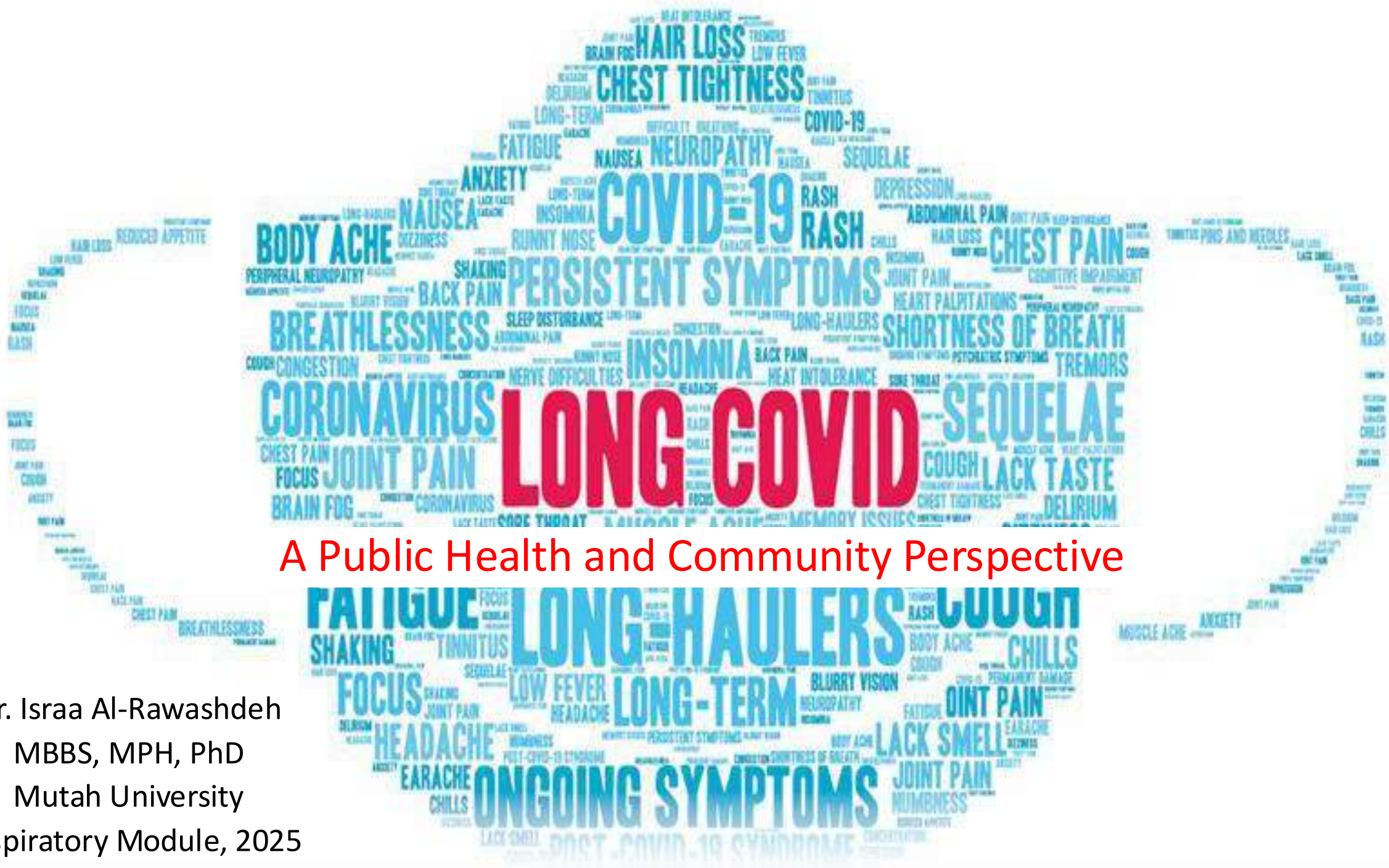

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Mutah University
Respiratory Module, 2025

Objectives:

- Define *Long COVID (Post-COVID Condition)* and describe its core clinical features.
- Summarize current evidence on its epidemiology and burden (2024–2025 data).
- Explain the biological mechanisms and risk factors proposed in recent literature.
- Discuss management and rehabilitation strategies recommended by international bodies.
- Identify public health and community implications

Introduction: Global situation

- More than 6 years into the pandemic !
- Over **704 million confirmed cases worldwide** (Worldometer, 2025).
- More than **7 million reported deaths** globally.
- WHO is currently tracking several SARS-CoV-2 variants:

- Variants of Interest: JN.1

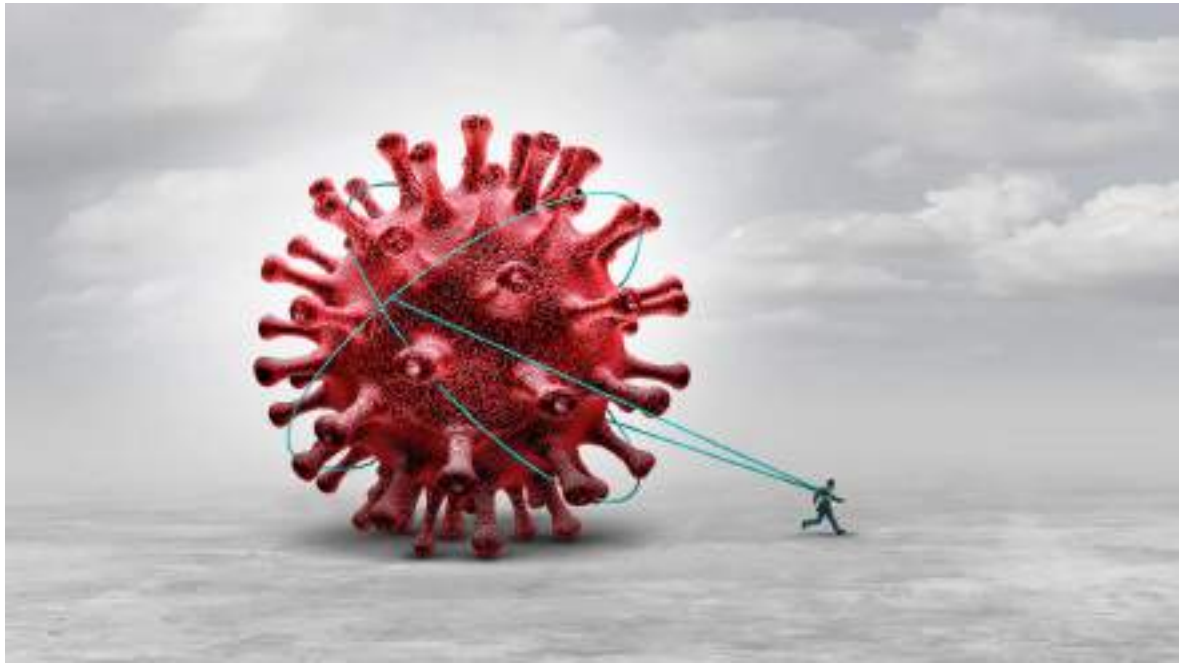
- Variants Under Monitoring: **XFG**, NB.1.8.1, LP.8.1, KP.3.1.1, and XEC

