

# Long-Term Health Effects Stemming from COVID-19 and Implications for the Social Security Administration: A Workshop

## What is Long COVID?

Stuart Katz, MD

NYU Grossman School of Medicine

PI NYU RECOVER Clinical Science Core

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**RECOVER**

Researching COVID to Enhance Recovery

*An Initiative Funded by the National Institutes of Health*

# Conflict of Interest Statement

- I am the contact Principal Investigator for the NYU RECOVER Clinical Science Core. RECOVER is an observational study of Long COVID funded by the National Institutes of Health.
- I have no financial or other conflicts of interest to report



# Objectives: What is Long COVID?

- What are the different names for Long COVID?
- What happens to people after SARS-CoV-2 infection over time?
- How does the SARS-CoV-2 virus cause changing symptoms over time?
- How do you recognize Long COVID?
- What are the risk factors for Long COVID?
- What are we doing to learn more about Long COVID?



# What are the different names for Long COVID?

- Long COVID was initially coined and popularized by patient advocacy groups to describe long-lasting symptoms after an acute COVID-19 infection
- Post-acute sequelae of COVID-19 (PASC) was introduced by the National Institutes of Health to encompass the total health care impact of COVID-19 over time
- Post-COVID condition is now used by WHO and CDC as an alternative to PASC
- Multisystem Inflammatory Syndrome in Children (MIS-C) is a rare type of Long COVID



# WHO COVID-19: Case Definitions

Updated in Public health surveillance for COVID-19, published 16 December 2020



Case Definitions

## Suspected case of SARS-CoV-2 infection

**A** A person who meets the clinical **AND** epidemiological criteria:  
**Clinical Criteria:**

- Acute onset of fever **AND** cough; OR
- Acute onset of **ANY THREE OR MORE** of the following signs or symptoms: Fever, cough, general weakness/fatigue<sup>1</sup>, headache, myalgia, sore throat, coryza, dyspnoea, anorexia/nausea/vomiting<sup>1</sup>, diarrhoea, altered mental status.

**AND**

**Epidemiological Criteria:**

- Residing or working in an **area with high risk of transmission of virus**: closed residential settings, humanitarian settings such as camp and camp-like settings for displaced persons; anytime within the 14 days prior to symptom onset; or
- Residing or travel to an **area with community transmission** anytime within the 14 days prior to symptom onset; or
- Working in **any health care setting**, including within health facilities or within the community; any time within the 14 days prior of symptom onset.

**B** A patient with **severe acute respiratory illness**:  
(SARI: acute respiratory infection with history of fever or measured fever of  $\geq 38^{\circ}\text{C}$ ; and cough; with onset within the last 10 days; and requires hospitalization).

## Probable case of SARS-CoV-2 infection

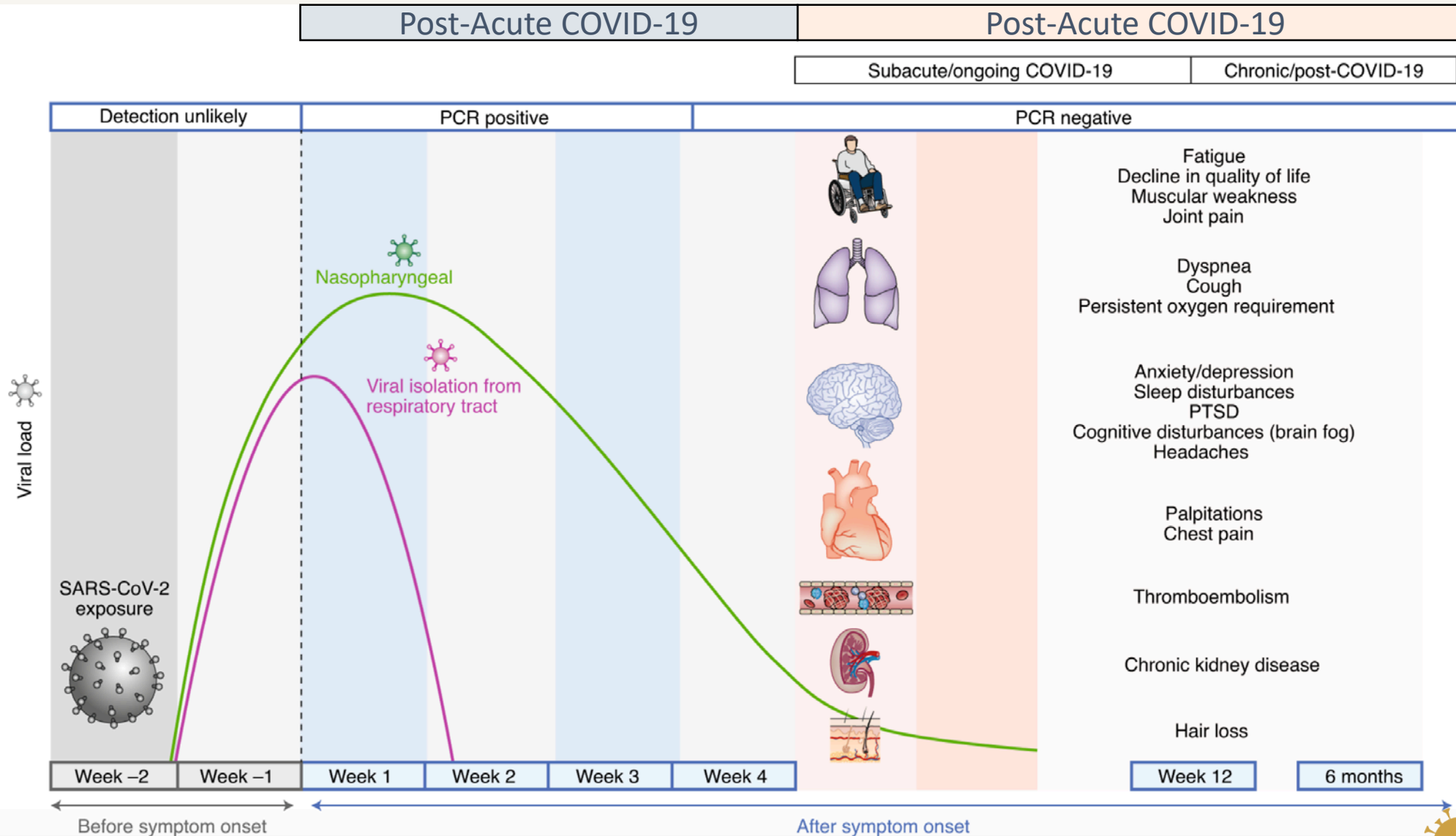
- A** A patient who meets **clinical criteria** above **AND** is a **contact of a probable or confirmed case**, or linked to a **COVID-19 cluster**<sup>3</sup>
- B** A **suspect case with chest imaging** showing findings suggestive of COVID-19 disease<sup>4</sup>
- C** A person with recent onset of **anosmia** (loss of smell) or **ageusia** (loss of taste) in the absence of any other identified cause.
- D** **Death**, not otherwise explained, in an adult with **respiratory distress** preceding death **AND was a contact of a probable or confirmed case** or linked to a **COVID-19 cluster**<sup>3</sup>

