



#### **POWER OF PROVIDERS**

Peer to Peer Learning Webinar

#### **Continuing Medical Education**

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Federation of State Medical Boards, Washington Medical Commission and the Washington State Department of Health. The Federation of State Medical Boards is accredited by the ACCME to provide continuing medical education for physicians.

The Federation of State Medical Boards designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

#### **Continuing Education**

 This nursing continuing professional development activity was approved by Montana Nurses Association, an accredited approver with distinction by the American Nurses Credentialing Center's Commission on Accreditation. Upon successful completion of this activity, 1.0 contact hours will be awarded.

 This program has been granted prior approval by the American Association of Medical Assistants (AAMA) for 1.0 administrative continuing education unit.

#### **Disclosures**

There are no relevant financial relationships with ineligible companies for those involved with the ability to control the content of this activity.

#### **Obtaining Continuing Education**

- Continuing education is available for physicians (MD, DO, ND), physician assistants, nurses (RN, ARNP, LPN), and medical assistants.
- Successful completion of this continuing education activity includes the following:
  - Attending the entire live webinar or watching the webinar recording.
  - Completing the evaluation after viewing the live webinar or webinar recording.
  - In the evaluation survey, please check Yes if you're interested in continuing education credit and specify which type you wish to obtain.
- Please note: CE certificates are NOT generated after evaluation completion—CE certificates
  will be sent by DOH within a few weeks after evaluation survey completion.
- The expiration date for credit for this webinar is 5/16/2024.

#### **Zoom Housekeeping**



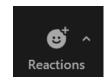
- Team shares information here
- Use for audience participation



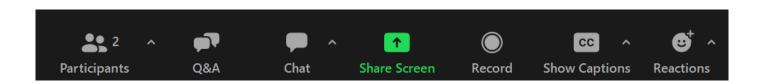
 Submit questions to presenter and team



 Click to enable automatic closed captions



 Click top-right arrow to hide participant reactions



## About the Power of Providers (POP) Initiative

- Support and equip health care providers to serve as trusted sources of COVID-19 vaccine information for their patients and their communities
- Respond to member requests for resources
- Work together to increase vaccine rates across the state



#### **Provider Commitment: SAVE**



SEEK: Seek your patients' COVID-19 vaccine status

ASK/EDUCATE: If your patient isn't vaccinated, ask them about the vaccine and offer education if they are unsure

VACCINATE: Provide patient with a COVID-19 vaccine or a referral to a location that provides them

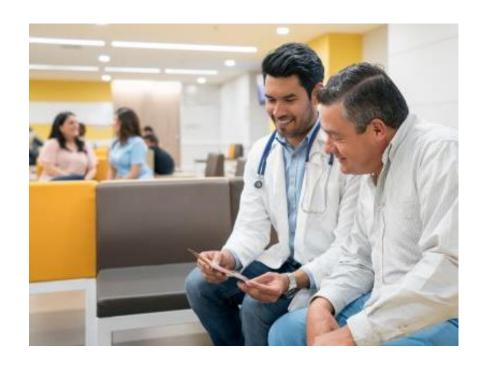
EMPOWER: Empower patients to share their vaccine status with their community

#### Who can join POP?

#### **Current Membership:**

- 4,500+ individuals
- 400 health care organizations
- 90 different health care roles
- Over 20 partnering health care associations

Any health care provider who engages with the people they serve about COVID-19 vaccinations is eligible—the ability to educate and refer is as important as administering the vaccine!



Visit our website to learn more at doh.wa.gov/joinpop. Fill out the member signup form to join.

#### **Current Resources**



#### **POP Shop**

Webpage to order free patient handouts, posters, discussion guides, other materials

doh.wa.gov/form/ pop-shop



#### **E-Newsletter**

New resources, timely and relevant updates for members



#### POP en Español

Updates, links, fact sheets, other resources for providers serving Spanish-speaking populations

doh.wa.gov/popesp

#### **Current Opportunities**



#### **Provider Advisory Group**

Multi-disciplinary group of POP members who inform and help guide our work.



#### Peer-to-Peer **Webinars**

- Learn about topics related to COVID from health care experts.
- To learn about upcoming topics, register, and view recordings, visit doh.wa.gov/POPwebinars



#### Member **Engagement**

POP staff are available and engaged in conversations with providers across the state to learn about your experiences, challenges, and feedback for DOH.

#### **Peer-to-Peer Webinars**

- Health care providers share expertise and knowledge with one another
- DOH provides meeting space only, not content

#### Long COVID series:

 March 29: Unmasking Long COVID: Insights and Updates from University of Washington Clinical Research – Dr. Helen Chu



#### **Today's Presenter**

#### Dr Eric J. Chow, MD, MS, MPH

- Chief of Communicable Disease
   Epidemiology and Immunization for
   Public Health Seattle & King County.
- Clinical Assistant Professor in the Division of Allergy and Infectious Diseases and in the Department of Epidemiology. At University of Washington.
- Helped characterize the initial cases of multi-system inflammatory syndrome in children in the United States.
- His peer reviewed publications and research interests focus on community respiratory virus epidemiology, extrapulmonary manifestations of respiratory viruses and emerging infectious diseases.