Introduction: From Pandemic to Post-Pandemic Era

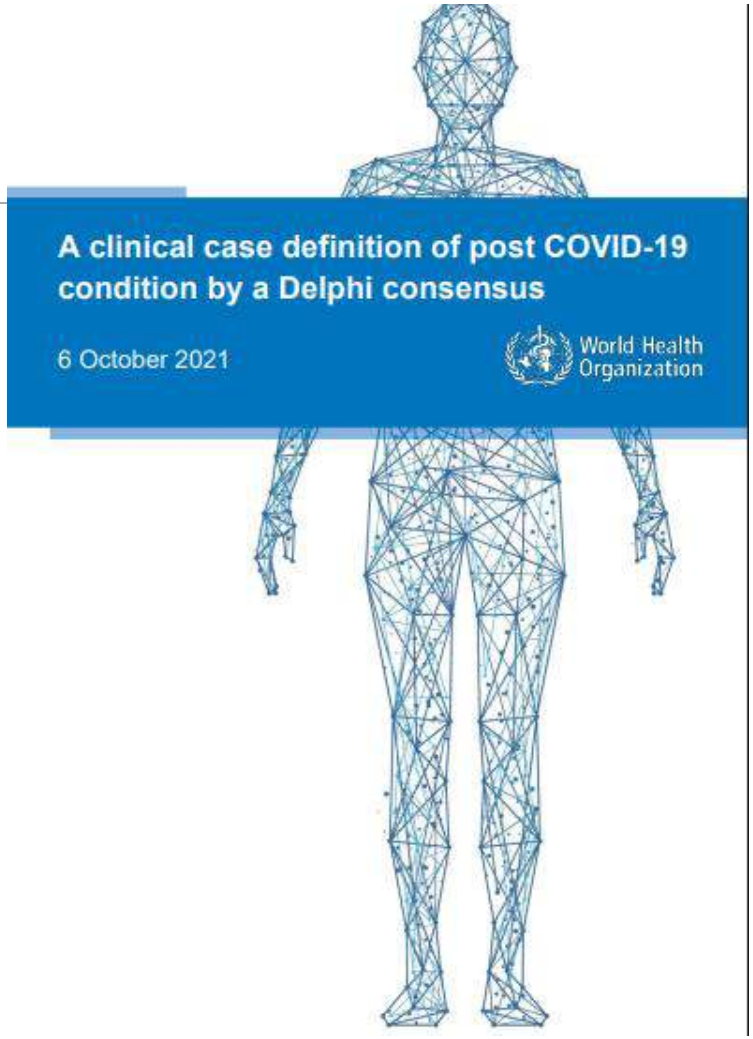
COVID-19 is no longer a global health emergency, but **its long-term impacts persist** (e.g. Long COVID or **Post-COVID Condition**).

Recognized globally as a **multisystem disorder** that extends beyond the lungs.

Long COVID is a global public health crisis. Over 400 million people worldwide have been affected by Long COVID, **with many additional cases likely undiagnosed or misclassified**.