## Confirmed case of SARS-CoV-2 infection

- A** A person with a positive **Nucleic Acid Amplification Test (NAAT)**
- B** A person with a **positive SARS-CoV-2 Antigen-RDT** **AND** meeting either the **probable case definition** or suspect criteria **A OR B**
- C** An **asymptomatic person with a positive SARS-CoV-2 Antigen-RDT** who is a **contact of a probable or confirmed case**

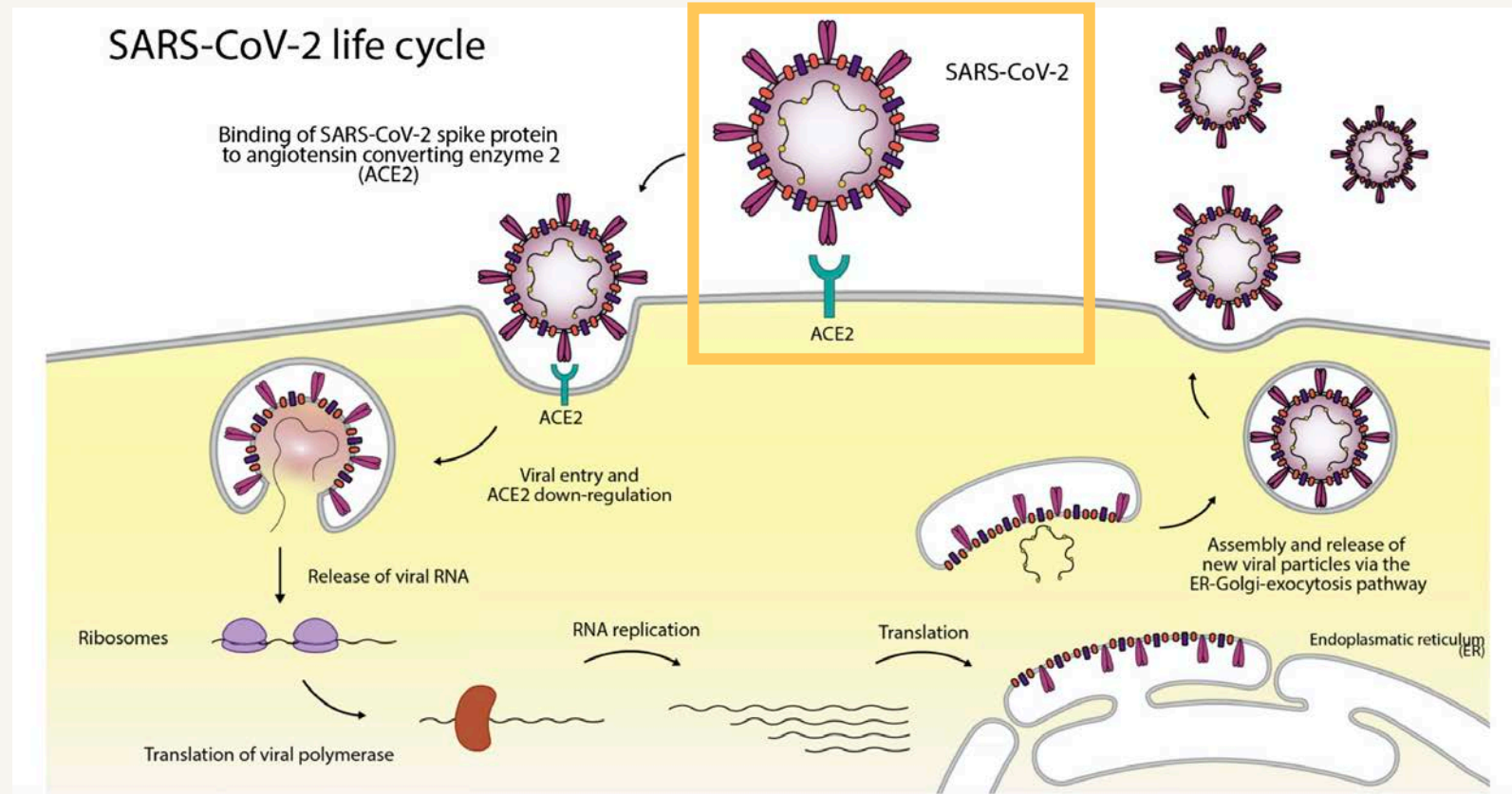
<sup>3</sup> A group of symptomatic individuals linked by time, geographic location and common exposures, containing at least **one NAAT-confirmed** case or at least **two** epidemiologically linked, symptomatic (meeting clinical criteria of Suspect case definition A or B) persons with **positive Ag-RDTs** (based on  $\geq 97\%$  specificity of test and desired  $>99.9\%$  probability of at least one positive result being a true positive)

