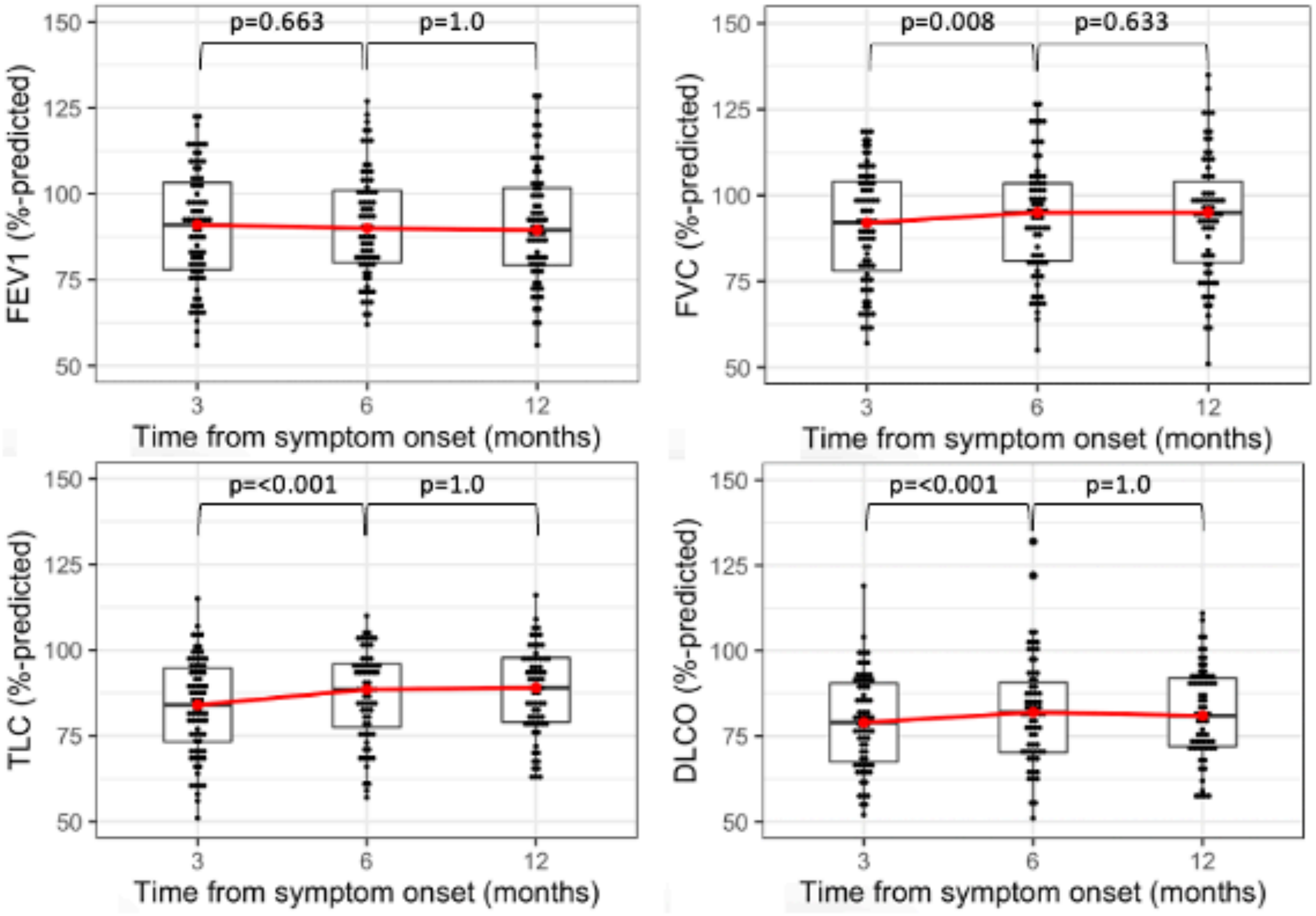

- FVC

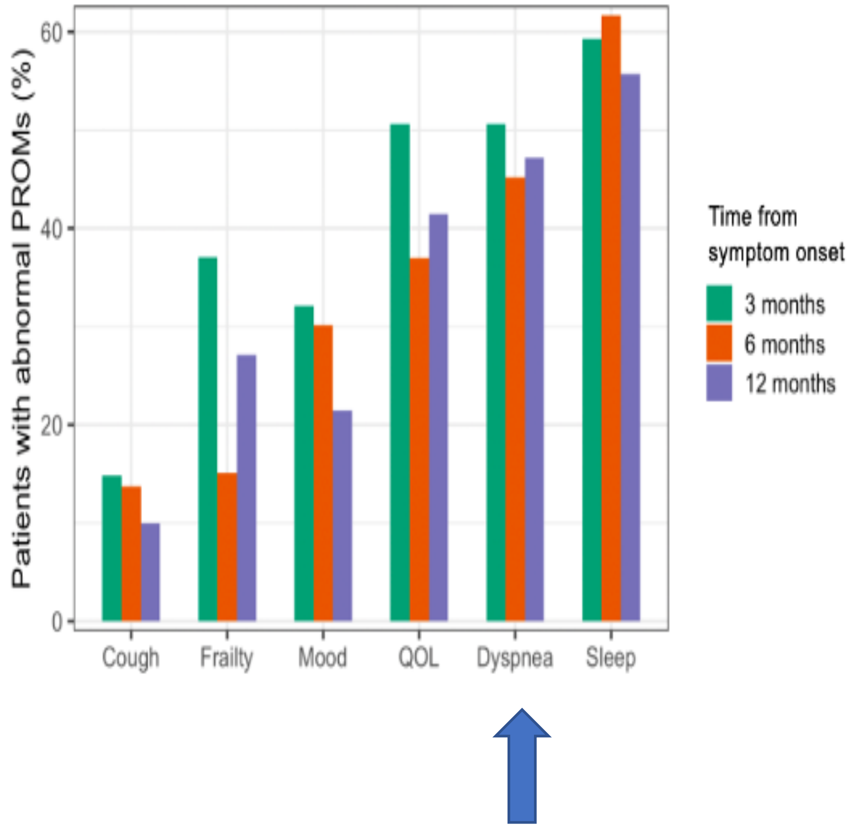

- reduced FEV1/FVC ratio



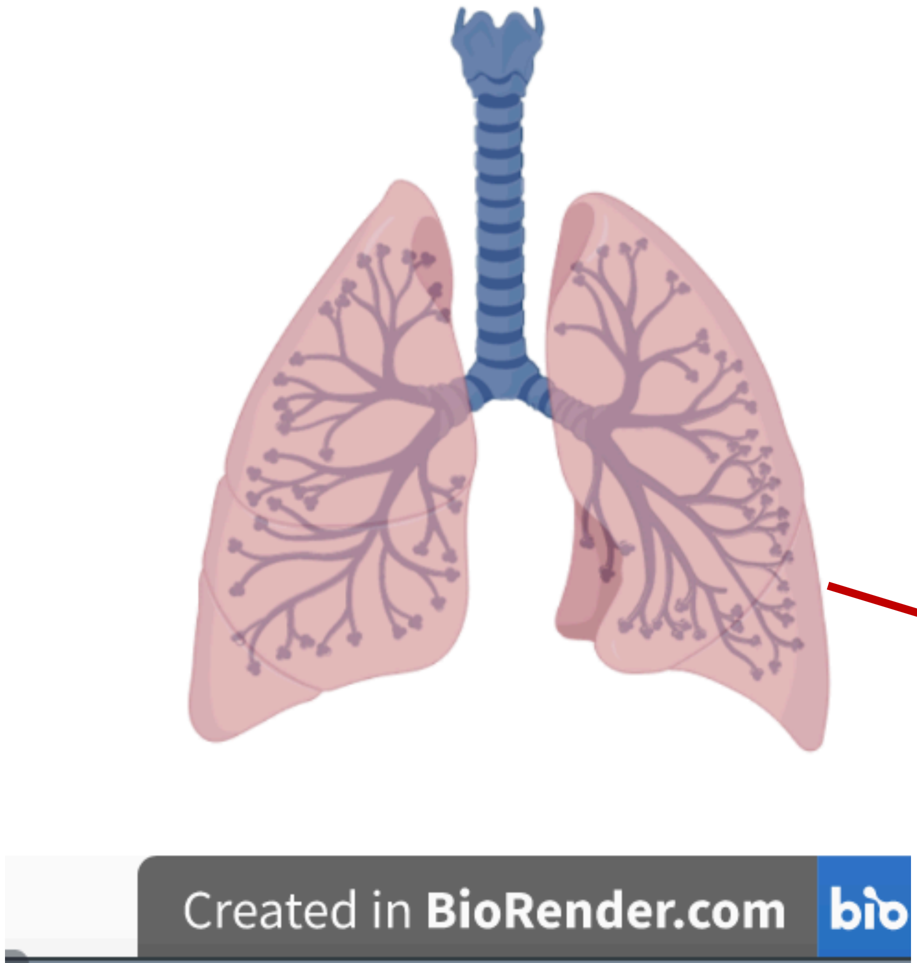

Wu X. et al. Lancet Resp med. 2021

Longitudinal study
Vancouver cohort
N = 73



# Long-term respiratory complications



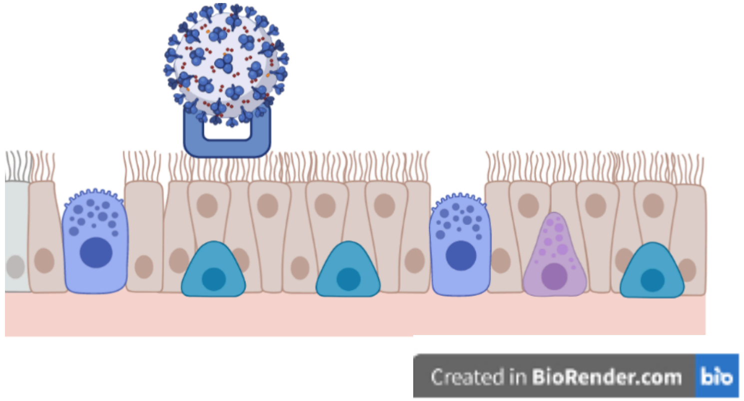

Small airway disease

# SARS-CoV-2 and small airway disease

**How can SARS-CoV-2 lead to airway involvement?**

**Few possible explanations**

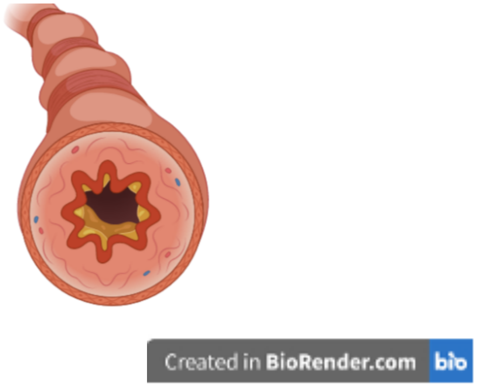
1




ACE2 receptors in airway tract, including small airways

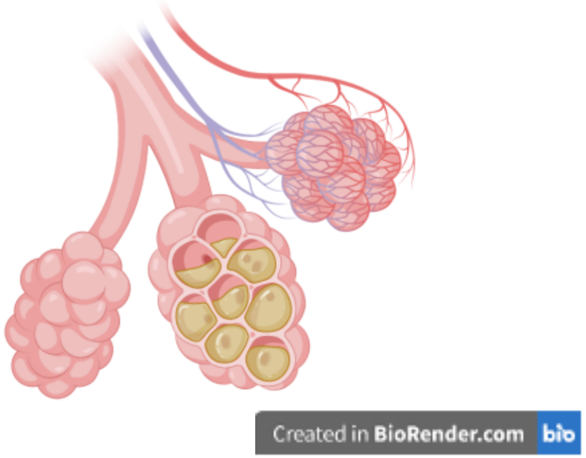
- Direct infection of the small airways leads to small airway disease