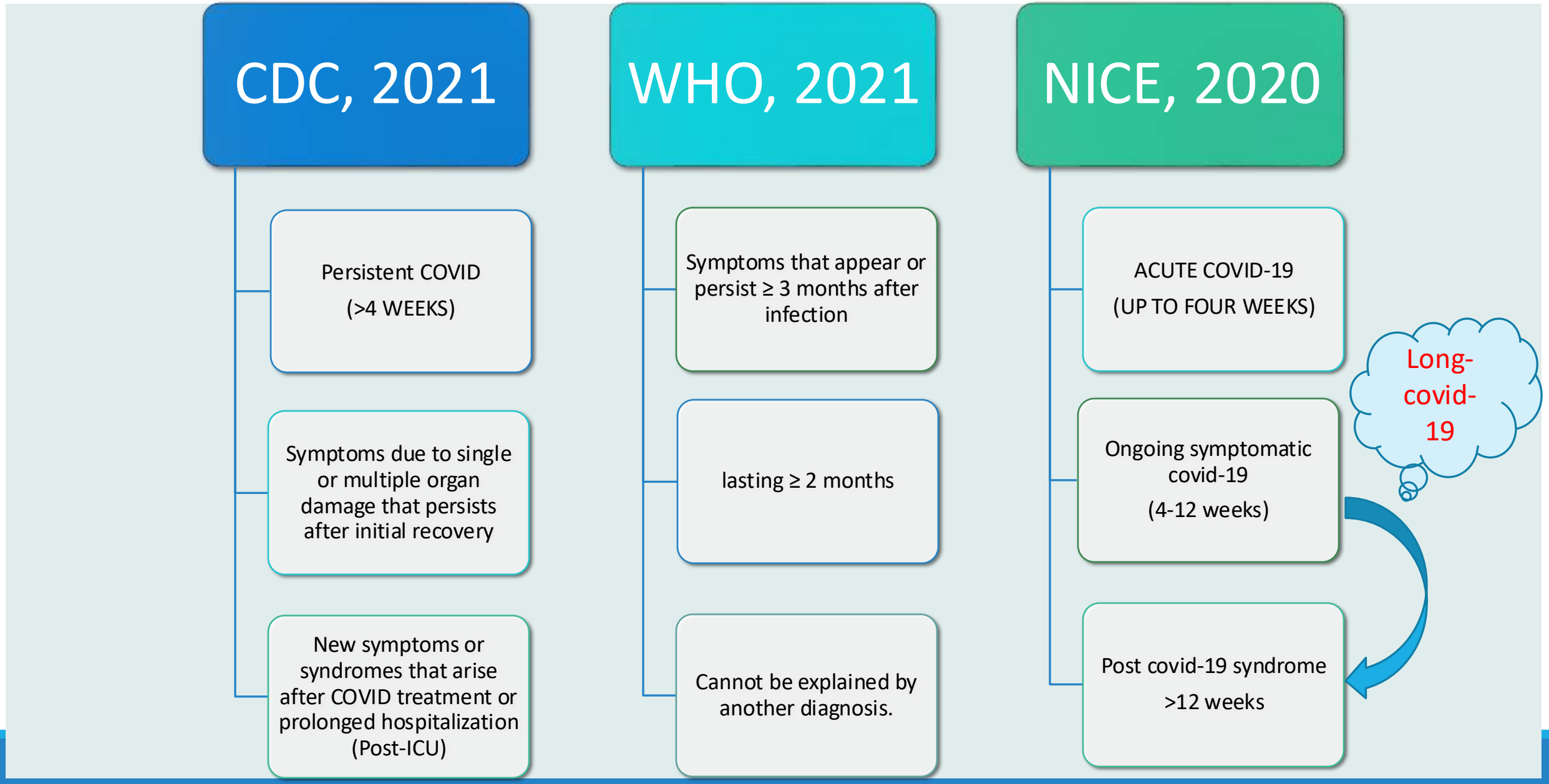
Definition & Diagnostic Criteria

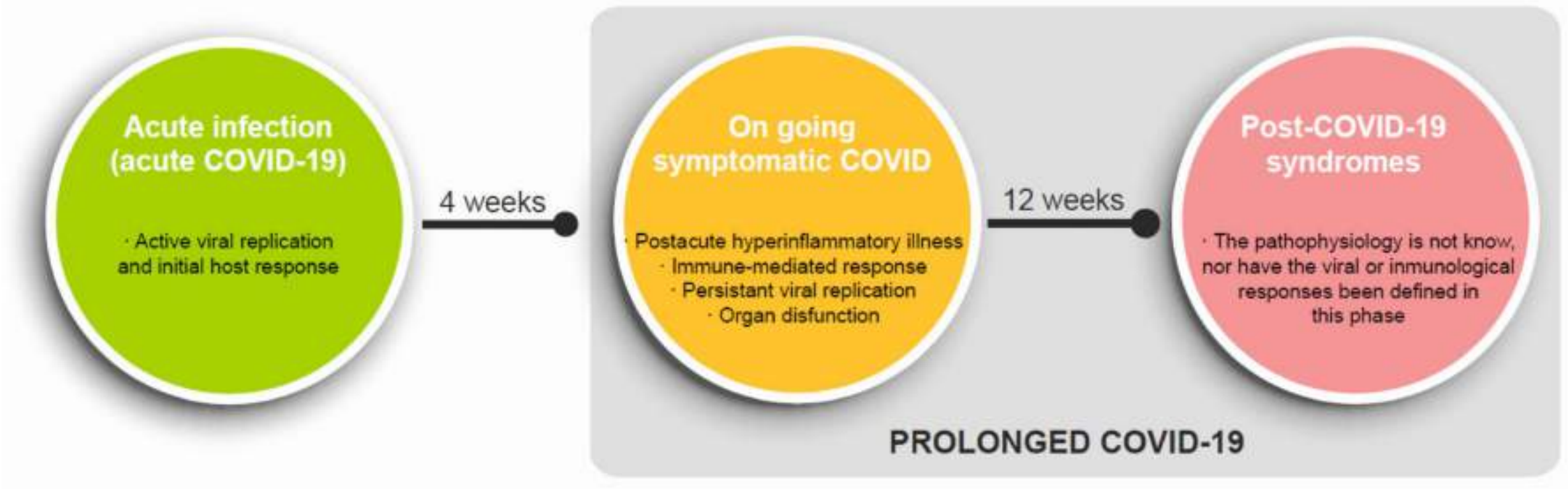


Post-COVID conditions, also known as long COVID, as an umbrella term for the long-term health consequences of a SARS-CoV-2 infection. These conditions can affect people who had a mild or asymptomatic initial infection and are present for four or more weeks after the infection.

Post COVID-19 condition occurs in individuals **with a history of probable or confirmed SARSCoV-2 infection**, **usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.** Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others* **and generally have an impact on everyday functioning.** Symptoms may be **new onset** following initial recovery from an acute COVID-19 episode **or persist** from the initial illness. Symptoms may also **fluctuate or relapse** over time.

Case definition categories:




Acute infection (acute COVID-19)
· Active viral replication and initial host response
4 weeks
On going symptomatic COVID
· Postacute hyperinflammatory illness
· Immune-mediated response
· Persistant viral replication
· Organ disfunction
12 weeks
Post-COVID-19 syndromes
· The pathophysiology is not know, nor have the viral or inmunological responses been defined in this phase
PROLONGED COVID-19