# Natural history of SARS-CoV-2 Infection





# SARS-CoV-2 Life Cycle in Acute COVID-19

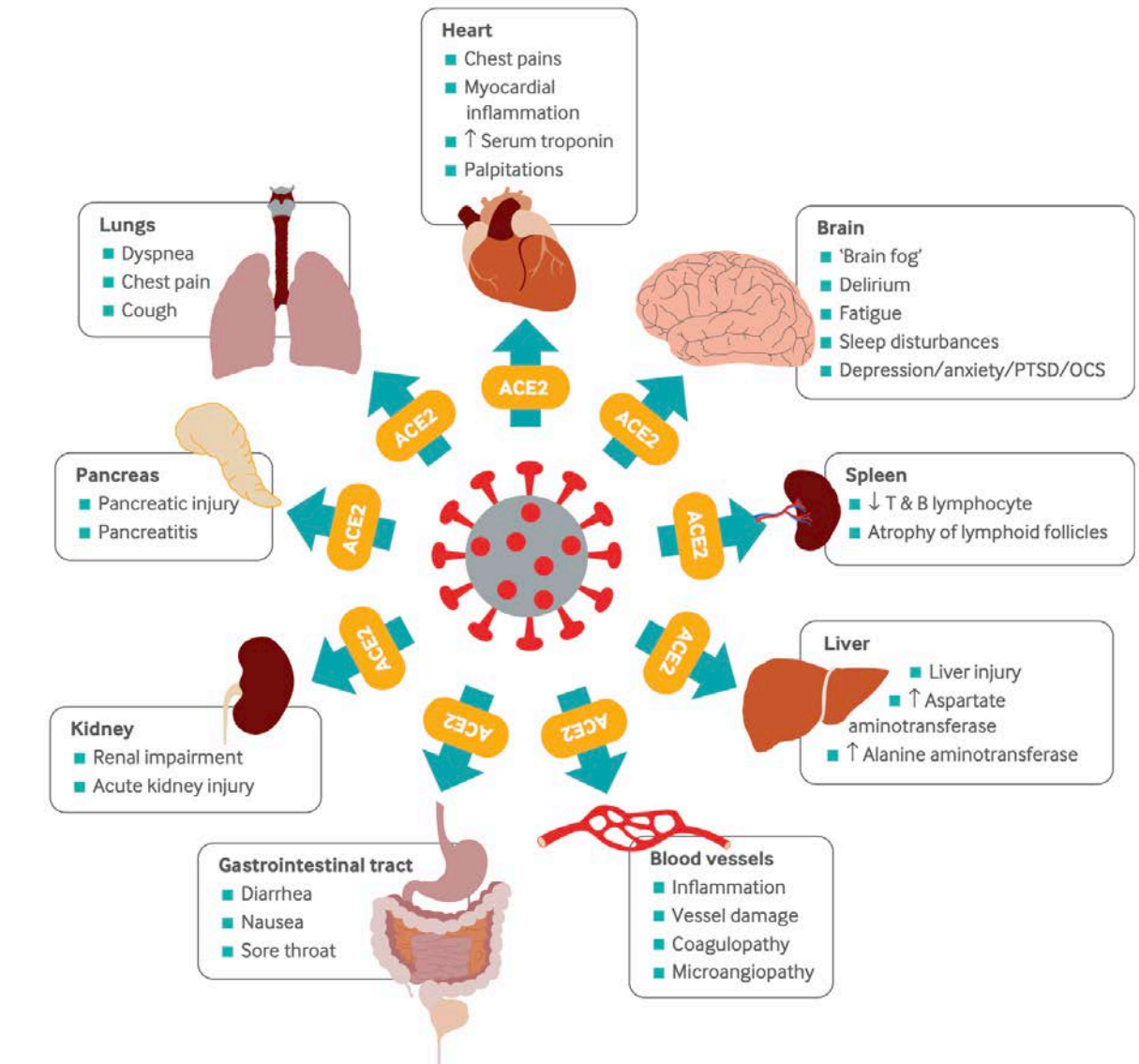


<https://doi.org/10.1007/s10096-020-04138-6>



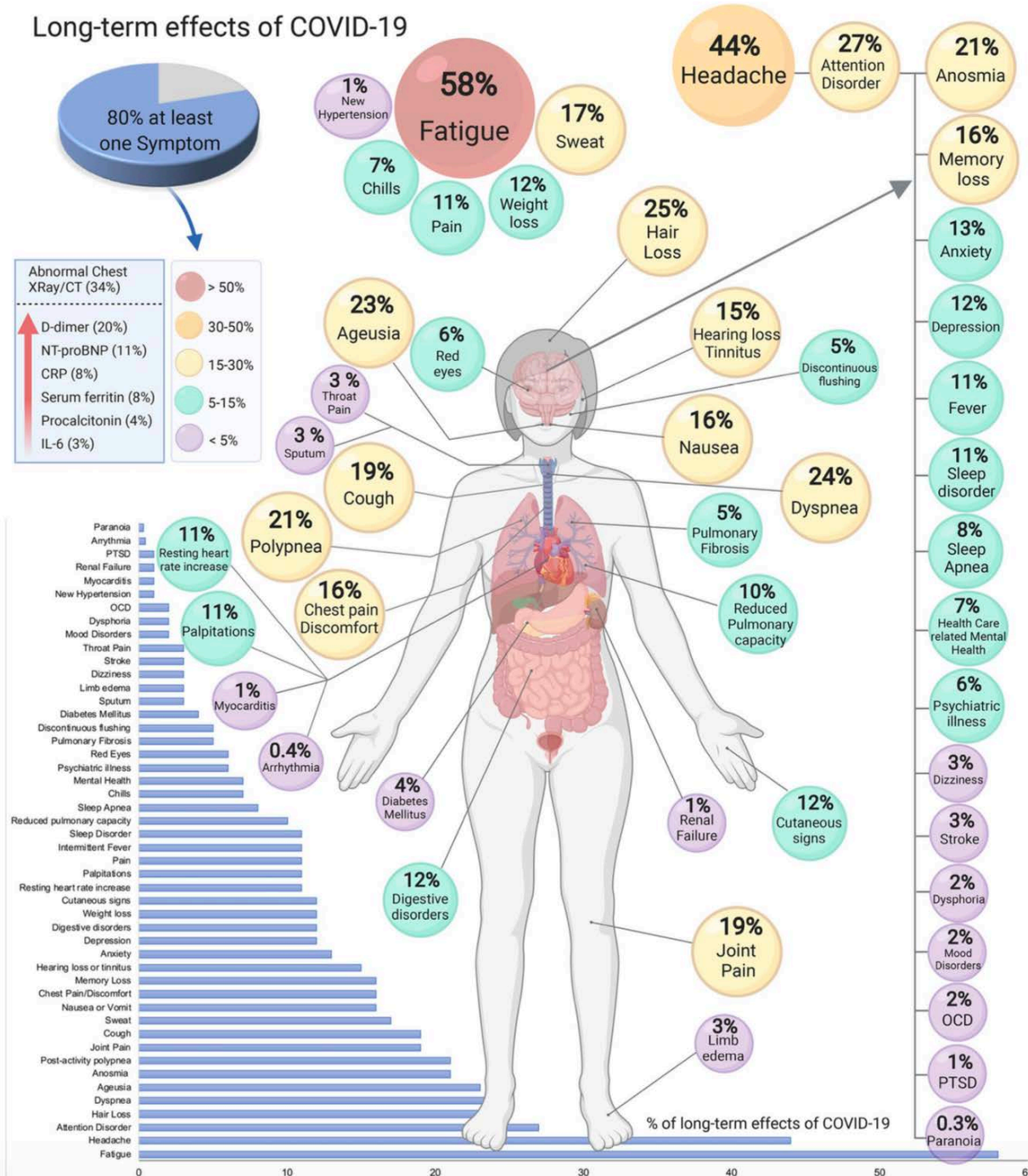
# SARS-CoV-2 Infection: Multi- organ Involvement

- ACE2 receptor is present on multiple cells types
- Widespread viral cell entry and replication
- Multiple organ involvement associated with diverse symptoms and organ dysfunction