# Post-COVID-19 Conditions: Expanding Our Understanding of the Long-term Sequelae of COVID-19

Eric J. Chow, MD, MS, MPH, FACP, FAAP

Chief of Communicable Disease
Epidemiology and Immunizations
Public Health – Seattle & King County

Clinical Assistant Professor
Division of Allergy and Infectious Diseases,
University of Washington

Clinical Assistant Professor
Department of Epidemiology, University of
Washington

# I have no disclosures to report.

### **Objectives**

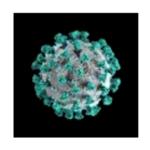
- 1. Summarize the terms and case definitions associated with post-COVID-19 conditions.
- 2. Recognize the clinical features commonly associated with certain phenotypes of post-COVID-19 conditions.
- 3. Review the known epidemiology and factors associated with the development of post-COVID-19 conditions.
- 4. Describe the possible etiologies and underlying pathophysiologic explanations for post-COVID-19 conditions.





**∜** CULTURE

**Q** SEARCH



#### Coronavirus Updates

THE CORONAVIRUS CRISIS

#### Fauci Estimates That 100,000 To 200,000 Americans Could Die From The Coronavirus

MARCH 29, 2020 · 2:17 PM ET





# 00000

## Hospitalizations

#### **Deaths**





# 6,693,491 Hospitalizations

(as of January 2024)

**Deaths** 





# 6,693,491 Hospitalizations

(as of January 2024)

1,167,210 **Deaths** 

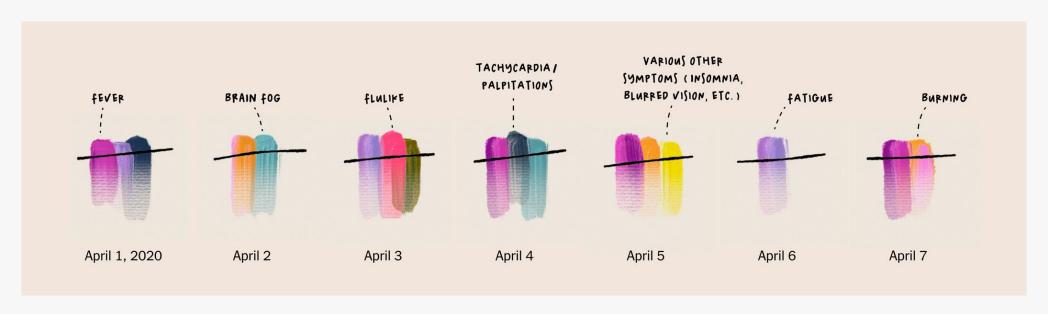
(as of January 2024)

"I am one of the lucky ones. I never needed a ventilator...But 27 days later, I still have lingering pneumonia. I use two inhalers, twice a day. I can't walk more than few blocks without stopping"

~ Mara Gay, New York Times Editorial Board Member

"I've come to realize that "long Covid" is a deceptive term for a condition that can trigger a diverse swarm of debilitating symptoms with no end in sight. What I've experienced is in no way just a lingering cough or a few weeks of fatigue after an acute COVID infection."

#### ~ Georgia Lupi



"I was also reading disheartening stories of perplexed and at times dismissive healthcare providers who reduced long-haul symptoms to 'anxiety attacks' or 'COVID-19-related hysteria.' This was a 'club' that none of us 'wanted' to join."

-Robin Macnofsky



# Characterized by over 200 symptoms have been reported.



**Fatigue** 



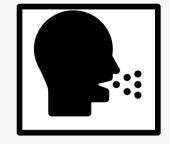
Shortness of breath



Chest pain or palpitations



**Anosmia** 



Cough



Dizziness or balance issues



Headache



Insomnia or sleep disturbances



Depression or anxiety



"...Under reasonable assumptions given the data available, long Covid could account for 15% of the nations... unfilled jobs."



"Approximately 18% of workers with Long COVID... could not return to work for more than 1 year"

New York State InsuranceFund



- 44% of people with post-COVID-19 conditions cannot work and those that do work 51% fewer hours.
- Up to \$9000 healthcare costs per person annually if extrapolating from chronic fatigue syndrome.
- As of January 2022, cost of post-COVID-19 conditions including lost wages and medical expenses is estimated to be >\$386 billion.

>773,000,000

Reported COVID-19 cases to WHO

(as of December 31 2023)

Assume

~10%

Experience post-COVID-19 conditions

~77,300,000

have had or is currently experiencing a post-COVID-19 condition



# A Diagnosis by Many Names and Definitions

Long COVID

Post-COVID-19 Condition Post-COVID-Conditions

Post-acute sequelae of SARS-CoV-2 Infection (PASC)

Persistent
Symptoms or
COVID-19
Consequences

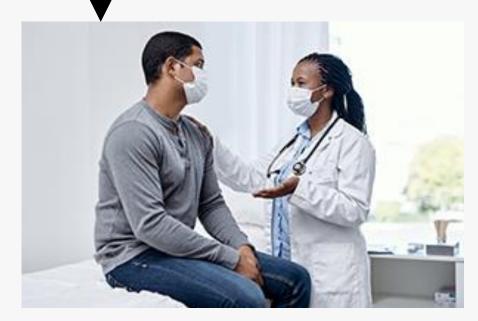
Ongoing symptomatic COVID-19

Post-COVID-19 syndrome

U09.9 Post-COVID-Condition, unspecified

Post-COVID-19 Conditions (PCC) Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) U09.9 Post-COVID
Condition,
unspecified

Post-COVID-19 Conditions (PCC) Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) U09.9 Post-COVID
Condition,
unspecified



- Patient driven by lived experience
- More commonly used in lay language
- Includes signs, symptoms, sequelae that persist or occur after acute COVID-19 experienced by individuals
- Progressive or relapse-remitting

Post-COVID-19 Conditions (PCC) Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) U09.9 Post-COVID Condition, unspecified







- Used by the medical, scientific, and public health communities
- Equivalent to "Long COVID" including direct and indirect effects of the virus
- Physical and mental health consequences present
   4+ weeks after acute infection