Epidemiology & Risk factors

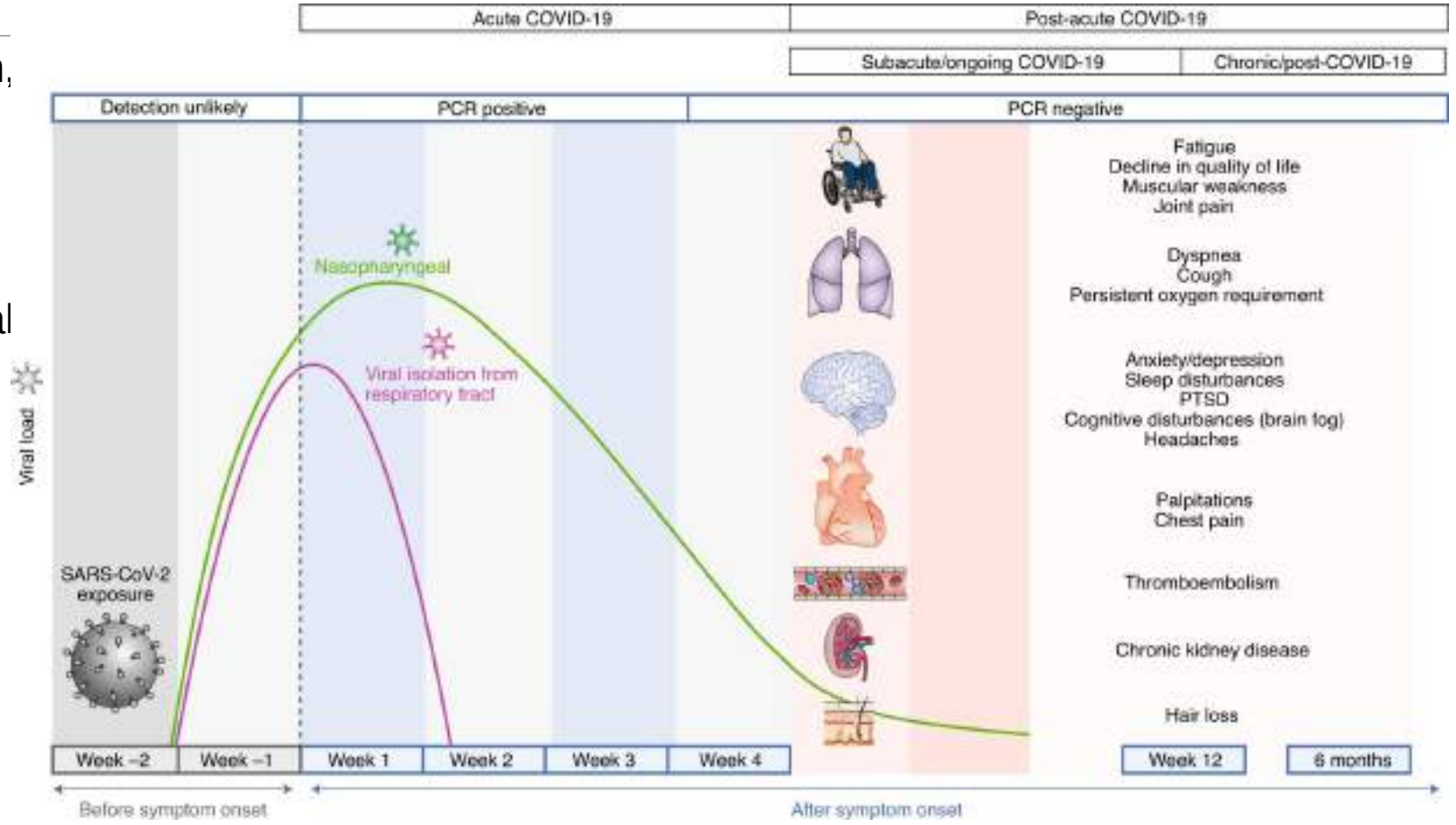
- **400 million people living with Long COVID** worldwide (Fact Sheet 2025).
- **Global prevalence** ≈ 13–16 % of all infected individuals ≥ 12 weeks post-infection.
- **Recovery from Long COVID is rare. Only 6-9% of people with Long COVID are recovered at 2-3 years**
- Regional data (EMRO / Jordan): No national surveillance yet; under-reporting expected.

Risk factors:
Female sex
Older age
Severe or hospitalized acute COVID
Reinfection: Each episode raises risk (1.7 × after two infections; 2.6 × after three)
Comorbidities (obesity, diabetes, asthma)
Smoking
Unvaccinated individuals (vaccination reduces risk by 30–50%)

Clinical Manifestations

- **Respiratory:** Dyspnea, chronic cough, chest tightness, ↓ lung capacity (> 50 %).
- **Neurological:** Brain fog, headache, poor concentration, paresthesia.
- **Cardiovascular:** Palpitations, postural tachycardia, chest pain.
- **Psychological:** Anxiety, depression, insomnia, memory deficits.
- **General:** Fatigue (~70 %), myalgia, exercise intolerance.
- **Other:** GI upset, altered smell/taste, menstrual irregularities.

- up to 25% unable to return to pre-illness work capacity.



Reference: ature Reviews Microbiology (2023); The Lancet (2024).