## Long-term effects of COVID-19



# What are the most common Post-COVID Symptoms?

## Key Take Away Points

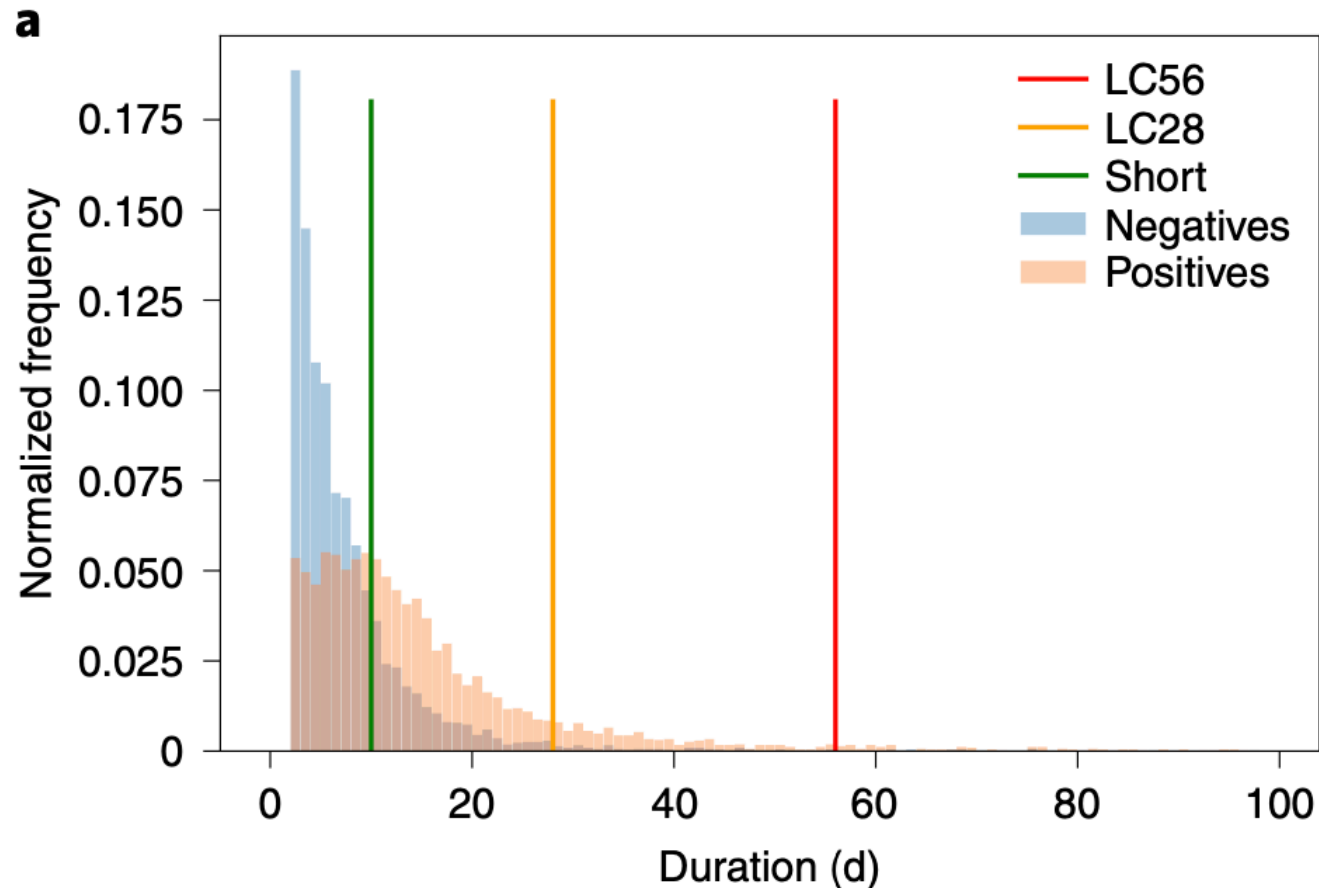
- Potential involvement of virtually all organ systems has been reported
- Many of the reports lack appropriate controls and are subject to bias
- US prevalence of PASC symptoms estimated to be 30%

Nature Scientific Reports (2021)