Post-COVID-19 Conditions (PCC) Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) U09.9 Post-COVID Condition, unspecified

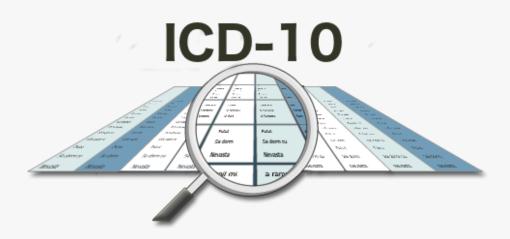
Post-COVID-19 Syndrome



National Institutes of Health

- Term used in NIH funded research studies such as RECOVER Study
- Focusing on the direct effects of the virus
- Persistent, relapsing or new symptoms or health effects after acute SARS-CoV-2 infection (present 4+ weeks after infection); definition evolving over time

Post-COVID-19 Conditions (PCC) Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) U09.9 Post-COVID Condition, unspecified



- International Classification of Diseases (ICD)-10 code
- No definition but establishes a link with COVID-19
- Not for acute COVID-19 unless in a setting of reinfection AND condition related to prior infection

Post-COVID-19 Conditions (PCC) Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) U09.9 Post-COVID Condition, unspecified



- UK based organization
- Long-term effects of COVID-19 divided into time periods: 4, 4-12, and >12
- Distinguishes between symptoms that are persistent after acute COVID-19 and symptoms/conditions that are new >12 weeks after infection

### NATIONAL ACADEMIES

Sciences
Engineering
Medicine

#### What We Heard:

# **Engagement Report on the Working Definition for Long COVID**

Presented to the Committee on Examining the Working Definition for Long COVID, at the National Academies of Sciences, Engineering, and Medicine

#### **JUNE 2023**

Prepared by EnSpark Consulting



"Long COVID is broadly defined as signs, symptoms and conditions that continue or develop after initial COVID-19 or SARS-CoV-2 infection.

The signs, symptoms and conditions are present four weeks or more after the initial phase of infection; may be multisystemic; and may present with a relapsing-remitting pattern and progression or worsening over time with the possibility of severe and life-threatening events even months or years after infection.

Long COVID is not one condition. It represents many potentially overlapping entities, likely with different biological causes and different sets of risk factors and outcomes."

~ U.S. Department of Health and Human Services 2022

#### **Upcoming Events**

12:00PM - 3:00PM (ET) MEETING 18

JANUARY 18, 2024

Examining the Working Definition for Long COVID - Committee Meeting 7

12:00PM - 3:00PM (ET) MEETING FEB 5

FEBRUARY 5, 2024

Examining the Working Definition for Long COVID - Committee Meeting 8



Health consequences (physical and mental) that can be present 4 or more weeks after infection with SARS-CoV-2

#### OR

Instances in which there is a lack of return to a usual state of health following acute COVID-19



### Characterized by over 200 symptoms have been reported.



**Fatigue** 



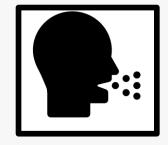
Shortness of breath



Chest pain or palpitations



**Anosmia** 



Cough



Dizziness or balance issues



Headache



Insomnia or sleep disturbances



Depression or anxiety

#### Persistent or New Symptoms and Conditions



**Fatigue** 



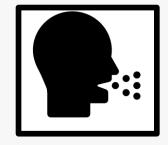
Shortness of breath



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**Anosmia** 



Cough



Dizziness or balance issues



Headache



Insomnia or sleep disturbances



Depression or anxiety

#### Increased Risk for New Health Conditions

Morbidity and Mortality Weekly Report

Post-COVID Conditions Among Adult COVID-19 Survivors Aged 18–64 and ≥65 Years — United States, March 2020–November 2021

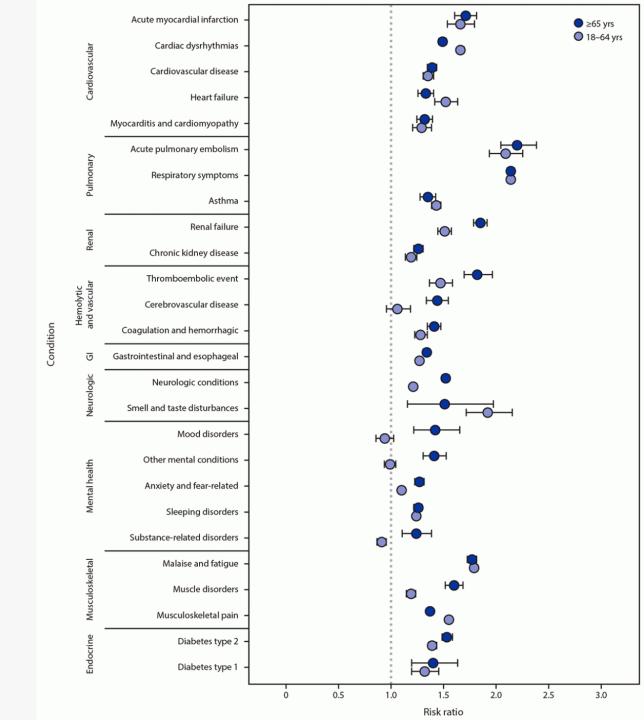
Lara Bull-Otterson, PhD1; Sarah Baca1,2; Sharon Saydah, PhD1; Tegan K. Boehmer, PhD1; Stacey Adjei, MPH1; Simone Gray, PhD1; Aaron M. Harris, MD1

Morbidity and Mortality Weekly Report

Post–COVID-19 Symptoms and Conditions Among Children and Adolescents — United States, March 1, 2020–January 31, 2022