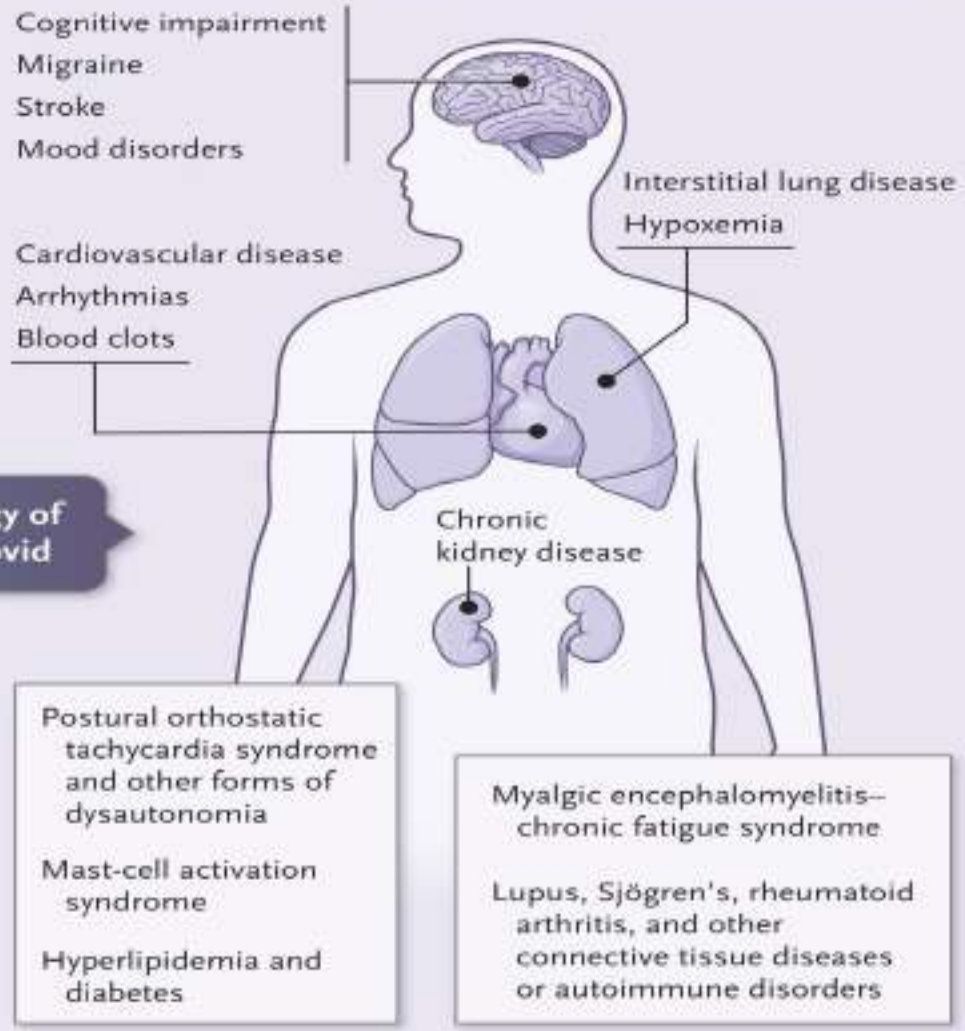
Acute SARS-CoV-2 Infection

Infection (recognized or unrecognized) may be asymptomatic, mild, or severe.

Common Symptoms
Can be mild to severe

- Postexertional malaise
- Persistent fatigue
- Difficulty concentrating
- Memory changes
- Recurring headaches
- Lightheadedness or fast heart rate
- Sleep disturbance
- Shortness of breath and cough
- Problems with taste
- Problems with smell
- Bloating, constipation, or diarrhea

Diagnosable Conditions
New or worsening of preexisting conditions



Pathology of Long Covid

- Postural orthostatic tachycardia syndrome and other forms of dysautonomia
- Mast-cell activation syndrome
- Hyperlipidemia and diabetes

- Myalgic encephalomyelitis–chronic fatigue syndrome
- Lupus, Sjögren's, rheumatoid arthritis, and other connective tissue diseases or autoimmune disorders

Important Features

Long Covid can affect children and adults, regardless of health, disability, socioeconomic status, age, sex, gender, sexual orientation, race, ethnicity, or geographical location.

Long Covid can resolve over a period of months or can persist for months or years.

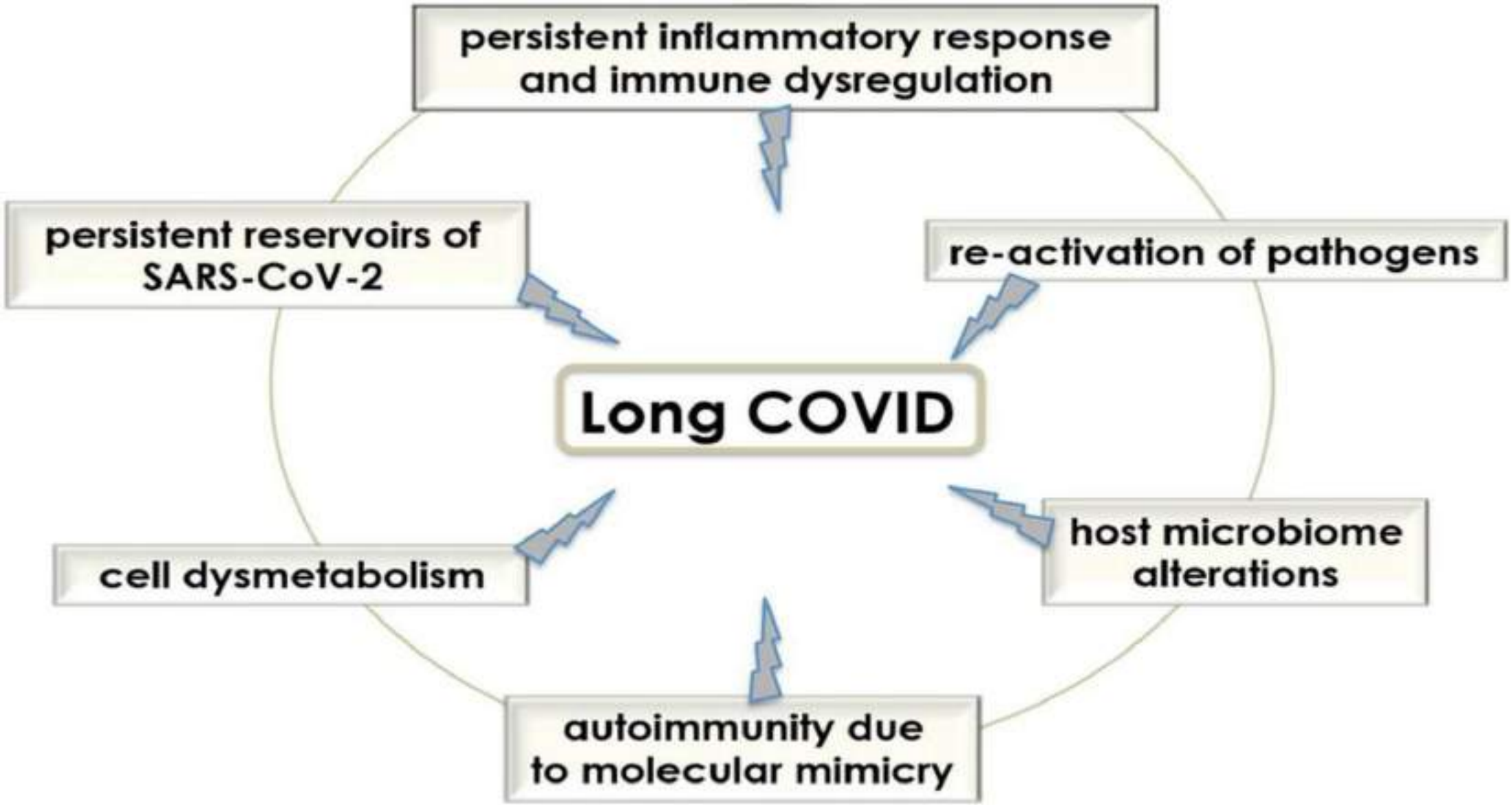
Long Covid can be diagnosed on clinical grounds. No biomarker currently available demonstrates conclusively the presence of long Covid.