11:16144<https://doi.org/10.1038/s41598-021-95565-8>

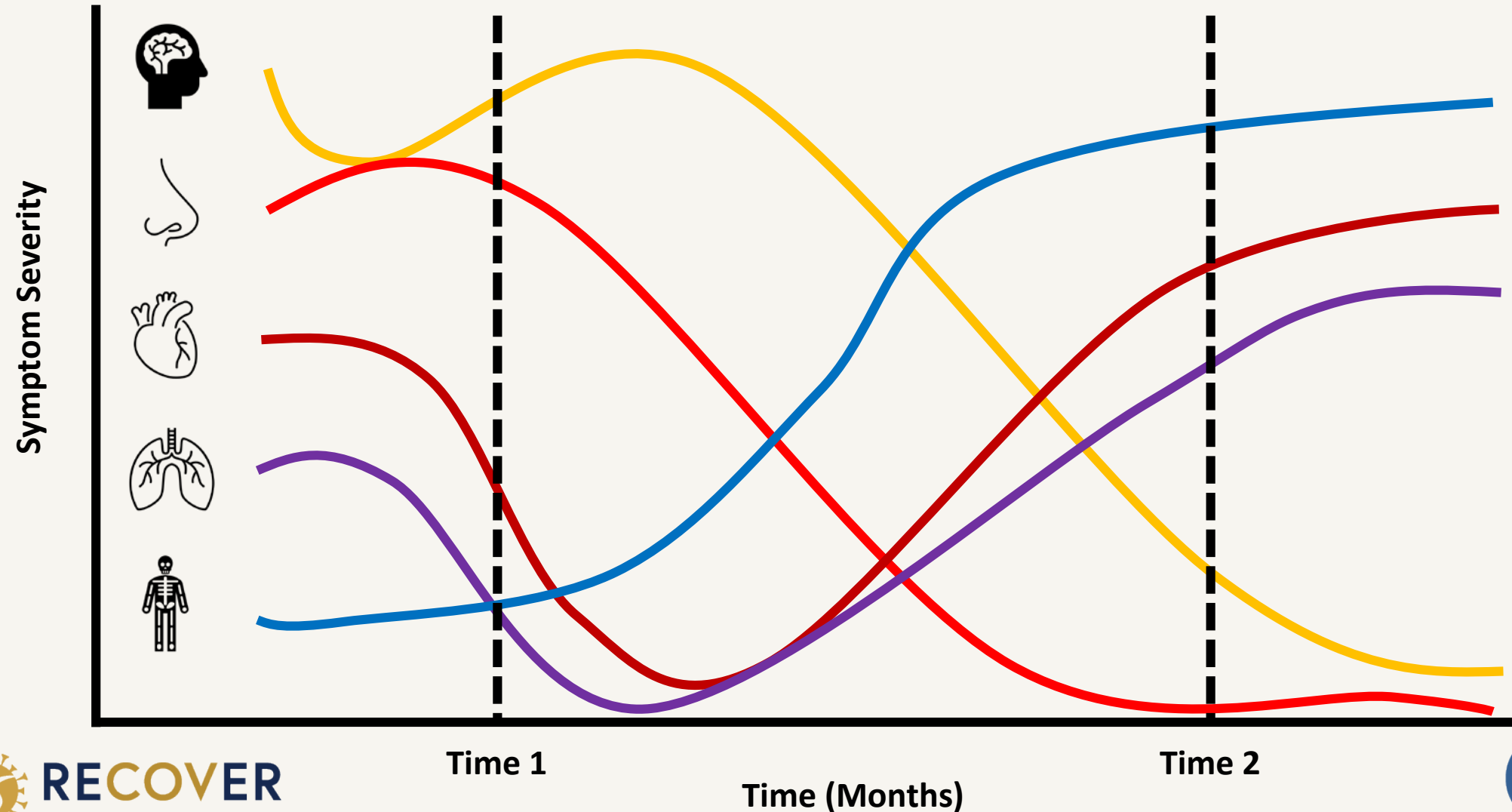
Preprint: <https://doi.org/10.1101/2021.11.15.21266377>

# How long do Post-COVID symptoms last?



- 4,182 users of the COVID Symptom Study App and matched controls from UK, US, and Sweden
- Recruited March-September 2020
- Controls
  - Median Duration 5 days
  - 2.4%  $\geq 28$  days
- Cases
  - Median Duration 11 days
  - 13.3%  $\geq 28$  days
  - 2.6%  $\geq 84$  days

# Long COVID Symptoms Change Over Time



Source	Text
Wellcome	Symptoms persisting beyond 4 weeks after symptom onset suggestive of COVID-19 (33).
Lancet	Multiorgan symptoms after COVID-19 are being reported by increasing numbers of patients. They range from cough and shortness of breath, to fatigue, headache, palpitations, chest pain, joint pain, physical limitations, depression, and insomnia, and affect people of varying ages. At the Lancet–Chinese Academy of Medical Sciences conference on 23 November 2020, Bin Cao presented data (in press at the Lancet) on the long-term consequences of COVID-19 for patients in Wuhan, and warned that dysfunctions and complications could persist in some discharged patients for at least 6 months. So-called long COVID is a burgeoning health concern and action is needed now to address it (34).
NICE	Signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis (35).
Scientific American	Individuals whose symptoms persist or develop outside the initial viral infection, but the duration and pathogenesis are unknown (36).
Royal Society	<p>The onset of persistent or recurrent episodes of one or more of the following symptoms, within x* weeks of infection with SARS-CoV-2 and continuing for y* weeks or more: severe fatigue, reduced exercise capacity, chest pain or heaviness, fever, palpitations, cognitive impairment, anosmia or ageusia, vertigo and tinnitus, headache, peripheral neuropathy, metallic or bitter taste, skin rash joint pain or swelling (3).</p> <p>* Maximum period between acquisition of the infection (if known) and the onset of symptoms, and the minimum duration of symptoms, should be specified in the definition.</p>
Haute Autorité de santé, France	Three criteria: Having presented with a symptomatic form of COVID-19; presenting with one or more initial symptoms 4 weeks after the start of the disease; and none of these symptoms can be explained by another diagnosis (37).
CDC	Long COVID: While most persons with COVID-19 recover and return to normal health, some patients can have symptoms that can last for weeks or even months after recovery from acute illness. Even people who are not hospitalized and who have mild illness can experience persistent or late symptoms (38).
Wikipedia	Condition characterized by long-term sequelae – persisting after the typical convalescence period – of coronavirus disease 2019 (COVID-19) (39).
Nature	Post-acute COVID-19 as persistent symptoms and/or delayed or long-term complications of SARS-CoV-2 infection beyond 4 weeks from the onset of symptoms (40).