2




Post-infectious constrictive bronchiolitis

3

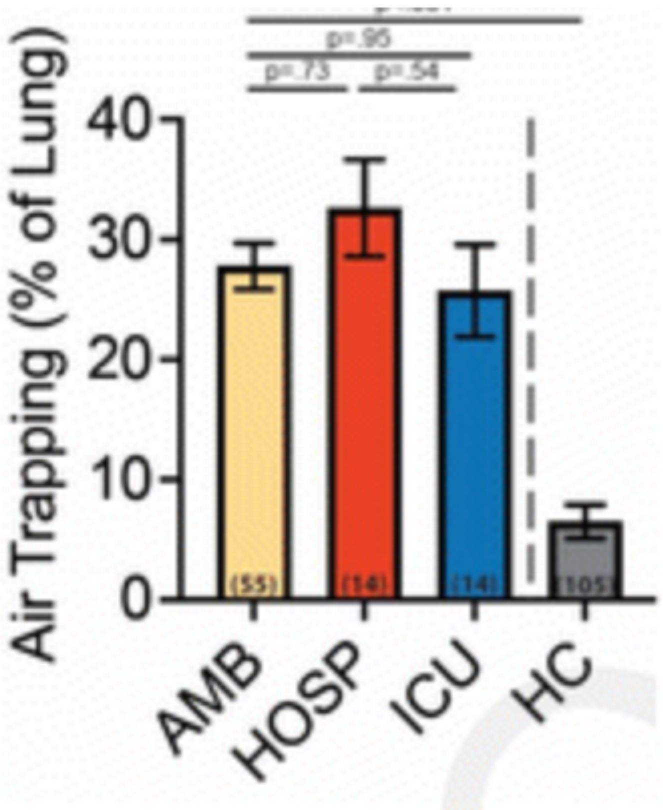



Organizing pneumonia → buds of inflammatory tissue
Fills up the small airways → small airway disease

Josalyn L. et al. Radiology. 2022

Radiology

# Quantitative Chest CT Assessment of Small Airways Disease in Post-Acute SARS-CoV-2 Infection




100 participants with Long COVID (smxs > 30 days post acute illness)
106 healthy participants

**Air trapping:**
7.2% Healthy Controls
25% Ambulatory during acute COVID-19
35% hospitalized during acute COVID-19
27% ICU 27.3% during acute COVID-19

**The median time from diagnosis to chest CT imaging was approximately 75 days.**

Josalyn L. et al. Radiology. 2022

Radiology

# Quantitative Chest CT Assessment of Small Airways Disease in Post-Acute SARS-CoV-2 Infection

NO evidence of airflow obstruction by spirometry in all groups

↓

Indicates small airway involvement. This may not be detected on spirometry, unless large percentage are obstructed

## SPIROMETRY

| Measurement | PASC group |
|---|---|
| **Median pre-bronchodilator FEV1/FVC** | Ambulatory: 79%<br>Hospitalized: 79%<br>ICU: 83% |
| **Response to bronchodilator** | Absent for all |

Josalyn L. et al. Radiology. 2022

# Key take away points

- CT imaging demonstrates findings indicative of small airway disease.
- This is often not captured on pulmonary function tests.

Question still remains:

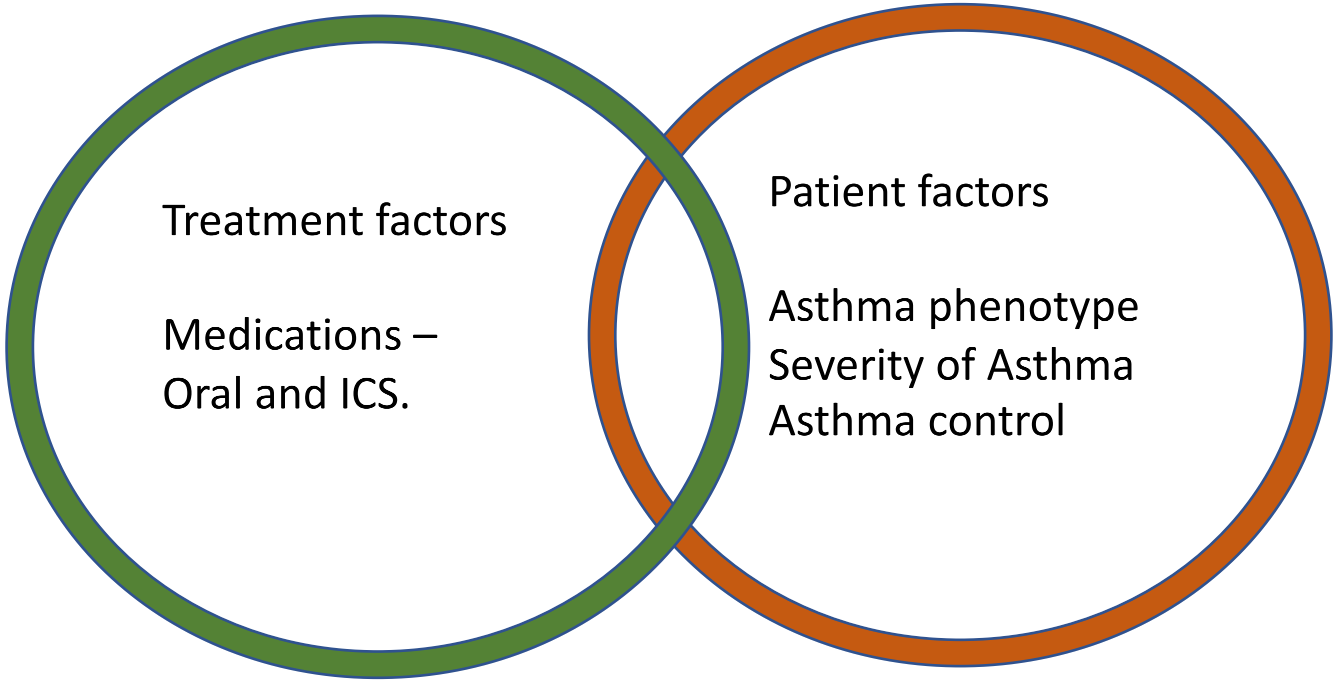
- ? How many will remain with abnormal findings, improve or recover
- ? What will be mechanism of persistent small airway disease (if it remains).
- ?how to prevent further progression of disease

What are the long-term impacts of COVID on patients with pre-existing airway disease

- Asthma

# Long-term impact of COVID on Asthma

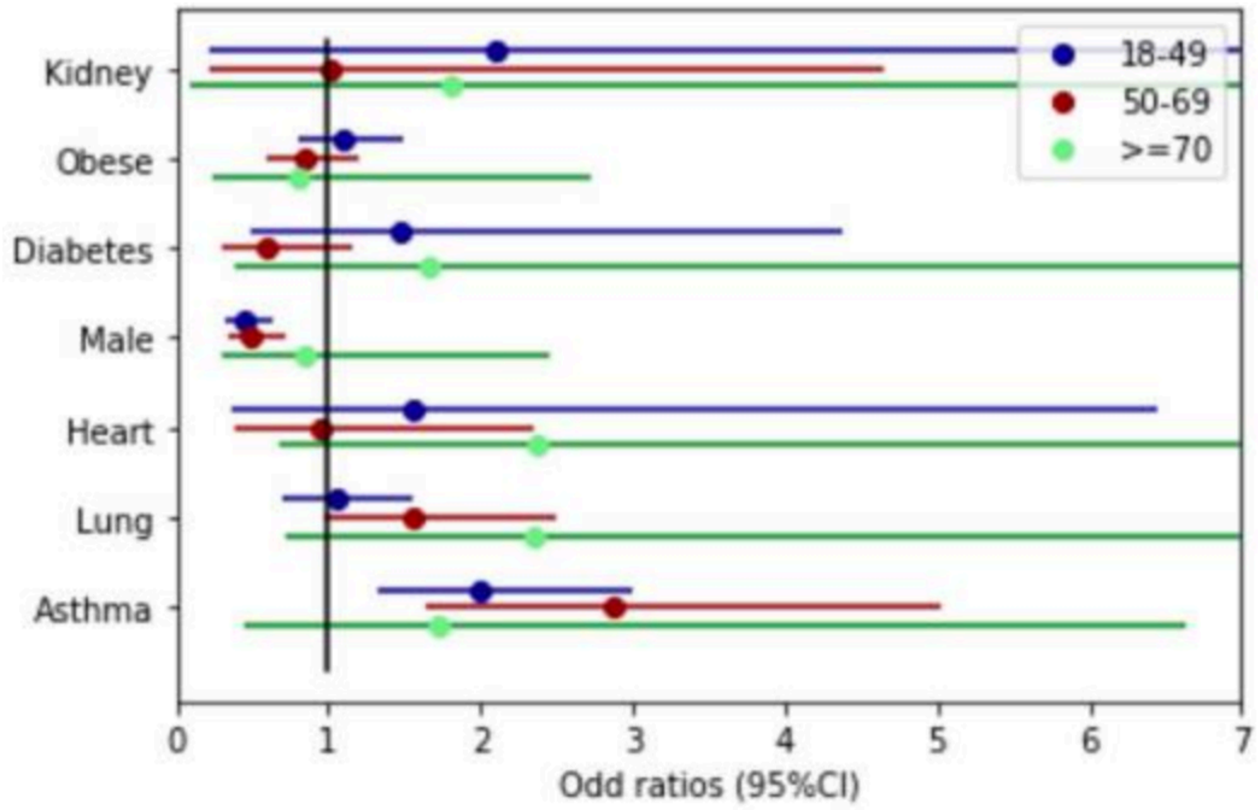
- The impact of COVID-19 on people with asthma is complex




Need to improve understanding of how COVID-19 impacts people with asthma, both acutely and longer-term.