Long Covid can impair affected patients' ability to work, attend school, and care for themselves and can have a profound emotional and physical effect on patients, families, and caregivers.

Long Covid is not a diagnosis of exclusion.

Diagnosable when symptoms or conditions are intermittently or continuously present for at least 3 months
Can be continuous from acute infection or delayed in onset

Source:
https://www.nejm.org/doi/full/10.1056/NEJMsb2408466


persistent inflammatory response and immune dysregulation
persistent reservoirs of SARS-CoV-2
re-activation of pathogens
Long COVID
cell dysmetabolism
host microbiome alterations
autoimmunity due to molecular mimicry

Respiratory Pathophysiology (Virology Journal 2022)

Mechanism	Respiratory Impact
Chronic low-grade inflammation	**sustained cytokine release → persistent fatigue & tissue injury and cough.**
Mast Cell Activation Syndrome (MCAS)	Overactivation of mast cells releases histamine and inflammatory mediators → airway hyperreactivity, bronchial inflammation, and chest tightness.
Immune Dysregulation:	Autoantibodies might target pulmonary tissue or vascular endothelium, leading to **ongoing inflammation or fibrosis-like changes.**
Endothelial & Microvascular Injury:	Damage to capillary networks reduces oxygen exchange and contributes to fatigue and exertional dyspnea.
Oxidative stress	Increased free radicals and mitochondrial dysfunction impair lung cell repair and resilience.
Viral Persistence / Reactivation	Remaining viral RNA or reactivation of latent viruses may sustain localized inflammation in the respiratory tract.

Reference: Cell, 2024; Frontiers in Immunology, 2023.

Associated Clinical and Laboratory Findings

Persistent respiratory symptoms were found in patients with:

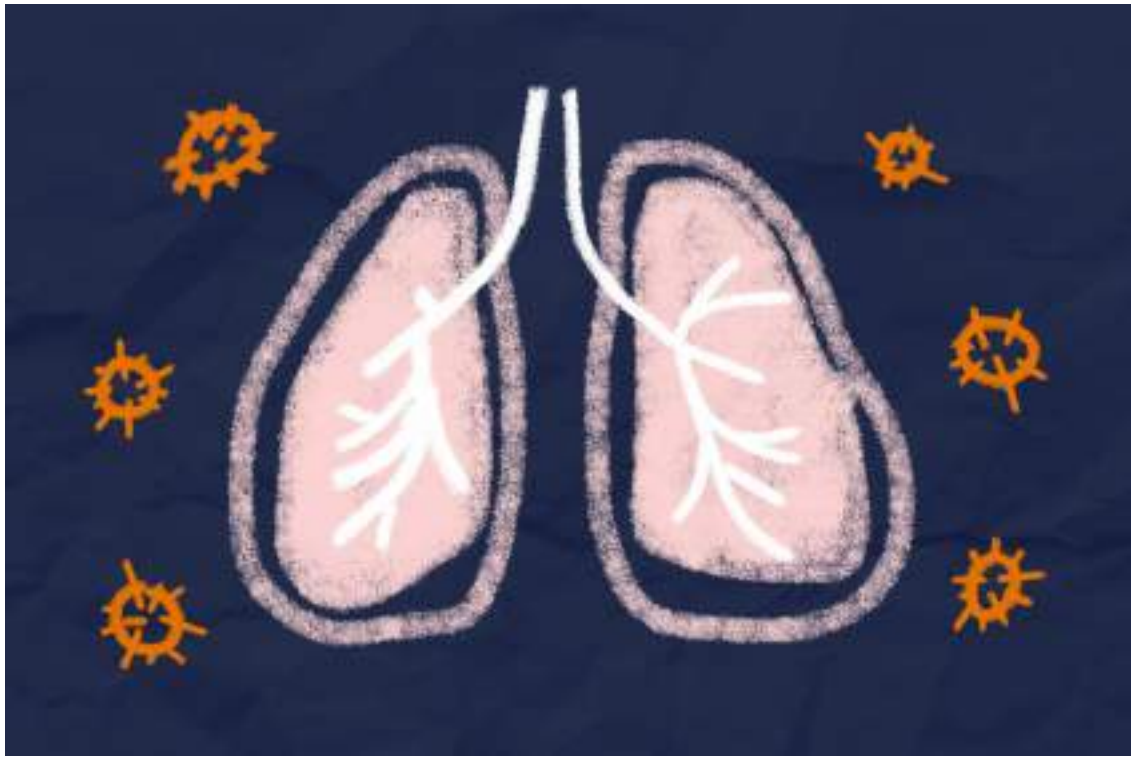
- Elevated **D-dimer** (suggesting microthrombotic activity).
- Prolonged **fatigue >10 weeks post-infection**.
- Normal imaging but abnormal **functional capacity tests**.

It is noted that **female sex** and **older age** increase the likelihood of developing post-COVID respiratory symptoms.

Lung recovery is gradual, and in some patients, function returns to near-normal within 6–12 months, while others show persistent limitations.