Lyudmyla Kompaniyets, PhD<sup>1</sup>; Lara Bull-Otterson, PhD<sup>1</sup>; Tegan K. Boehmer, PhD<sup>1</sup>; Sarah Baca<sup>1,2</sup>; Pablo Alvarez, MPH<sup>1,2</sup>; Kai Hong, PhD<sup>1</sup>; Joy Hsu, MD<sup>1</sup>; Aaron M. Harris, MD<sup>1</sup>; Adi V. Gundlapalli, MD, PhD<sup>1</sup>; Sharon Saydah, PhD<sup>1</sup>

# Health Conditions in Adults





#### **Acute Cardiovascular Events**



**Acute Pulmonary Events** 



**Kidney Disease** 



**Hematologic Diseases** 



**Gastrointestinal Disorders** 



**Neurologic Disorders** 



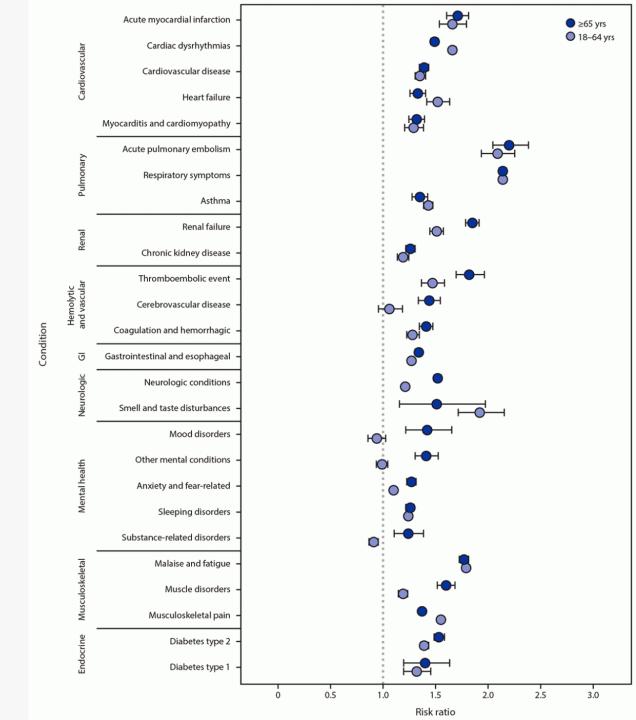
**Mental Health Disorders** 



Musculoskeletal/Rheumatic Disorders



**Endocrine Disorders** 



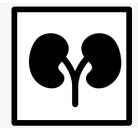
# Health Conditions in Children

TABLE 3. Adjusted hazard ratios of selected potential post–COVID-19 symptoms and conditions among children and adolescents aged 2–17 years with and without COVID-19, by age group — HealthVerity medical claims database, United States, March 1, 2020–January 31, 2022

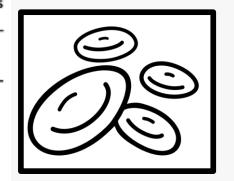
	Adjusted hazard ratio (95% CI)*		
Outcome	Aged 2–4 yrs	Aged 5–11 yrs	Aged 12–17 yrs
Symptom			
Smell and taste disturbances	1.22 (0.70-2.15)	0.94 (0.83-1.07)	1.23 (1.16-1.31) <sup>†</sup>
Circulatory signs and symptoms	1.17 (1.12–1.23) <sup>†</sup>	1.11 (1.08–1.13) <sup>†</sup>	1.04 (1.02-1.06) <sup>†</sup>
Malaise and fatigue	1.13 (1.05-1.22)†	1.08 (1.05-1.12) <sup>†</sup>	1.03 (1.01-1.04)†
Musculoskeletal pain	1.16 (1.10–1.21)†	1.06 (1.04-1.07)†	1.00 (0.99-1.01)
Dizziness and syncope	1.08 (0.90-1.29)	1.03 (0.99-1.08)	1.00 (0.98-1.02)
Gastrointestinal and esophageal disorders	1.15 (1.10–1.20)†	1.02 (1.00-1.04)†	0.97 (0.95-0.99)†
Sleeping disorders	0.99 (0.93-1.06)	0.89 (0.86-0.92)†	0.91 (0.89-0.94)†
Respiratory signs and symptoms	1.07 (1.04–1.10)†	0.93 (0.92-0.94)†	0.88 (0.87-0.89)†
Symptoms of mental conditions	1.03 (0.97-1.10)	0.92 (0.90-0.95)†	0.89 (0.86-0.91)†
Condition			
Acute pulmonary embolism	5	5	2.03 (1.61-2.56)†
Myocarditis and cardiomyopathy	2.39 (1.57-3.65)†	2.84 (2.39-3.37)†	1.66 (1.48-1.88) <sup>†</sup>
Venous thromboembolic event	5	2.69 (1.73-4.19) <sup>†</sup>	1.52 (1.22-1.91) <sup>†</sup>
Acute and unspecified renal failure	1.52 (1.07-2.14)†	1.38 (1.16-1.63) <sup>†</sup>	1.27 (1.15-1.40) <sup>†</sup>
Type 1 diabetes	1.01 (0.57-1.78)	1.31 (1.13–1.53) <sup>†</sup>	1.20 (1.09-1.33) <sup>†</sup>
Coagulation and hemorrhagic disorders	1.47 (1.20-1.80) <sup>†</sup>	1.28 (1.15-1.43) <sup>†</sup>	1.10 (1.03-1.19)†
Type 2 diabetes	1.24 (0.85-1.81)	1.14 (1.02-1.28) <sup>†</sup>	1.18 (1.11-1.24) <sup>†</sup>
Cardiac dysrhythmias	1.44 (1.22-1.70)†	1.23 (1.14–1.32)†	1.12 (1.08–1.17)†
Cerebrovascular disease	1.66 (0.85-3.23)	1.14 (0.79-1.64)	1.18 (0.93-1.48)
Chronic kidney disease	0.86 (0.54-1.36)	1.04 (0.83-1.31)	1.12 (0.96-1.31)
Asthma	1.12 (1.07–1.18)†	1.02 (1.00-1.05)†	0.96 (0.94-0.98)†
Muscle disorders	0.87 (0.77-0.98)†	0.86 (0.82-0.91)†	0.96 (0.93-0.99)†
Neurological conditions	0.98 (0.93-1.04)	0.96 (0.93-0.98)†	0.91 (0.89-0.93)†
Anxiety and fear-related disorders	0.91 (0.83-1.00)	0.86 (0.83-0.88)	0.84 (0.82-0.85)†
Mood disorders	0.82 (0.62–1.08)	0.73 (0.69–0.77)†	0.80 (0.77-0.83) <sup>†</sup>