Philip KEJ et al. BMJ open res. 2022

# Long-term impact of COVID on Asthma



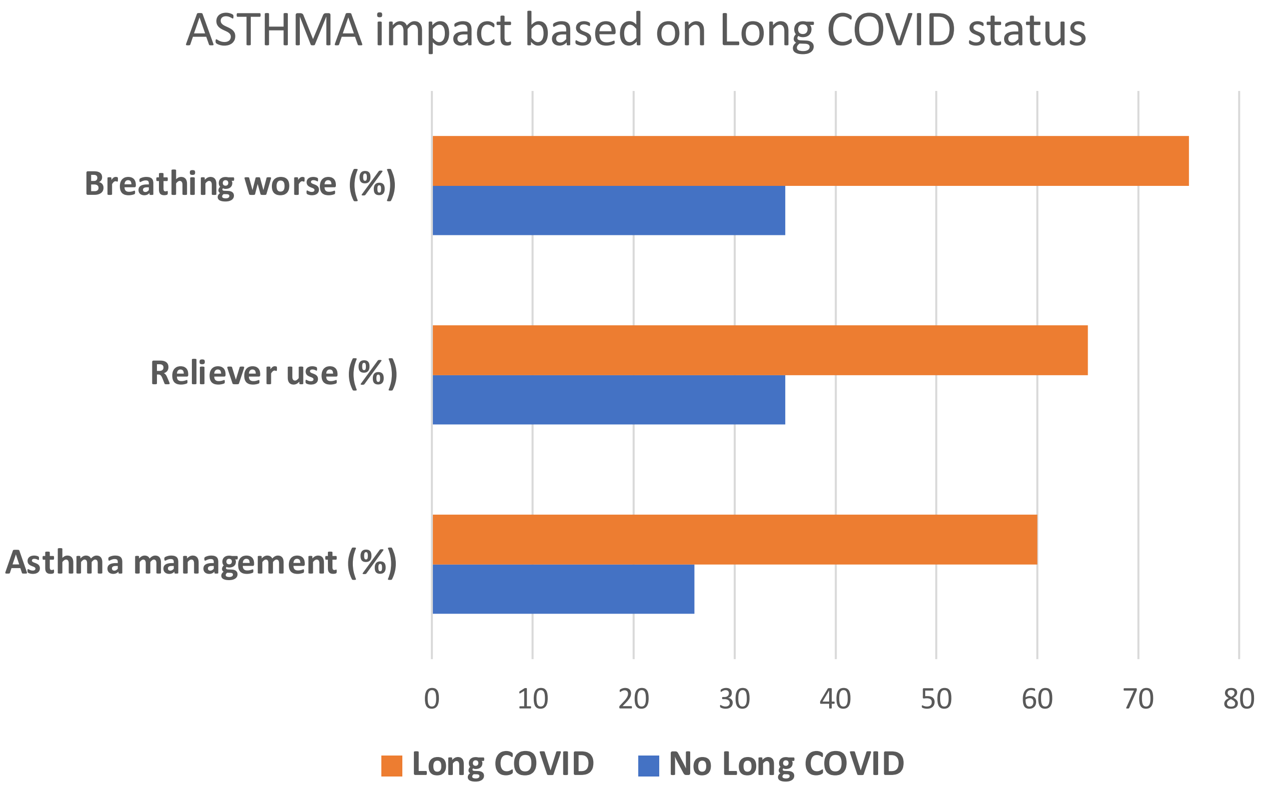

| | LONG COVID | Matched negative controls | P-value |
|---|---|---|---|
| Asthma (%) | 15.8** | 13.7 | <0.05 |

**Asthma was the only pre-existing condition significantly associated with Long COVID (smxs > 28 days) (OR = 2.14)**

Sudre CH et al. nat med. 2021

# UK study: Long COVID in Asthma

- 471 asthma patients with reported COVID (based on survey responses)




Key findings:

- Long COVID individuals had:

1. Breathing worse
2. Asthma management worse
3. Higher rescue inhaler use

Philip KEJ et al. BMJ open res. 2022

# Patient experience..

**Theme 1:**
**The severity and duration of symptoms described varied between people.**

- Nearly **half ongoing symptoms weeks to many months later**
- Recovery: highly variable
  - **relapsing recoveries** 'slow and unpredictable'
  - episodic worsening of symptoms after initial improvements
  - 'It comes and goes in waves' (female, aged 40–49).

Over half believed that they had long COVID

**Theme 2:**
**symptom overlap and interaction between COVID-19 and asthma.**

- **Frequent reports of additional features atypical from norm – " my asthma changed massively".**
- **COVID-19 often seen as causing a protracted asthma exacerbation.**
- psychological impacts - anxiety were often mentioned – worsened asthma

Philip KEJ et al. BMJ open res. 2022

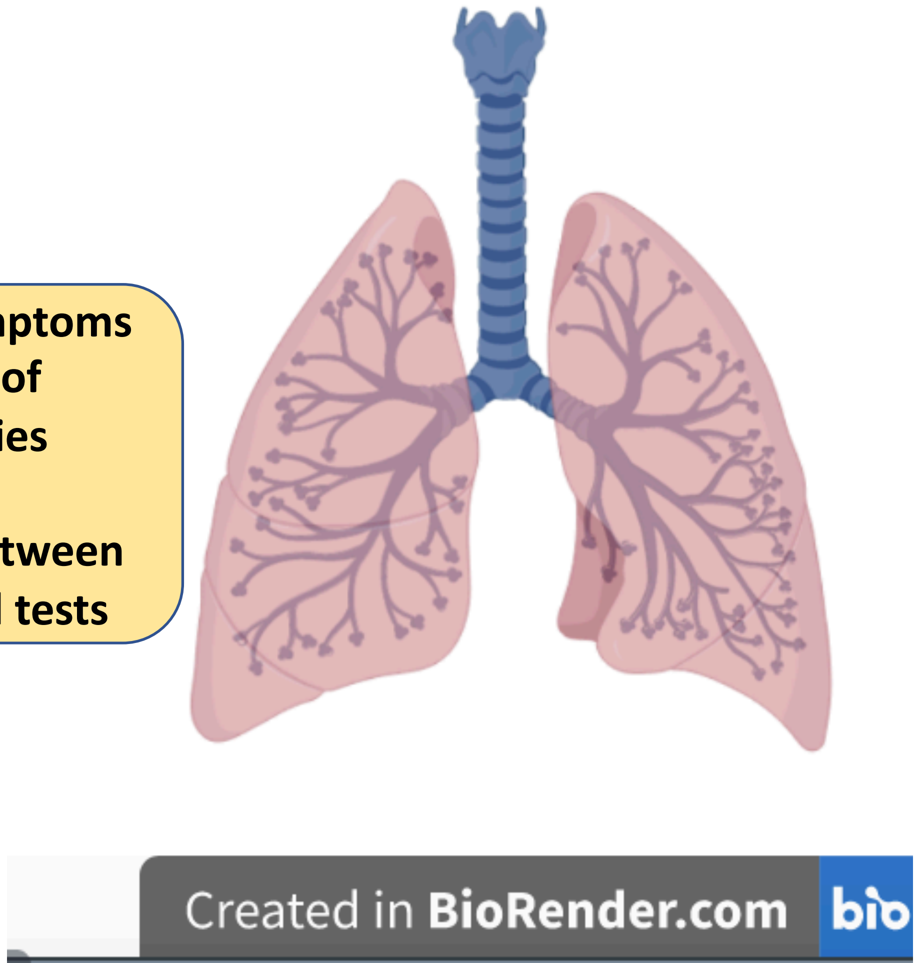
# Key take away points: UK STUDY

- Data suggests - people with asthma may have protracted symptoms due to COVID-19
- Require confirmation in further studies w/ non-asthmatic comparison.
- Persisting symptoms: it is unclear if due to long COVID vs destabilised asthma, or a combination of factors

# Long-term respiratory complications

**Respiratory symptoms in absence of abnormalities**

**Discordance between symptoms and tests**



# Dyspnea is multidimensional..

**Sensory–perceptual experience**

what breathing feels like to a person

**Affective distress**

How distressing breathing feels.

**Symptom impact or burden**

How dyspnea/breathlessness affects functional ability, employment (disability), quality of life, or health status.

# Case 1

Mr. AL

61 year old male

COVID-19 in March 2021, hospitalized never intubated,

At discharge quite weak, fatigued, anxious about his symptoms.

Post COVID he has had a very low recovery.

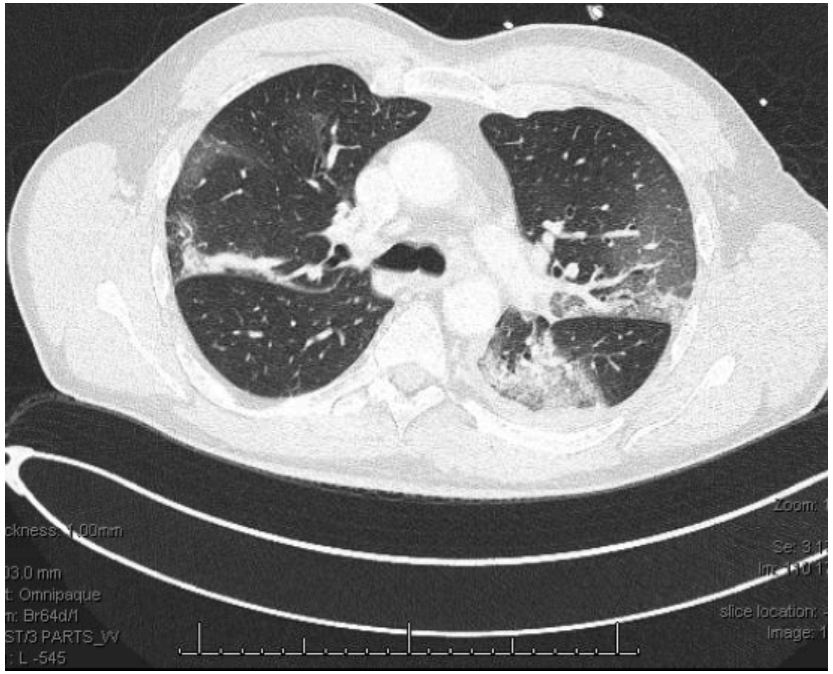
2 months post illness, he experiences fatigue, dyspnea and cough which is the most bothersome symptom.