Pulmonary Complications in Post-COVID Syndrome

- **Radiological abnormalities** persisted in **71%** , correlated with elevated **BUN**.
- **Functional lung disorders** (e.g., reduced diffusion capacity) were present in **25%** , correlated with higher **D-dimer** levels.
- **42% of survivors** showed decreased **lung diffusion capacity (DLCO)** three months after discharge.
- **Up to 50%** continued to have **persistent pulmonary abnormalities or fibrosis** at 6 months.



Radiological and functional sequelae

Residual CT abnormalities (ground-glass opacities, fibrotic streaks) may remain up to six months post-infection.

Impaired gas exchange can occur even in patients with normal CT scans, indicating microvascular or interstitial changes.

Reduced maximal aerobic capacity was observed in recovered patients versus healthy controls, showing ongoing exercise limitation.

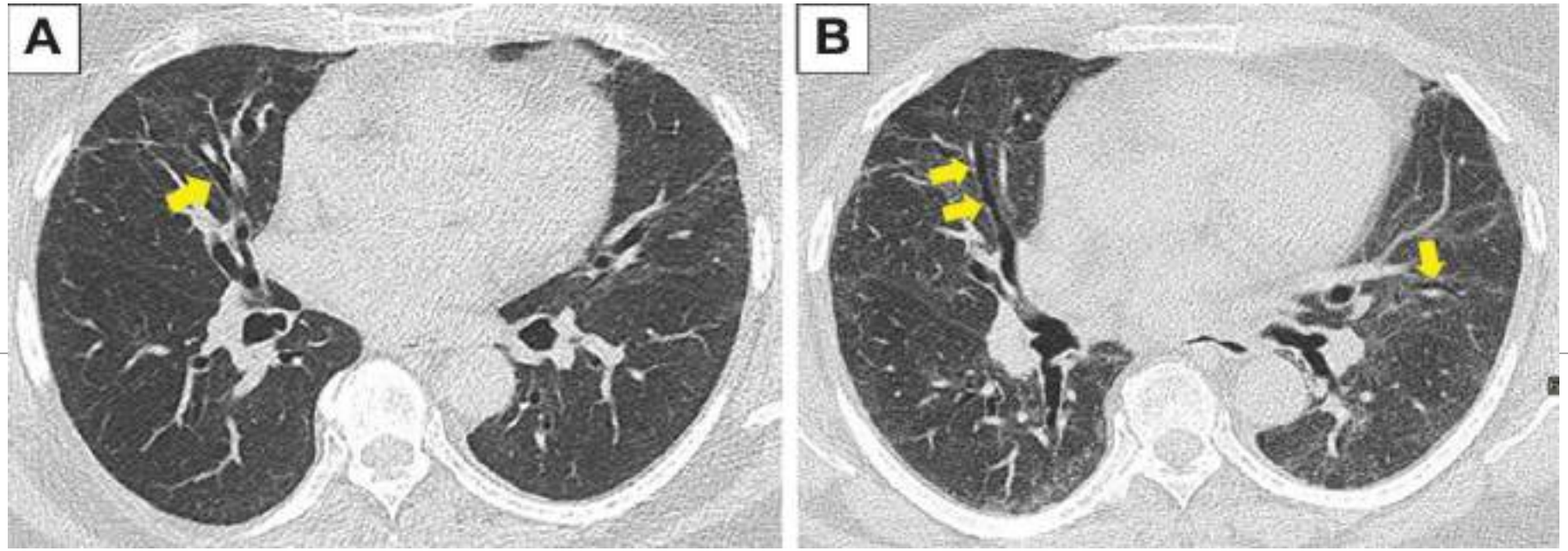


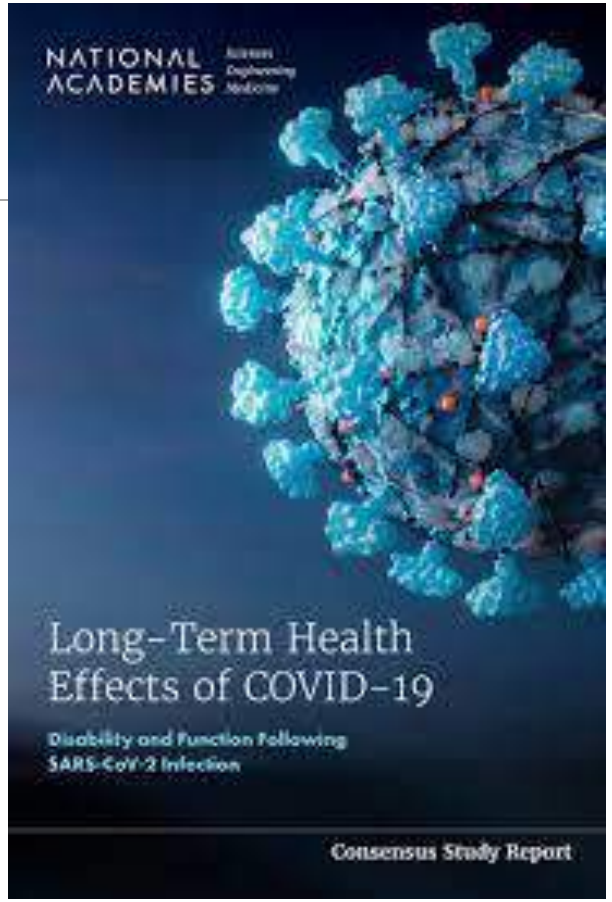
Figure 6: Paired axial unenhanced CT scans in a 59-year-old man at **(A)** 3 months and **(B)** 1 year after hospital discharge for COVID-19. Images show widespread residual bilateral ground-glass opacification, a few band opacities, and, importantly, evidence of traction bronchiectasis in the middle and left lower lobes (arrow in **A**) at 3 months. There is a reduction in the extent of ground-glass opacification and bands but with persistent traction brochiectasis (arrows in **B**) at 1-year follow-up.