WHAT IS LONG COVID?

RESEARCH ~

NEWS & EVENTS >

ABOUT THE INITIATIVE ~

### RECOVER: Researching COVID to Enhance Recovery

The National Institutes of Health (NIH) created the RECOVER Initiative to learn about the long-term effects of COVID.

The goal of RECOVER is to rapidly improve our understanding of and ability to predict, treat, and prevent PASC (post-acute sequelae of SARS-CoV-2), including Long COVID.

LEARN MORE ABOUT LONG COVID





Research

#### JAMA | Original Investigation

### Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection

Tanayott Thaweethai, PhD; Sarah E. Jolley, MD, MS; Elizabeth W. Karlson, MD, MS; Emily B. Levitan, ScD; Bruce Levy, MD; Grace A. McComsey, MD; Lisa McCorkell, MPP; Girish N. Nadkarni, MD, MPH; Sairam Parthasarathy, MD; Upinder Singh, MD; Tiffany A. Walker, MD; Caitlin A. Selvaggi, MS; Daniel J. Shinnick, MS; Carolin C. M. Schulte, PhD; Rachel Atchley-Challenner, PhD; RECOVER Consortium Authors; Leora I. Horwitz, MD; Andrea S. Foulkes, ScD; for the RECOVER Consortium

# Acute Cohort

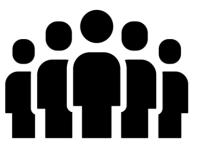
(within 30 days after acute infection)

# Post-acute Cohort

(30 days to 3 years after acute infection)

# Uninfected Cohort

(No evidence of current or prior infection)



# Acute Cohort

(within 30 days after acute infection)

# Post-acute Cohort

(30 days to 3 years after acute infection)

# Uninfected Cohort

(No evidence of current or prior infection)





# Acute Cohort

(within 30 days after acute infection)

# Post-acute Cohort

(30 days to 3 years after acute infection)

# Uninfected Cohort

(No evidence of current or prior infection)







85 sites across the US

### **Acute Cohort**

(within 30 days after acute infection)

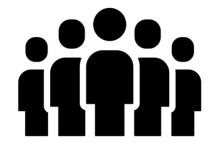
### Post-acute **Cohort**

(30 days to 3 years after acute infection)

### Uninfected **Cohort**

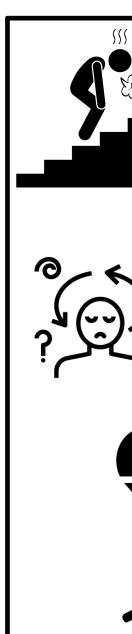
(No evidence of current or prior infection)







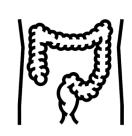
85 sites across the US











































1.Symptoms assigned a value

2.Score was totaled to provide the individual's PASC score

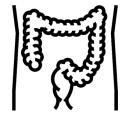
3.Using a PASC score threshold of 12 or greater to identify individuals with PASC





















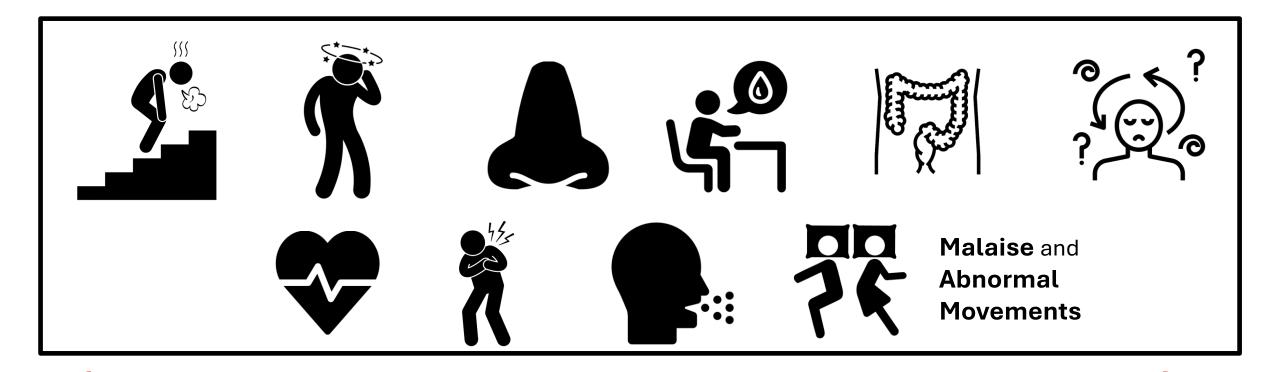


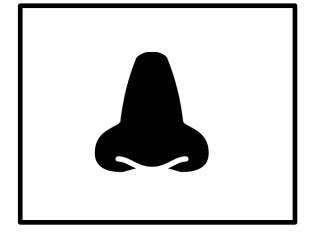
3. Should also note that 4% of people without a history of COVID-19 also

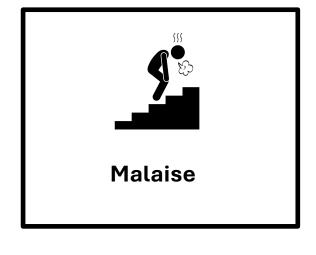
Among infected cohort,
 23% were PASC positive.