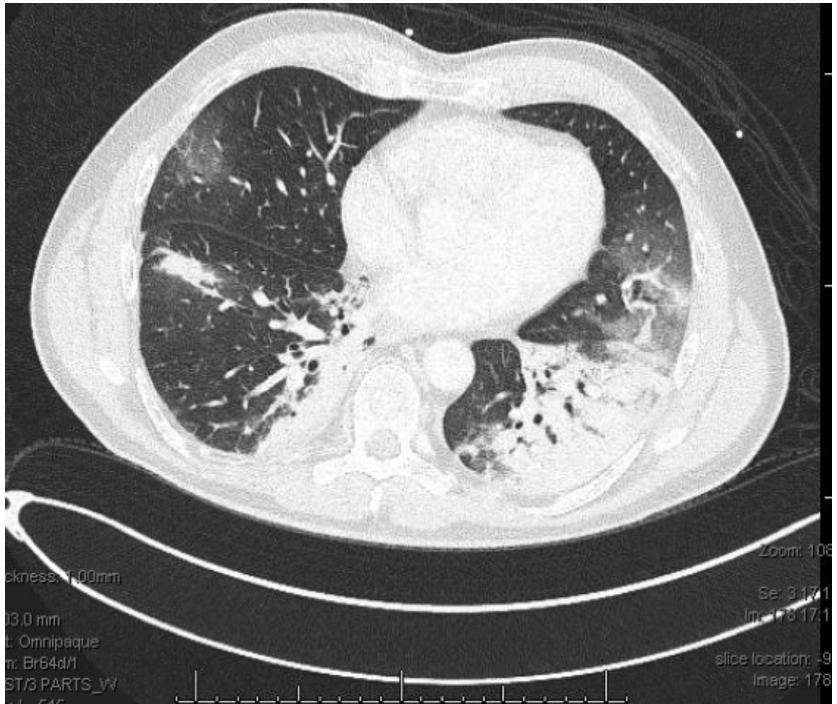
He has cough nearly on daily basis, lasting for few minutes.

# Case 1: Physiology measurements

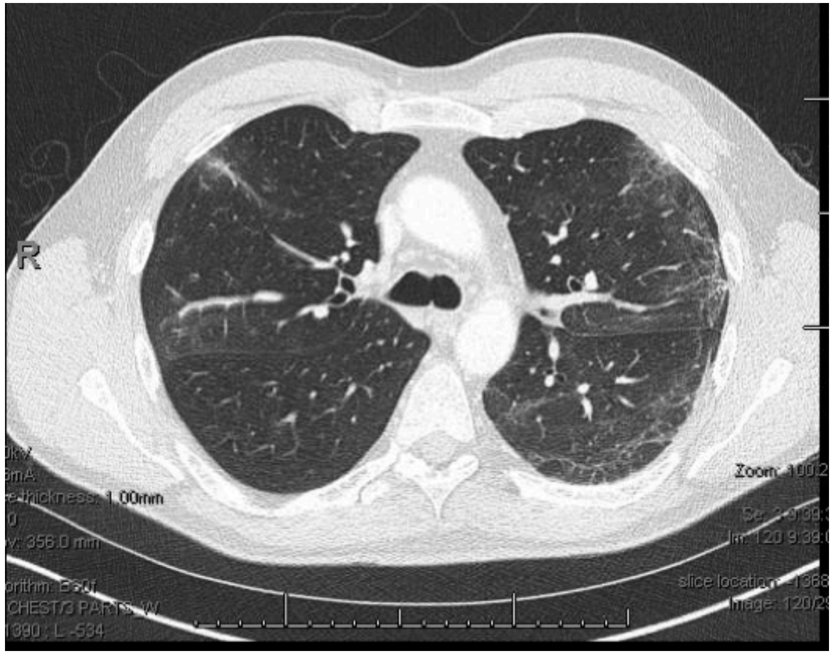
| Measurement | 6 months | 9 months | 12 months |
|---|---|---|---|
| FVC (L, % predicted) | 3.81L (94%) | 4.12L (103%) | 4.32L (106% |
| FEV1/FVC (%) | 84% | 89% | 87% |
| DLCO (% predicted) | 70% | | 75% |
| 6-MWT, distance (m) | 400m | | |
| Methacholine challenge test | | | Absence of AHR |

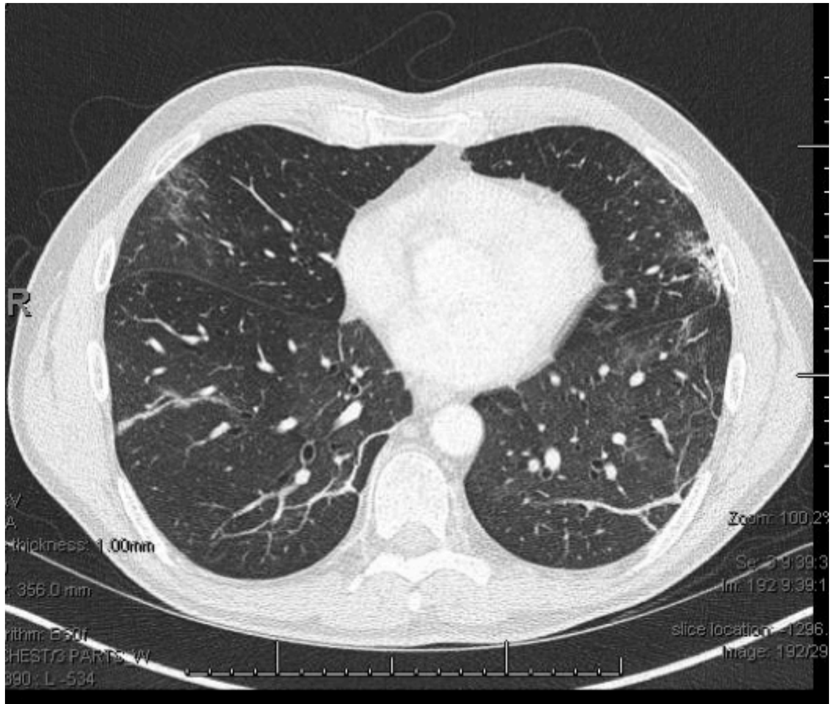
**Week 1**





**Week 10**





# Case 1 clinical course

**Therapies tried:**

- Symbicort
- Ventolin
- Pantoprazole
- Codeine syrup

Non-pharmacologic: PT, OT, pulm rehab.

Visit 1

**Main resp issues:**
Persistent coughing
Prolonged episodes of cough associated with dyspnea

Other issues:
Depression, fatigue, myalgias, generalized weakness

Visit 2

**Main resp issues:**
Cough is less frequent, 1-2 times / day.

Dyspnea with limited activity present

Visit 3

**Main resp issues:**
Cough is less frequent
Dyspnea occurs with more rigorous tasks (climbing stairs, fast pace walk)

**Improvement in clinical symptoms lags behind**
**Improvement in radiologic and physiologic measurements**

# Case 2

Mr. TL is a 55 year old

- COVID-19 in April 2021, warranting intubation, ECMO VV for 90 days, tracheostomy.
- Therapies for COVID in hospital included dexamethasone, tocilizumab, prednisone for organizing pneumonia due to COVID-19 (2 months duration).
- He was discharged to rehab facility.

# Case 2: Physiology

6 months post illness

| Spirometry<br>Reference set: GLI 2012 by Quanjer et al. | Pre Best | LLN | ULN | Ref | % Ref |
|---|---|---|---|---|---|
| FVC(L) | 2.12 | 3.7 | | 4.84 | 44 |
| FEV1(L) | 1.93 | 2.9 | | 3.78 | 51 |
| FEV1/FVC(%) | 91 | 67 | 88 | 78 | |
| FEF25-75(L/S) | 5.05 | 0.0 | | 2.91 | 174 |
| PEF(L/S) | 9.65 | 7.2 | | 9.58 | 101 |
| FIVC(L) | 2.19 | 3.7 | | 4.84 | 45 |
| F50Ex/In(%) | 321 | — | | 0.00 | — |

Normal Range - Ref. Values

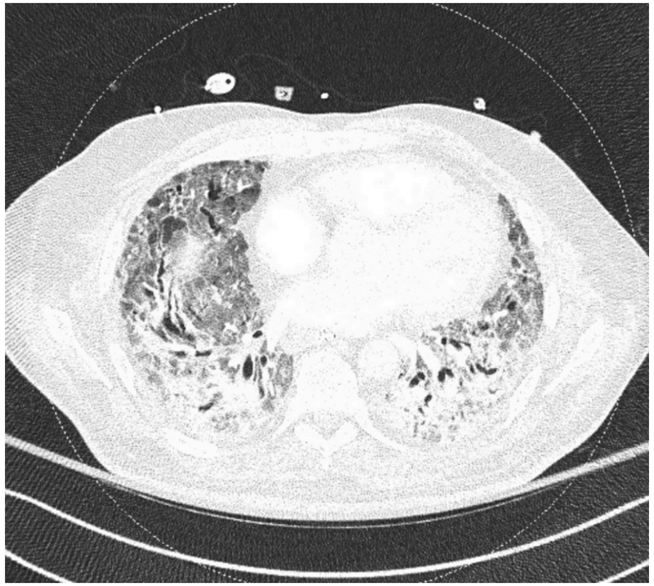
| Lung Volumes (via Pleth)<br>Reference set: Gutierrez, et al 2004 | Pre | LLN | ULN | Ref | % Ref |
|---|---|---|---|---|---|
| TLC(L) | 3.63 | 6.1 | 8.7 | 7.40 | 49 |
| VC (Pl.)(L) | 2.12 | 4.1 | 6.1 | 5.12 | 41 |
| IC (Pl.)(L) | 1.63 | 3.1 | 4.7 | 3.91 | 42 |
| FRC (Pl.)(L) | 2.00 | 2.4 | 4.7 | 3.55 | 56 |
| ERV (Pl.)(L) | 0.60 | — | — | 0.00 | — |
| RV(L) | 1.51 | 1.5 | 3.0 | 2.27 | 66 |
| RV/TLC(%) | 42 | 26 | 44 | 35 | |

| Diffusion Capacity (DLCO)<br>Reference set: GLI 2017 | Pre | LLN | ULN | Ref | % Ref |
|---|---|---|---|---|---|
| DLCO(mL/mmHg/Mi) | 9.8 | 21.6 | 36.8 | 28.6 | 34 |
| DLCO cor(mL/mmHg/Mi) | 11.2 | 21.6 | 36.8 | 28.6 | 39 |
| KCO(DLCO/L) | 3.53 | 3.3 | 5.6 | 4.36 | 81 |
| Va(L) | 2.78 | 5.3 | 7.9 | 6.60 | 42 |
| IV(L) | 2.02 | 4.1 | 6.1 | 5.12 | 40 |