# Clinical Case Definitions of Long-COVID

## WHO Consensus Definition

“Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS- CoV-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.”



# CDC Guidance: Post-COVID Conditions

- The term “Post-COVID Conditions” is an umbrella term for the wide range of physical and mental health consequences experienced by some patients that are present four or more weeks after SARS-CoV-2 infection, including by patients who had initial mild or asymptomatic acute infection.
- Objective laboratory or imaging findings should not be used as the only measure or assessment of a patient’s well-being; lack of laboratory or imaging abnormalities does not invalidate the existence, severity, or importance of a patient’s symptoms or conditions.
- Understanding of post-COVID conditions remains incomplete and guidance for healthcare professionals will likely change over time as the evidence evolves.





# What are the Risk Factors for Post-COVID Condition?

- More acute COVID-19 symptoms
- More severe acute COVID-19 symptoms
- Hospitalization during acute COVID-19
- Pre-existing co-morbidities
- Effects of race, ethnicity, variants, vaccinations still uncertain

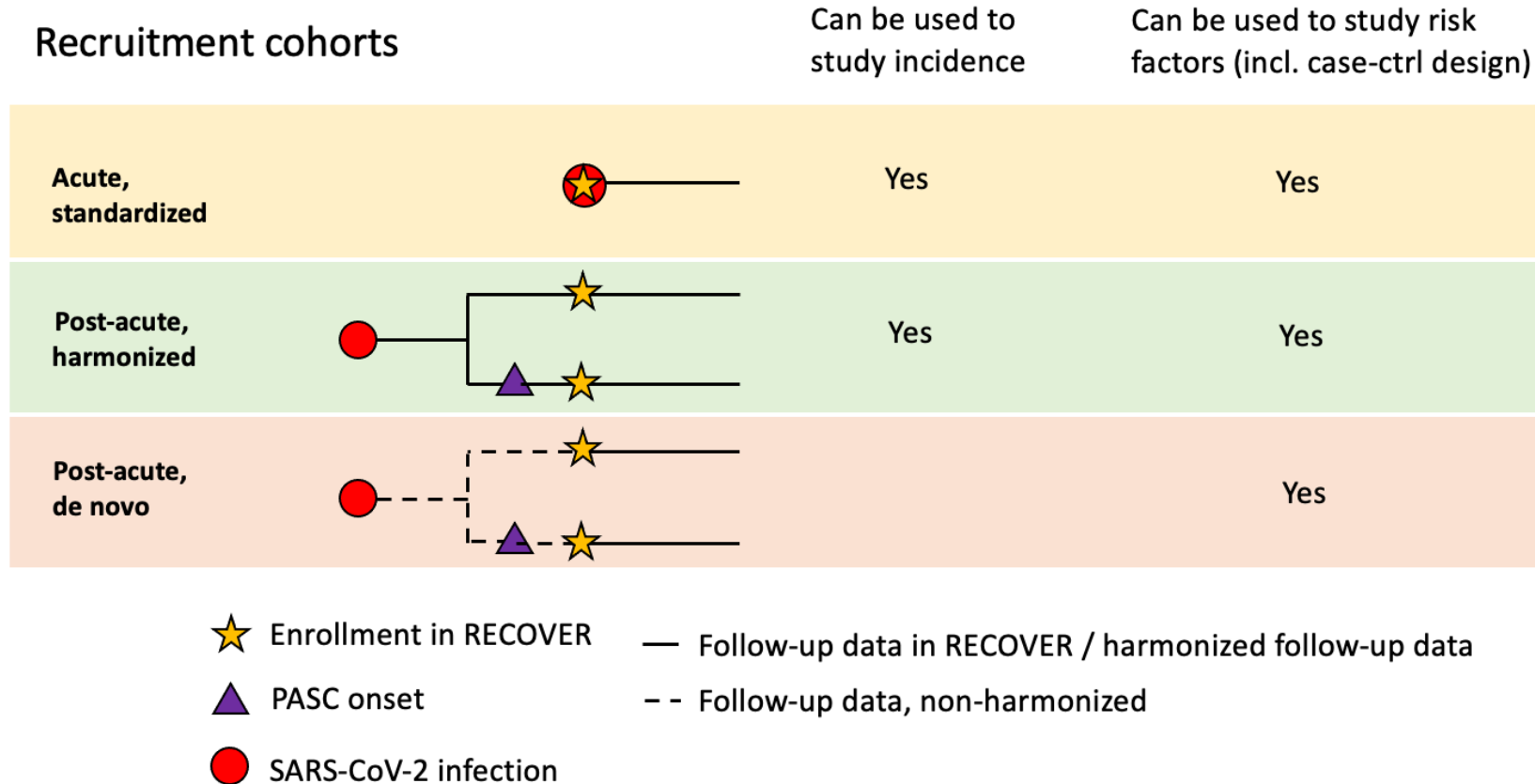


# What is being done to learn more about Long COVID?

- RECOVER is an NIH-funded multisite observational study designed to increase understanding of the epidemiology and mechanisms of Long COVID.
- In the RECOVER studies, we are trying to find out
  - How many people are getting Long COVID.
  - Why some people get Long COVID and others do not.
  - What symptoms people feel when they get Long COVID.
  - How long people feel sick when they get Long COVID.
  - What causes Long COVID to happen.