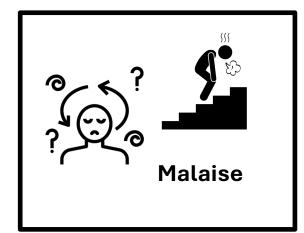
 Among acute cohort during the Omicron period,
 10% were PASC positive.

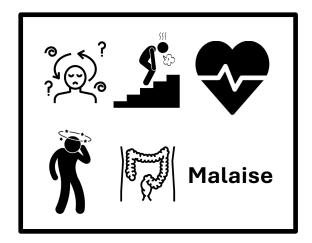
met PASC score cutoff.







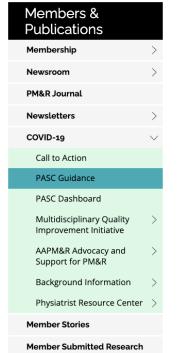






Home / Members & Publications / COVID-19 / PASC Guidance

#### **PASC Consensus Guidance**



The Academy has undertaken comprehensive efforts to support our call for a national plan to address Post-Acute Sequelae of SARS-CoV-2 infection (PASC or Long COVID) and the 3 to 10 million Americans it is affecting.

AAPM&R understands the need for focused, meaningful, and ongoing clinical exchange between the medical community to assess and implement appropriate clinical practice for treating and following all long-term COVID issues, not just those issues requiring PM&R intervention, is necessary. Therefore, AAPM&R has gathered a multidisciplinary collaborative with goals to foster engagement and share experiences to propel the health system towards defining standards of care for persons experiencing Long COVID-19/PASC.

#### **Published Guidance**

The collaborative is working to publish guidance on a rolling basis. Writing groups are working within a consensus process with 3 waves. All published guidance will be linked here as it becomes available.



- Neurological Symptoms
- Automatic Dysfunction
- Fatigue
- Cognitive Symptoms
- Cardiovascular
   Complications
- Breathing Discomfort
- Pediatrics



Low and slow

Gradual increases

Titrated work hours



>773,000,000

Reported COVID-19 cases to WHO

(as of December 31 2023)

Assume

~10%

Experience post-COVID-19 conditions

~77,300,000

have had or is currently experiencing a post-COVID-19 condition



The in the Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study

Aranka V Ballering, Sander K R van Zon, Tim C olde Hartman, Judith G M Rosmalen, for the Lifelines Corona Research Initiative\*



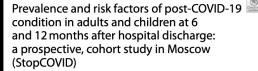
Post-COVID-19 condition occurs in 1 in 8 adults with COVID-19 in the general population.



Post-COVID Conditions Among Adult COVID-19 Survivors Aged 18–64 and ≥65 Years — United States, March 2020-November 2021

Lara Bull-Otterson, PhD1; Sarah Baca1.2; Sharon Saydah, PhD1; Tegan K. Boehmer, PhD1; Stacey Adjei, MPH1; Simone Gray, PhD1; Aaron M. Harris, MD1

Approximately 1 in 5 adults (18-64 years) and 1 in 4 older adults (≥65 years) had a health condition that may be related to previous SARS-CoV-2 infection.



Ekaterina Pazukhina<sup>1,2†</sup>, Margarita Andreeva<sup>3†</sup>, Ekaterina Spiridonova<sup>3†</sup>, Polina Bobkova<sup>3†</sup>, Anastasia Shikhaleva<sup>3</sup> Yasmin El-Taravi<sup>3†</sup>, Mikhail Rumyantsev<sup>3†</sup>, Aysylu Gamirova<sup>3†</sup>, Anastasiia Bairashevskaia<sup>3</sup>, Polina Petrova<sup>3</sup> Dina Baimukhambetova<sup>3</sup>, Maria Pikuza<sup>3</sup>, Elina Abdeeva<sup>3</sup>, Yulia Filippova<sup>3</sup>, Salima Deunezhewa<sup>3</sup>, Nikita Nekliudov<sup>3</sup> Polina Bugaeva<sup>3</sup>, Nikolay Bulanov<sup>4</sup>, Sergey Avdeev<sup>5</sup>, Valentina Kapustina<sup>6</sup>, Alla Guekht<sup>7,8</sup>, Audrey DunnGalvin<sup>3,5</sup> Pasquale Comberiati<sup>10</sup>, Diego G. Peroni<sup>10</sup>, Christian Apfelbacher<sup>11</sup>, Jon Genuneit<sup>12</sup>, Luis Felipe Reyes<sup>13,14</sup> Caroline L. H. Brackel 15,16, Victor Fomin 17, Andrey A. Svistunov 17, Peter Timashev 18, Lyudmila Mazankova 19 Alexandra Miroshina<sup>20</sup>, Elmira Samitova<sup>1920</sup>, Svetlana Borzakova<sup>821</sup>, Elena Bondarenko<sup>3</sup>, Anatoliy A. Korsunskiy<sup>3</sup> Gail Carson<sup>22</sup>, Louise Sigfrid<sup>22</sup>, Janet T. Scott<sup>23</sup>, Matthew Greenhawt<sup>24</sup>, Danilo Buonsenso<sup>2</sup> Malcolm G. Semple<sup>28,29</sup>, John O. Warner<sup>30</sup>, Piero Olliaro<sup>22</sup>, Dale M. Needham<sup>31,32,33</sup>, Petr Glybochko<sup>1</sup> enis Butnaru<sup>17</sup>, Ismail M. Osmanov<sup>8,20†</sup>, Daniel Munblit<sup>3,7,30\*†</sup> and Sechenov StopCOVID Research Tean



Prevalence of post-COVID-19 conditions estimated to be 1 in 3 adults and 1 in 10 children who were hospitalized with COVID-19.