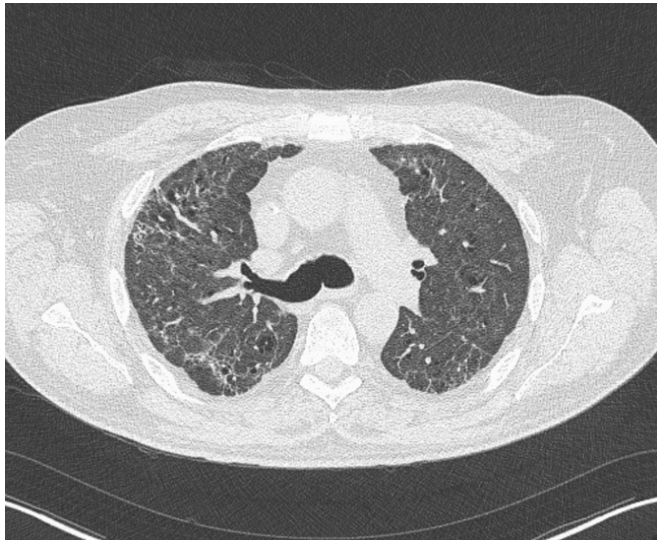
| Resistance<br>Reference set: DuBois 1959 | Pre | LLN | ULN | Ref | % Ref |
|---|---|---|---|---|---|
| RAW(cmH2O/L/S) | — | | | 1.25 | — |

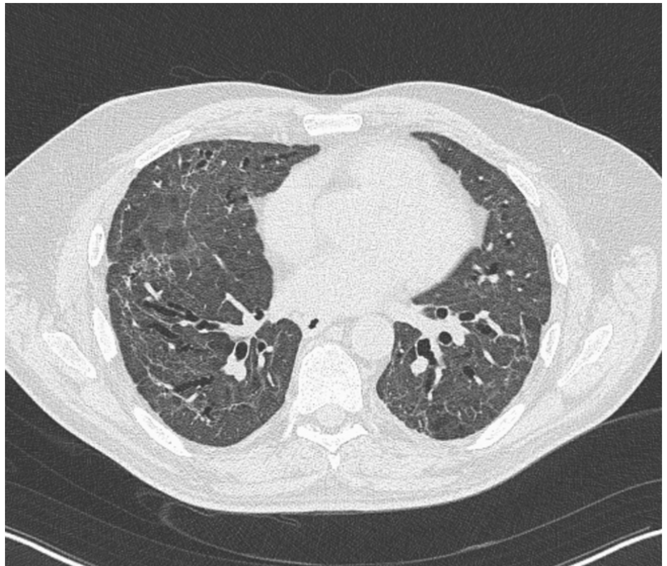
# Case 2: Radiology

Acute illness



3-months f/u





# Case 2: Clinical course

- 3 months post-illness, patient remained on oxygen supplementation 3-5LPM, able to walk few steps, limited due to dyspnea and using 4-wheel walker.
- 6 minutes walk test is 110 m

- 6 months post-illness, off O2 supp. mMRC 1.

# Dyspnea post COVID 19

**Organ damage during acute phase of illness**

- Endothelial injury and microangiopathy Leading to autonomic dysfunction
- Cardiac injury
- Treatment factors ICU related complications

**Persistent symptoms In absence of sig. organ damage**

**Mechanisms of persistent dyspnea**

1. Deconditioning
2. Hyperventilation
3. Gas exchange changes
4. Autonomic dysfunction
5. weakened respiratory muscles

Motiejunaite J. Frontiers. 2021

# In some cases respiratory symptoms present despite radiologic and physiologic improvement

Most of the data supports the hypothesis that alteration in pulmonary function does not entirely account for persistent symptoms

Motiejunaite J. Frontiers. 2021

# Dyspnea Post COVID-19

- Exercise intolerance cannot reliably investigated using resting investigations

- Physiology measurements during exercise are more informative

# Data from CPET STUDY

CHEST® JOURNAL

## Persistent Exertional Intolerance After COVID-19

**Study Overview:**

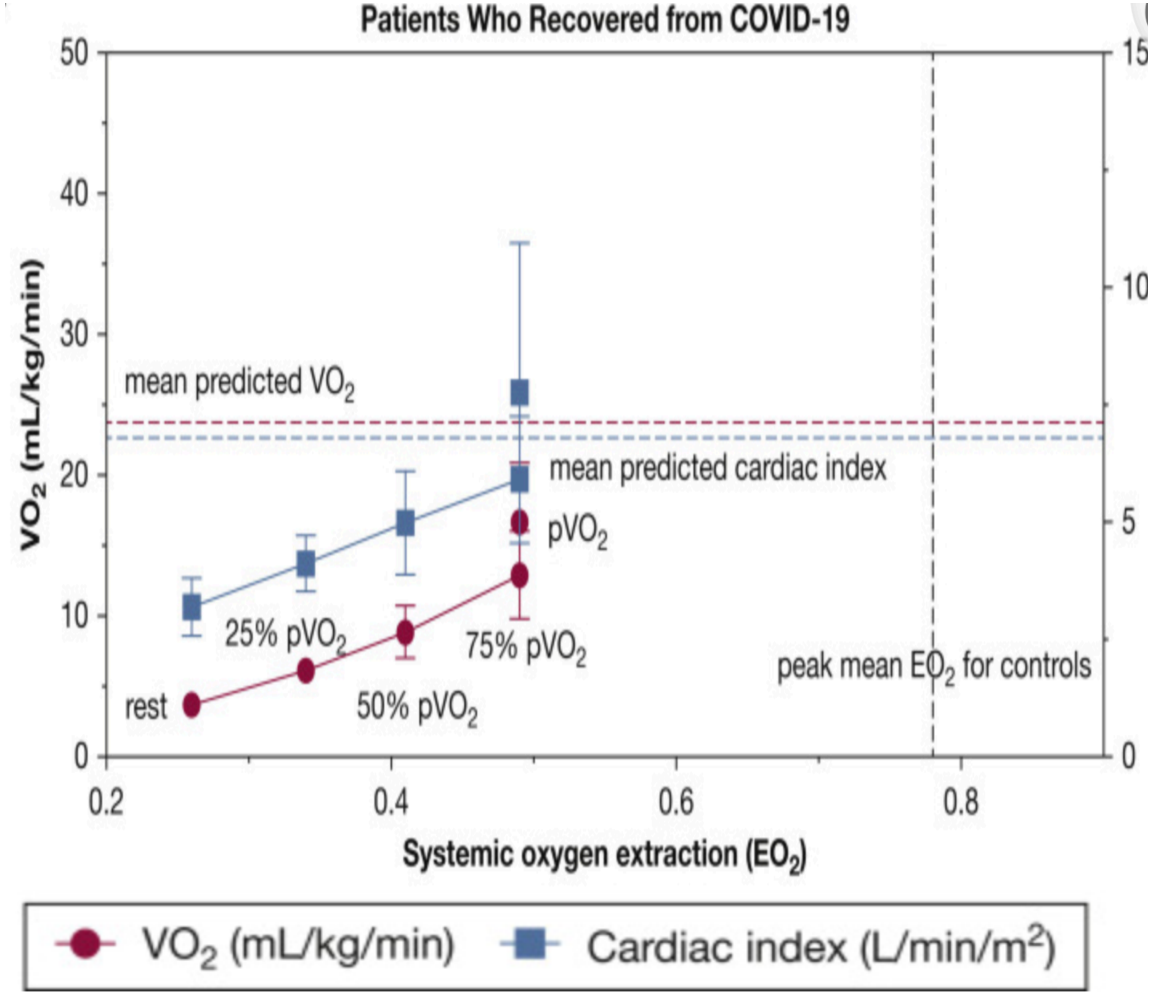
- **10 patients with normal CT scan, normal Echo.**
- **11 months post acute illness, not hospitalized.**
- invasive cardiopulmonary exercise testing for unexplained exercise intolerance after mild COVID-19.

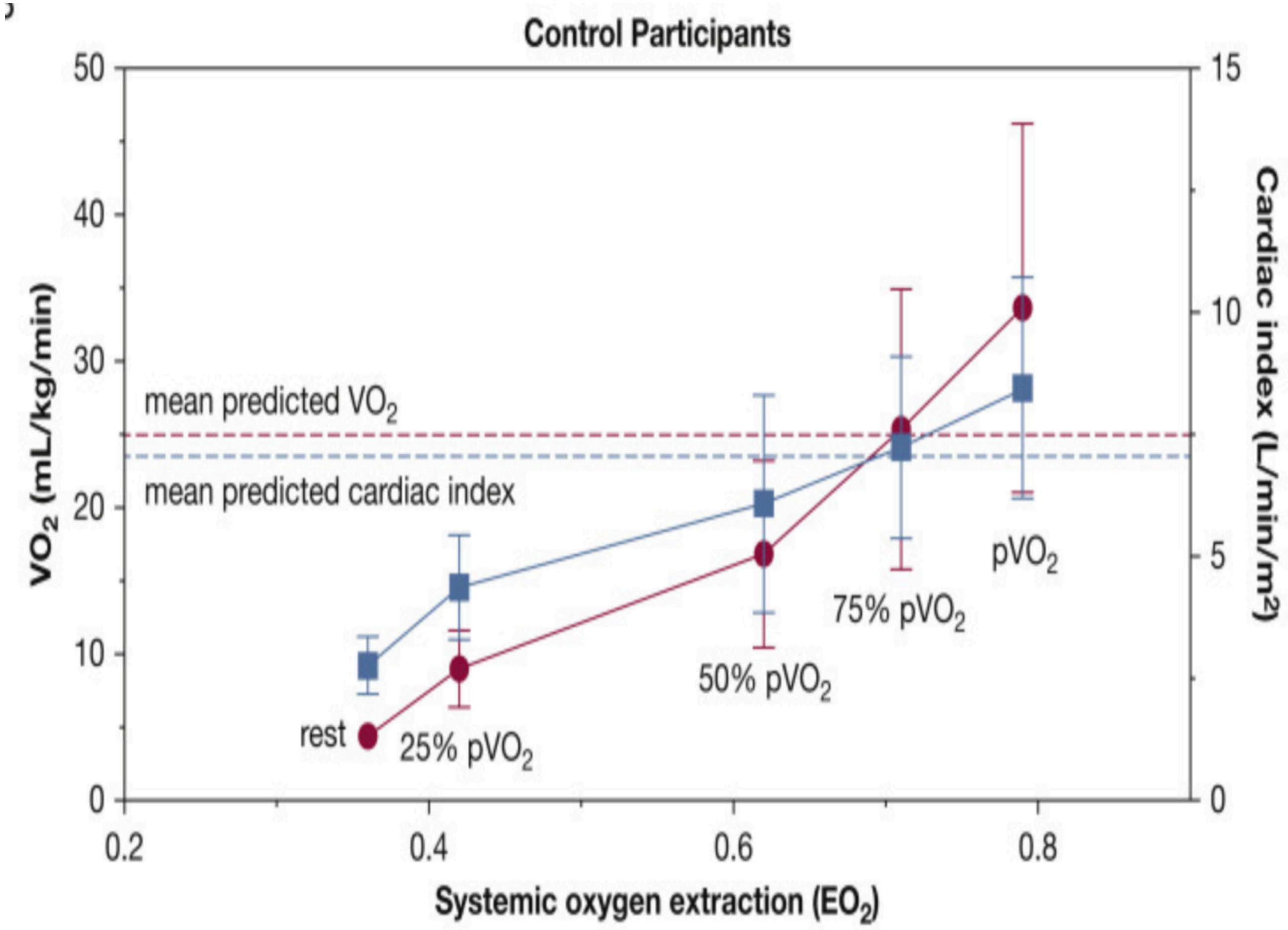
**STUDY AIM: Characterize the CAUSE OF persistent exercise intolerance among patients who have recovered from COVID-19 without evidence of cardiopulmonary disease or anemia using invasive CPET**