# Who can participate in RECOVER?



RECOVER is a meta-cohort study that includes people with and without a history of COVID-19. The different cohorts include:

- Pregnant women and their infants
- Children
- Adults

# What is the study plan for RECOVER?



The RECOVER main protocols will enroll patients with and without COVID infection, and with and without PASC.

There are about 200 enrolling sites.

Participant biospecimens will be collected at study sites and stored in a biorepository.

Learn more at [Recovercovid.org](https://Recovercovid.org)

Recruitment in all 50 States  
Hospitals/Clinics/Communities/Electronic Health Records  
Diverse population with and without COVID-19  
Infants/Children/Adults/Pregnant women



**Tier 1** Screening Tests (40,000 participants)  
What are the symptoms of PASC?  
What is the risk of PASC after COVID-19?  
How does pandemic-related stress impact PASC?

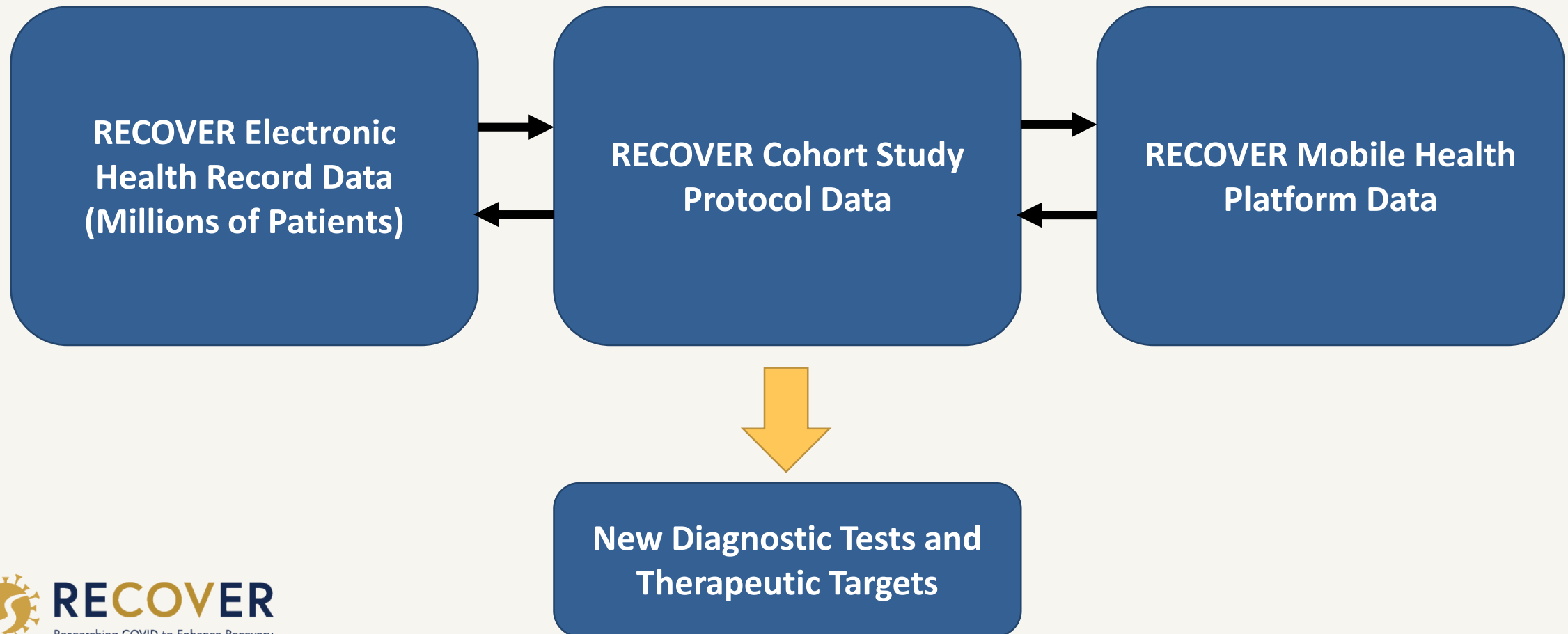


**Tier 2** Series of Clinical Tests over 2-4 years (10,000 participants)  
What are the risk factors for PASC?  
What is the time course of PASC?  
How does PASC affect child development?



**Tier 3** Advanced Testing (4,500 participants)  
What are the causes of PASC?  
How does PASC affect organ function over time?  
Is PASC associated with new onset chronic diseases?

# RECOVER Cohort Studies: Integration of Real World Data from Electronic Health Records





# Summary: What is Long COVID?

- Long COVID is umbrella term for the wide range of physical and mental health consequences experienced by some patients that are present four or more weeks after SARS-CoV-2 infection.
- The most common COVID symptoms are fatigue, headache, brain fog, shortness of breath, hair loss, pain.
- Understanding of post-COVID conditions remains incomplete and guidance for healthcare professionals will likely change over time as the evidence evolves.
- The RECOVER Initiative is designed to increase understanding of Long COVID and provide information to develop new diagnostic tests and treatment approaches for Long COVID



# Selected Bibliography: What is Long COVID?

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