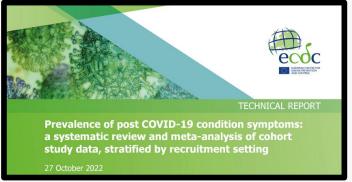
months after SARS-CoV-2 infection (long COVID) among adolescents in England (CLoCk): a national matched cohort study



Terence Stephenson, Snehal M Pinto Pereira, Roz Shafran, Bianca L de Stavola, Natalia Rojas, Kelsey McOwat, Ruth Simmons, Maria Zavala,  $Lauren\ O'Mahoney, Trudie\ Chalder, Esther\ Crawley, Tamsin\ J\ Ford,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CLoCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Isobel\ Heyman,\ Olivia\ Swann,\ Elizabeth\ Whittaker,\ CloCk,\ Anthony\ Harnden,\ Mandala Harnden,\ Mandala$ Consortium, Shamez N Ladhani



Among non-hospitalized adolescents aged 11-17 years, there were 13.2% more individuals reporting symptoms and 14% more reporting ≥3 symptoms at 3 months among those with COVID-19 compared to those without.



The Journal of Infectious Diseases

MAJOR ARTICLE







Global Prevalence of Post-Coronavirus Disease 2019

(COVID-19) Condition or Long COVID: A Meta-Analysis and Systematic Review

Chen Chen, 1.a Spencer R. Haupert, 1.a Lauren Zimmermann, 1.2.0 Xu Shi, 1 Lars G. Fritsche, 1.3.4 and Bhramar Mukherjee 1,2.3.4.5.0

Department of Biostatistics, School of Public Health, University of Michigan, Ann Arbor, Michigan, USA: "Pongel Cancer For Precision Health Data Science, University of Michigan, Ann Arbor, Michigan, USA: "Enter for Statistical Genetics, School of Public Health, University of Michigan, Ann Arbor, Michigan, USA: "Center for Statistical Genetics, School of Public Health, University of Michigan, Ann Arbor, Michigan, USA

"USA: and "Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan, USA



Coronavirus (COVID-19)

Home // Policy Watch // Long COVID: What Do the Latest Data Show?

Long COVID: What Do the Latest Data Show?

Alice Burns 🗹 Ian 26, 2023

Jan 26, 2023







#### Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection

Tanayott Thaweethai, PhD; Sarah E. Jolley, MD, MS; Elizabeth W. Karlson, MD, MS; Emily B. Levitan, ScD; Bruce Levy, MD; Grace A. McComsey, MD; Lisa McCorkell, MPP; Girish N. Nadkarni, MD, MPH; Sairam Parthasarathy, MD; Upinder Singh, MD; Tiffany A. Walker, MD; Caitlin A. Selvaggi, MS; Daniel J. Shinnick, MS; Carolin C. M. Schulte, PhD; Rachel Atchley-Challenner, PhD; RECOVER Consortium Authors; Leora I. Horwitz, MD; Andrea S. Foulkes, ScD; for the RECOVER Consortium



Prevalence of any post COVID-19 condition symptom was estimated to be **51% among** community setting cohorts.



Estimated global prevalence of post-COVID-19 conditions estimated to be 43% among those with prior SARS-CoV-2 infection.



15% of US adults reported ever having longCOVID; 28% of adults with previous COVID-19 reported ever having long COVID



Among adult study participants first infected on or after December 1, 2021 and enrolled within 30 days of infection, 10% were PASC positive at 6 months.

10-30% of non-hospitalized cases

50-70% of hospitalized cases

10-12% of vaccinated cases





 People of all ages are at risk for post-COVID-19 conditions



 People of all ages are at risk for post-COVID-19 conditions

 Highest percentages of diagnoses between ages 36 and 50 years



 People of all ages are at risk for post-COVID-19 conditions

 Highest percentages of diagnoses between ages 36 and 50 years

 Risk appears higher in older age groups with similar acute disease severity

#### **Acute COVID-19**

Asymptomatic

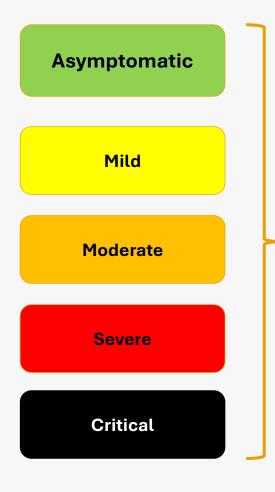
Mild

Moderate

Severe

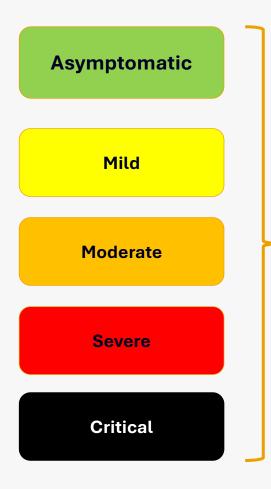
Critical

#### **Acute COVID-19**



 People with all acute disease severities are at risk for post-COVID-19 conditions including those who had asymptomatic or mild infection.