Inderjit. S. et al. Chest. 2022

# Data from CPET STUDIES

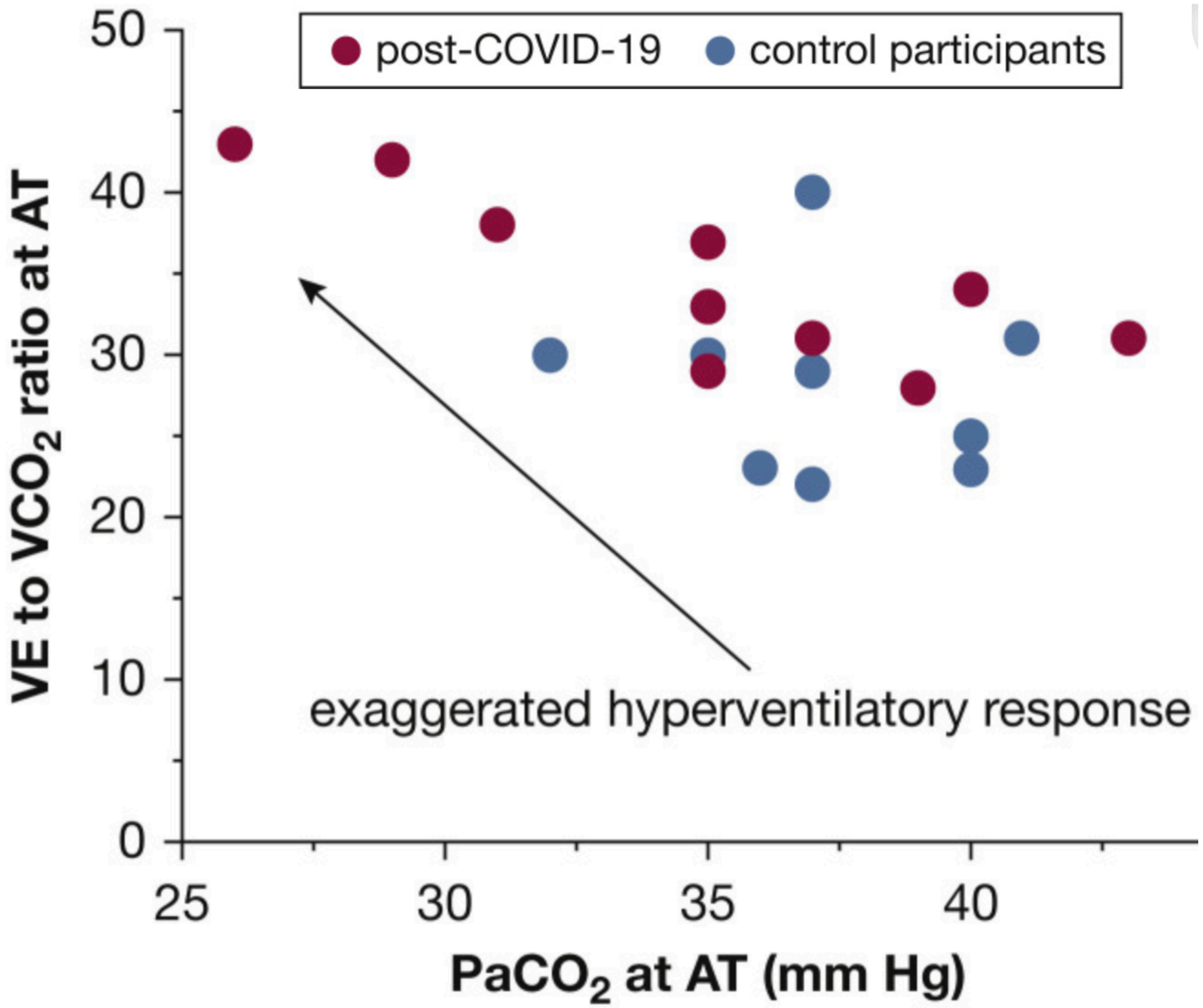
Markedly reduced aerobic capacity




Inderjit. S. et al. Chest. 2022

# Data from CPET STUDIES




Post COVID-19 → ventilatory inefficiency

- **Recovered COVID : [VE/$VCO_2$] slope: 35 ± 5**
- **Control group: VE/VCO2 slope 27 ± 5; *P* = .01)**

Inderjit. S. et al. Chest. 2022

# Data from CPET STUDIES

| | Post COVID-19 | Control | |
|---|---|---|---|
| Cardiac output, % predicted | 115 ± 44 | 123 ± 34 | .64 |
| Cardiac index, L/min/$m^2$ | 7.8 ± 3.1 | 8.4 ± 2.3 | .59 |
| Stroke volume index, mL/$m^2$ | 54.1 ± 20.8 | 63.5 ± 22.2 | .34 |

Inderjit. S. et al. Chest. 2022

# Results: Post COVID patients

***Fick's Principle***

**Reduced**

$$CO = \frac{VO_2}{C_a - C_v}$$

Normal

**Reduced**

the depressed peak $VO_{2}$--> driven primarily by reduced systemic $EO_2$

Inderjit. S. et al. Chest. 2022

# Results: Post COVID patients

***Fick's Principle***

Normal

Reduced

$$CO = \frac{VO_2}{C_a - C_v}$$

Reduced

| | Post COVID | Control | P value |
|---|---|---|---|
| **Peak $MvO_2$, %** | **50** | **22** | **<0.001** |

Depressed peak $VO_2$ → driven primarily by reduced systemic $EO_2$ → reduced oxygen diffusion in peripheral microcirculation

Inderjit. S. et al. Chest. 2022

# CPET DATA: Other studies

| | |
|---|---|
| Motiejunaite J. | 8 patients case series.<br>No previous medical history<br>**Mild COVID, normal PFTs, normal CT scan**<br>3 months post smxs.<br>CPET, ABG analsyis |

All pts:

- Dyspnea, dizziness w/ CPET

VE/VCO2 high

- 5/8 = hyperventilation

Resp alkalosis

3/8 = resp alkalosis with low PaCO2 with exertion.

Hypothesis: hyperventilation-induced hypocapnia following COVID-19 infection responsible for persistent smxs at 3 months.

# Key take away points

- Post COVID exercise limitation is due to a peripheral, rather than a central, cardiac limit to aerobic exercise
- Exaggerated hyperventilatory response during exercise

# What is missing..

- CPET data demonstrates abnormalities in Post COVID patients, providing an explanation for persistent dyspnea
- **Next steps:**
  - Larger cohort studies
  - How to apply this information to tailor rehab programs
  - Additional data can be obtained eg: Orthostatic assessment (? Preload dysfunction), breathing pattern assessment (? Hyperventilation syndrome)

# Applying concepts to clinical practice

- When should we order pulmonary investigations?
- What about lab biomarkers? E.g. D-dimer?
- What are the long-term impacts of COVID on patients with underlying pulmonary conditions:
  - Asthma
  - ILD

# Applying concepts to clinical practice

When should we order pulmonary investigations?

# How do symptoms change over time? Respiratory

HOSPITALIZED COVID-19 SURVIVORS

**3 months**

- **Dyspnea: 81% (mMRC >1)**
- **Dyspnea severity score (UCSD) – 10 (median)**
- Cough severity (cough VAS) - 30 mm (median)

**6 months**

- **Dyspnea: 30% & 26%**
- **Dyspnea severity score – 9 (median)**
- Cough severity– 24 mm (median)

**12 months**

- **Dyspnea: 5% & 30%**
- **Dyspnea severity score – 9 (median)**
- Cough severity – 15 mm (median)

**Data from prospective cohort studies**


Huang L, Lancet. et al 2021
Wu X. et al. Lancet Resp med. 2021
Shah AS. et al. Thorax. 2020
Shah AS.et al. ERJ open. 2021

# Role of diagnostic testing in Post COVID-19 assessment

## Diagnostic Testing

- **Role of diagnostic testing for assessment and monitoring**
  - **rule out serious causes**
  - There is no specific testing protocol for post COVID-19 assessment.
  - It should be directed based on symptoms.

## What is the usefulness of pulmonary testing?

Pulmonary testing is reasonable in select patients – e.g. slower than expected improvement, severe residual symptoms.

# Applying concepts to clinical practice

**What is the usefulness of pulmonary function tests?**

- Offer tests and investigations tailored to individuals’ signs and symptoms to find out if symptoms are likely to be caused by post-COVID-19 syndrome or could be a new, unrelated diagnosis.

# Applying concepts to clinical practice

What about lab tests biomarkers? E.g. D-dimer?

# Impact of persistent D-dimer elevation following recovery from COVID-19

**Antje Lehmann[1]*, Helmut Prosch[2], Sonja Zehetmayer[3], Maximilian Robert Gysan[1], Dominik Bernitzky[1], Karin Vonbank[1], Marco Idzko[1], Daniela Gompelmann[1]**

**1** Department of Medicine II, Division of Pulmonology, Medical University of Vienna, Vienna, Austria, **2** Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria, **3** Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Vienna, Austria

129 patients, enrolled 6 months after COVID-19 illness
Tests:
Lab test: D-dimer.
CTPE if elevated D-dimer.