Clinical Consequences

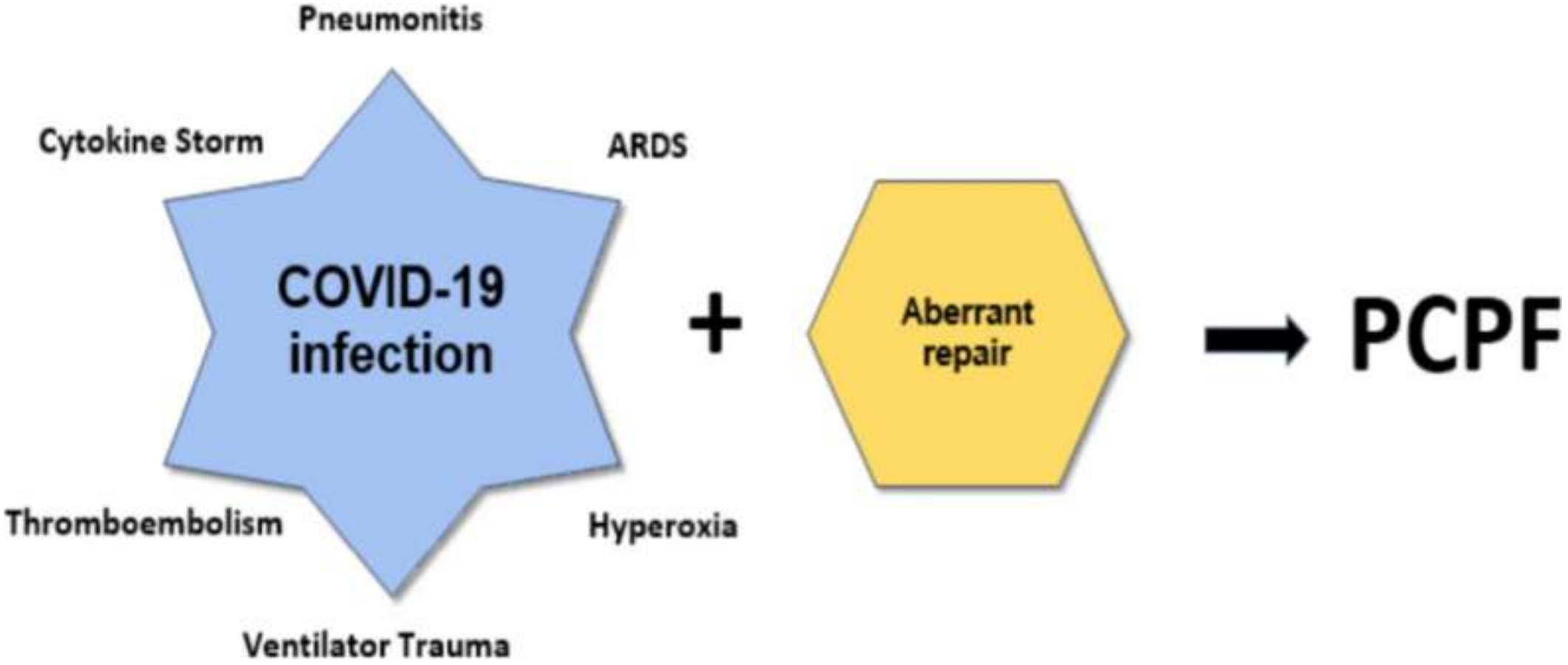
The combined effects of **cytokine storm, acute lung injury (ALI), ARDS, ventilation trauma, hypoxia, and hyperoxia** can lead to **aberrant tissue repair → post-COVID pulmonary fibrosis (PCPF)**.

Fibrosis and scarring are likely causes of **chronic cough** and **dyspnea** in Long COVID patients.

However, some patients experience persistent dyspnea **even after radiological and functional improvement**, indicating **additional mechanisms** (e.g., autonomic dysfunction, microvascular changes, or immune dysregulation).



COVID-19 and the risk of Post-COVID pulmonary fibrosis (PCPF)



Management & Rehabilitation

***No curative therapy yet* → focus on symptom control & functional recovery**.

- **Multidisciplinary care:** primary care + pulmonary rehab + mental health.

Non-pharmacologic:
- Pulmonary & physical rehabilitation programs (breathing training).
- Cognitive behavioral therapy for fatigue/anxiety and memory training for brain fog.
- Gradual pacing of physical activity (“energy management”) (not forced exercise).

Clinical follow-up:
- **Monitor for complications:** cardiac, thrombotic, respiratory.
- Referral to *Post-COVID Clinics* if available.

Community role:
- Patient education, community support improve long-term outcomes. , peer support, tele-rehab initiatives.

Reference: BMJ, 2024; Cochrane Rapid Review, 2023.

Public Health Implications

- ✓Approximately **400 million individuals worldwide** are currently affected by Long COVID.
- ✓The **global economic burden** exceeds **$1 trillion annually** (WHO & World Bank, 2025).
- ✓The overall impact is **comparable to major chronic diseases** such as diabetes and heart failure.
- ✓Significant impact on **workforce productivity**, **mental health**, and **health-care utilization**.

Reference: WHO EMRO 2024 report on Post-COVID Recovery.

Challenges:

- Chronic illness model: Requires long-term health-system adaptation.
- Lack of standardized care pathways.
- Under-diagnosis, especially in low-resource settings.
- Need for national surveillance and post-COVID registries.
- Medical provider education about Long COVID is inadequate. Only 7% of physicians are very confident diagnosing Long COVID and only 4% are very confident treating it. A majority of Long COVID patients have experienced a negative experience with a healthcare provide
- Economic burden: Lost productivity = up to 1% of national GDP.
- Equity issues: Marginalized groups have less access to rehab and psychological care

Policy priorities:

- Integrate Long COVID care into primary health services.
- Integrate Long COVID into chronic-disease registries
- Develop rehabilitation centers and community awareness campaigns.
- Development of tele-health follow-up.
- Improve structured referral pathways.

Explained: Long COVID

Q: What is **Long COVID?**

A: About 10% of individuals with COVID-19 infection will continue to have symptoms lasting more than 12 weeks.

Most common symptoms:

Fatigue, shortness of breath, pain, anxiety and depression, trouble thinking/concentrating ("brain fog")

Vaccines reduce the chance of getting infected with COVID-19 by about

85%

Vaccines reduce the chance of developing Long COVID-19 in breakthrough infections by about

50%