15% with high D-dimer, median 94 days
1 patient = acute PE
1 patient = CTEPH

High D-dimer common in:
- Severe SARS-Co—2
- Hospitalized patients

Lehmann A. Plos one. 2021

## Prolonged elevation of D-dimer levels in convalescent COVID-19 patients is independent of the acute phase response

Liam Townsend[1,2] | Helen Fogarty[3,4] | Adam Dyer[5] | Ignacio Martin-Loeches[6] | Ciaran Bannan[1] | Parthiban Nadarajan[7] | Colm Bergin[1] | Cliona O'Farrelly[8,9] | Niall Conlon[10,11] | Nollaig M. Bourke[5] | Soracha E. Ward[3] | Mary Byrne[4] | Kevin Ryan[4] | Niamh O'Connell[4] | Jamie M. O'Sullivan[3] | Cliona Ni Cheallaigh[1,2] | James S. O'Donnell[3,4,12]

150 patients

4 months post acute illness: outpatient & hospitalized patients.

Elevated D-dimer:

25% patients up to 4 months post-SARS CoV- 2 infection.

More common in individuals w/ severe acute disease and in older patients.

21% were outpatients with mild illness

8 patients had CTPE – no evidence of PE.

Lehmann A. Plos one. 2021

# Applying concepts to clinical practice

**What about lab tests biomarkers? E.g. D-dimer?**

- Further adequately powered studies will be required to elucidate the mechanisms underlying elevated D-dimer levels during COVID-19 convalescence
- Need to reconsider standard VTE algorithms in this context

Lehmann A. Plos one. 2021

# Learning Objectives

- ***How to apply pulmonary rehabilitation strategies to clinical practice***
- ***How to support and improve functional status and quality of life for patients living with long term respiratory consequences of COVID-19***

# Role of Pulmonary rehabilitation in recovery Post COVID-19

- Pulmonary rehab can improve the functional status, dyspnea, and quality of life in those with chronic respiratory diseases

# Questions..

- Does pulmonary rehab help improve post COVID symptoms?
- Is virtual pulmonary rehab an option?

# Does pulmonary rehab help improve post COVID symptoms?

**Literature review:**

- 11 studies address this question
- All included hospitalized patients with persistent symptoms
- Dyspnea, fatigue most common

PR sessions: Variable
PR settings: Variable ( outpatient, inpatient, ward, virtual, tele-rehab, mixed)
PR timing after acute COVID-19: Variable, ranging from 10 days – 125 days following acute illness

# Does pulmonary rehab help improve post COVID symptoms? Randomized control trial

Respiratory rehabilitation in elderly patients with COVID-19: A randomized controlled study

Kai Liu[a,1], Weitong Zhang[b,1], Yadong Yang[c,1], Jinpeng Zhang[c,1], Yunqian Li[a], Ying Chen[d,*]

- ≥ 6 months after the onset of other acute diseases.
- 72 participants
- Measurements:
  - Full PFT
  - 6-min walk distance test
  - Quality of life assessments

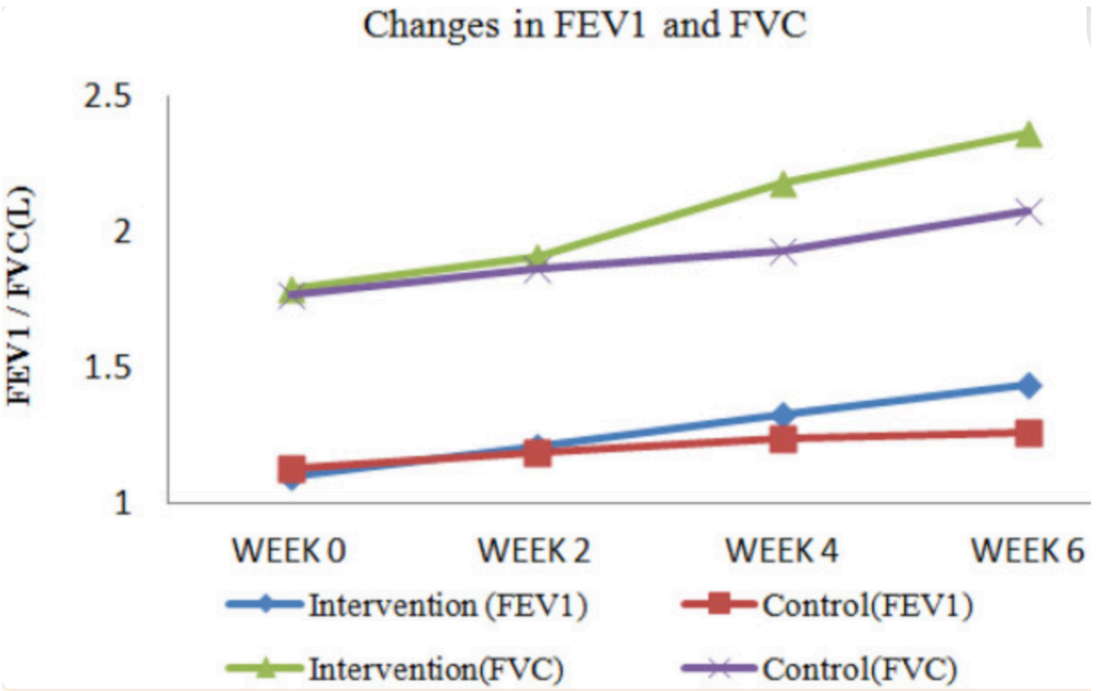
**Interventions included:**
**(1) respiratory muscle training**
**(2) cough exercise**
**(3) diaphragmatic training**
**(4) stretching exercise; and (5) home exercise.**
**pursed-lip breathing and coughing training**

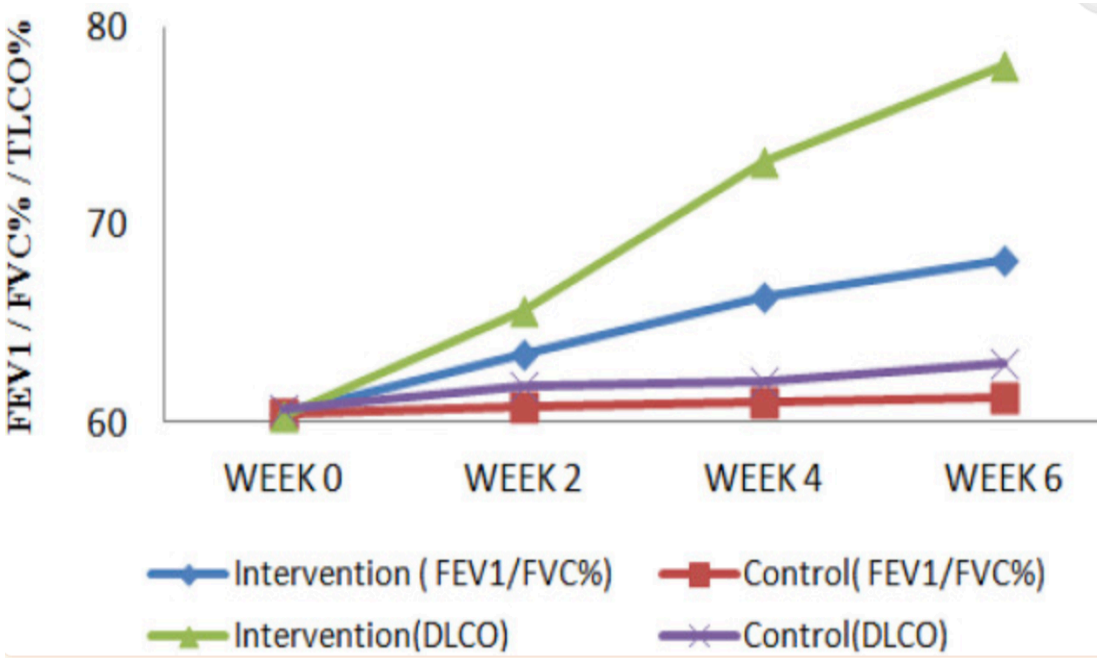
**2 sessions per week for 6 weeks)**

Liu K. Complement Ther Clin Pract. 2020

# Respiratory rehabilitation in elderly patients with COVID-19: A randomized controlled study

Kai Liu [a,1], Weitong Zhang [b,1], Yadong Yang [c,1], Jinpeng Zhang [c,1], Yunqian Li [a], Ying Chen [d,*]



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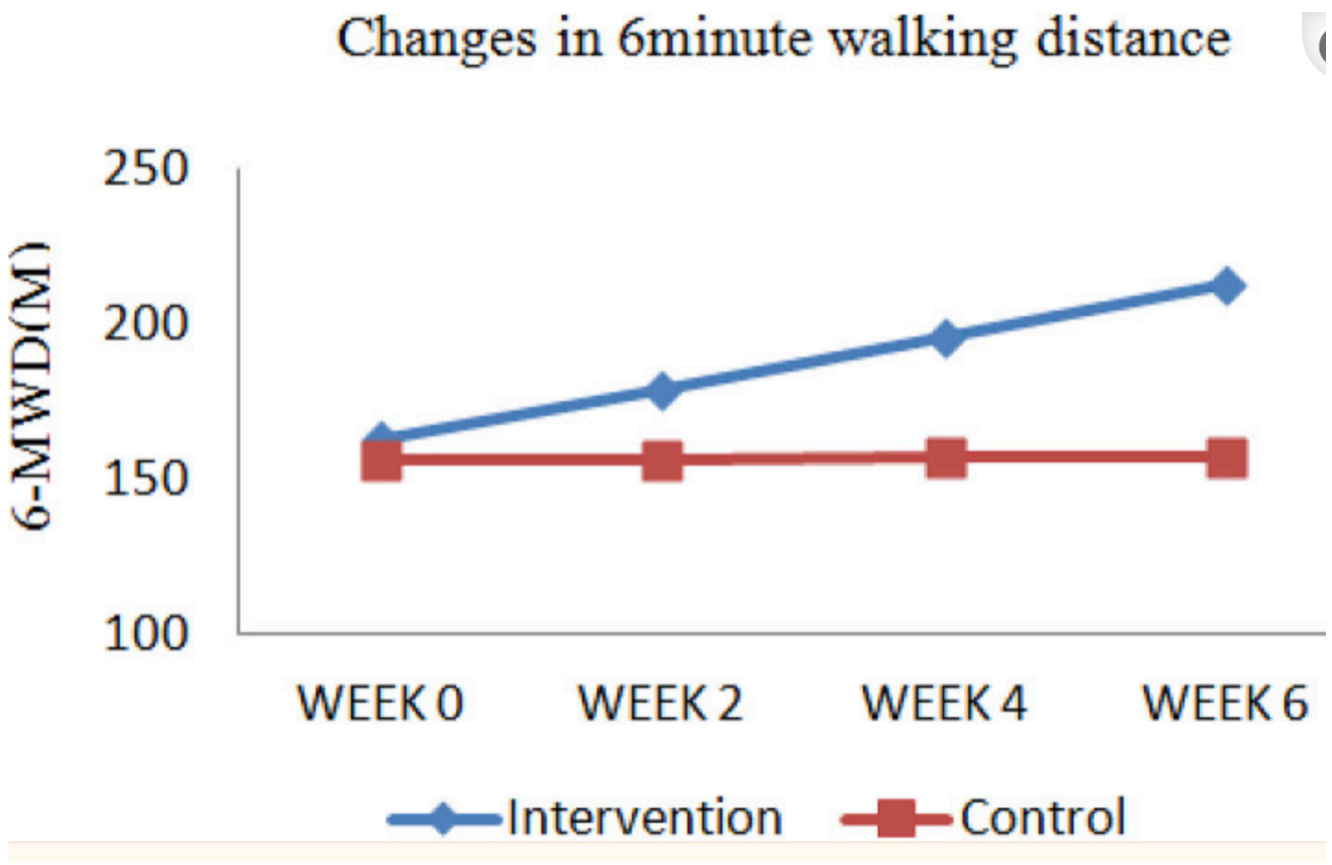


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**Summary of findings**

- Significant improvements in:

❖ Physiologic measurements

❖ Exercise endurance: 6MWD

❖ Quality of life, and self-rated anxiety compared to their baseline values and to control participants.

# Is virtual pulmonary rehab effective at improving Post COVID symptoms?

# Feasibility of tele-rehabilitation in survivors of COVID-19 pneumonia



- A pilot study
- 1 month program, 1 hour daily sessions at home, video call with physiotherapist twice a week.

**INCLUSION CRITERIA**

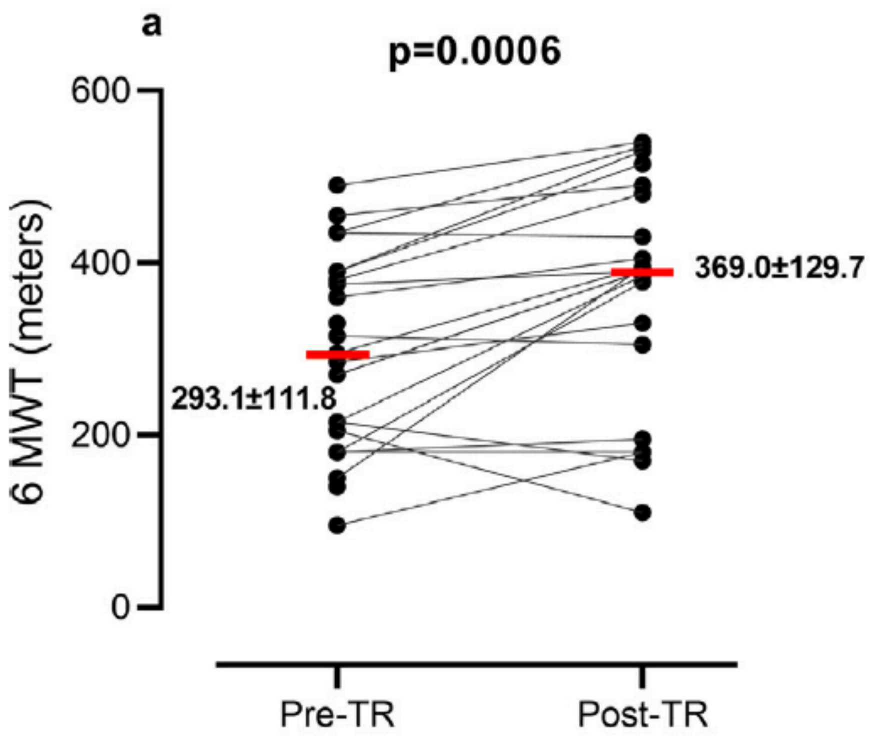
- clinically stable
- resting hypoxemia or exercise-induced desaturation
- exercise limitation (6MWT: <70% of predicted)
- home internet

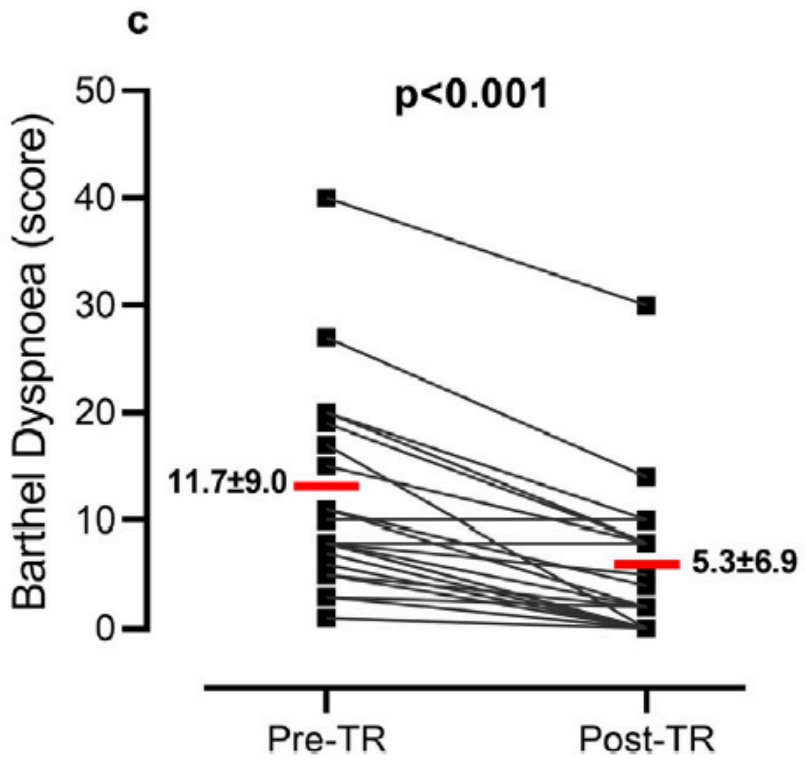
Paneroni M. Pulmonology. 2022

# Feasibility of tele-rehabilitation in survivors of COVID-19 pneumonia

Distance walked in 6MWT increased in 75.0%

Barthel dyspnoea improved in 83.3%




Exercise capacity and Barthel dyspnoea significantly improved.

Paneroni M. Pulmonology. 2022

# Pulmonary rehabilitation position statement for COVID-19: Canadian Thoracic Society (CTS)

# Pulmonary rehabilitation guidelines CTS

- 6-8 weeks after COVID-19 encourage patients to resume regular daily activities

**Patients who can be considered for PR after COVID-19**

| |
|---|
| New or ongoing respiratory symptoms (dyspnea and/or cough and/or exercise intolerance) and functional limitations (difficulty in performing daily activities) after resolution of acute COVID-19* <br><br> AND |
| New or ongoing requirement for supplemental oxygen after resolution of acute COVID-19* <br><br> OR <br><br> AT LEAST ONE OF: <br><br> • Persistent radiographic pulmonary abnormality (ie, Chest X-ray and/or CT chest demonstrating new/persistent reticular changes and/or fibrosis after resolution of acute COVID-19)* <br><br> or <br><br> • Pulmonary Function Test results demonstrating new/persistent reduction in lung volumes, airflow limitation, and/or reduction in diffusing capacity after resolution of acute COVID-19* |

Canadian Thoracic Society position statement on rehabilitation for COVID-19 and implications for pulmonary rehabilitation.
https://doi.org/10.1080/24745332.2021.1992939

# Pulmonary rehabilitation guidelines

| | |
|---|---|
| ERS/ATS | “The international task force suggests that COVID-19 survivors with **pre-existing/ongoing lung function impairment at 6–8 weeks following hospital discharg**e should receive a comprehensive pulmonary rehabilitation programme” |
| British Thoracic Society | Survivors of COVID-19 who were either managed in the community or admitted to hospital and who require rehabilitation should be referred to their local PR service **at least 6-8 weeks after recovery from COVID-19** |

# Pulmonary rehabilitation CTS: Post COVID

- Recommendations for adapting pulmonary rehabilitation for patients with post COVID-19 conditions

1. beginning at lower intensities for aerobic exercise
2. conservative progression
3. Monitor symptoms to prevent post-exertional malaise
4. Gradual introduction of strengthening exercises

Canadian Thoracic Society position statement on rehabilitation for COVID-19 and implications for pulmonary rehabilitation.
https://doi.org/10.1080/24745332.2021.1992939

# What should be considered before PR referral?

**Complications of COVID-19 that need to be considered at the time of the initial assessment**

**Acute Deep Vein Thrombosis and Pulmonary embolism**

- rehabilitation can be considered in the absence of bleeding or other complications.

**Myocarditis**

- It is recommended that PR should be delayed for at least six months in COVID-19 patients recovering from myocarditis

Canadian Thoracic Society position statement on rehabilitation for COVID-19 and implications for pulmonary rehabilitation.
https://doi.org/10.1080/24745332.2021.1992939

# Learning Objectives

- ***Locating respiratory tools and resources***

RACE

# Living with Persistent Post-COVID Symptoms

Are you a BC resident struggling with post-COVID symptoms and looking for help?

Provincial Health Services Authority

## Managing Breathlessness in Post COVID-19 Recovery

**Post COVID-19**
**Interdisciplinary Clinical Care Network**
Recovery | Care | Research | Education

It is very common for people recovering from COVID-19 to feel breathless. Breathlessness can occur for many reasons. It can make people feel scared, anxious or panicky and it may limit their activities.

The following ideas may help you feel less breathless. You might find some of them more helpful than others. Try them out and use the ones that you find most helpful:

# Post-COVID Recovery clinics

There are four PHSA Post-COVID Recovery Clinics in the province

## Eligibility criteria

Referrals are only accepted for patients who have unexplained, persistent symptoms for more than 12 weeks post-symptom onset, thought to be related to COVID-19, AND who were

- confirmed COVID positive (NAAT or serology),
- official epi-linked cases, OR
- symptomatic in January to May 2020 and did NOT have access to a COVID-19 test.

These clinics are **NOT** for cases requiring urgent care.

THE UNIVERSITY OF BRITISH COLUMBIA

# Thank you

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