#### **Acute COVID-19**



 People with all acute disease severities are at risk for post-COVID-19 conditions including those who had asymptomatic or mild infection.

 Most cases are in individuals with mild infection given the proportion of people with non-severe acute infection.

## **Acute COVID-19**

**Asymptomatic** Mild **Moderate** Severe **Critical** 

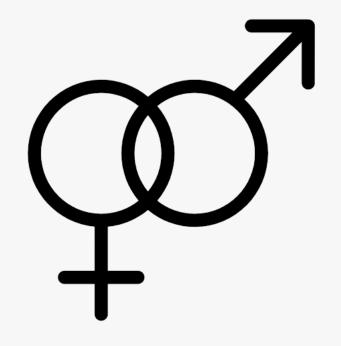
 People with all acute disease severities are at risk for post-COVID-19 conditions including those who had asymptomatic or mild infection.

 Most cases are in individuals with mild infection given the proportion of people with non-severe acute infection.

 However, people with more severe acute COVID-19 are more at risk for post-COVID-19 conditions.







Prevalence of described cases appears to be higher in women

# There are likely racial and ethnic disparities.

Morbidity and Mortality Weekly Report

# Trends in Racial and Ethnic Disparities in COVID-19 Hospitalizations, by Region — United States, March–December 2020

Sebastian D. Romano, MPH<sup>1</sup>; Anna J. Blackstock, PhD<sup>1</sup>; Ethel V. Taylor, DVM<sup>1</sup>; Suad El Burai Felix, MPH<sup>1</sup>; Stacey Adjei, MPH<sup>1</sup>; Christa-Marie Singleton, MD<sup>1</sup>; Jennifer Fuld, PhD<sup>1</sup>; Beau B. Bruce, MD, PhD<sup>1</sup>; Tegan K. Boehmer, PhD<sup>1</sup>

## **Annals of Internal Medicine**

REVIEW

# Racial and Ethnic Disparities in COVID-19-Related Infections, Hospitalizations, and Deaths

## **A Systematic Review**

Katherine Mackey, MD, MPP; Chelsea K. Ayers, MPH; Karli K. Kondo, PhD; Somnath Saha, MD, MPH; Shailesh M. Advani, MD, MPH; Sarah Young, MPH; Hunter Spencer, DO; Max Rusek, MD; Johanna Anderson, MPH; Stephanie Veazie, MPH; Mia Smith, MPH; and Devan Kansagara, MD, MCR

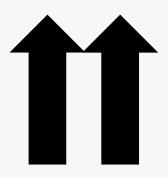
# When compared to White populations, Black and Hispanic populations have:

When compared to White populations, Black and Hispanic populations have:



Rates of SARS-CoV-2 infections

When compared to White populations, Black and Hispanic populations have:



Rates of SARS-CoV-2 infections



Risk of hospitalization due to COVID-19

## Racial/Ethnic Disparities in Post-acute Sequelae of SARS-CoV-2 Infection in New York: an EHR-Based Cohort Study from the RECOVER Program



Dhruv Khullar, MD, MPP<sup>1,2</sup>, Yongkang Zhang, PhD<sup>1</sup>, Chengxi Zang, PhD<sup>1</sup>, Zhenxing Xu, PhD<sup>1</sup>, Fei Wang, PhD<sup>1</sup>, Mark G. Weiner, MD<sup>1</sup>, Thomas W. Carton, PhD<sup>3</sup>, Russell L. Rothman, MD, MPP<sup>4</sup>, Jason P. Block, MD, MPH<sup>5</sup>, and Rainu Kaushal, MD, MPH<sup>1</sup>

<sup>1</sup>Department of Population Health Sciences, Weill Cornell Medicine, New York, NY, USA; <sup>2</sup>Department of Medicine, Weill Cornell Medicine, New York, NY, USA; <sup>3</sup>Louisiana Public Health Institute, New Orleans, LA, USA; <sup>4</sup>Institute for Medicine and Public Health, Vanderbilt University Medical Center, Nashville, TN, USA; <sup>5</sup>Department of Population Medicine, Harvard Pligrim Health Care Institute, Harvard Medical School, Boston, MA, USA.

## Racial/Ethnic Disparities in Post-acute Sequelae of SARS-CoV-2 Infection in New York: an EHR-Based Cohort Study from the RECOVER Program



Dhruv Khullar, MD, MPP<sup>1,2</sup>, Yongkang Zhang, PhD<sup>1</sup>, Chengxi Zang, PhD<sup>1</sup>, Zhenxing Xu, PhD<sup>1</sup>, Fei Wang, PhD<sup>1</sup>, Mark G. Weiner, MD<sup>1</sup>, Thomas W. Carton, PhD<sup>3</sup>, Russell L. Rothman, MD, MPP<sup>4</sup>, Jason P. Block, MD, MPH<sup>5</sup>, and Rainu Kaushal, MD, MPH<sup>1</sup>

<sup>1</sup>Department of Population Health Sciences, Weill Cornell Medicine, New York, NY, USA; <sup>2</sup>Department of Medicine, Weill Cornell Medicine, New York, NY, USA; <sup>3</sup>Louisiana Public Health Institute, New Orleans, LA, USA; <sup>4</sup>Institute for Medicine and Public Health, Vanderbilt University Medical Center, Nashville, TN, USA; <sup>5</sup>Department of Population Medicine, Harvard Pligrim Health Care Institute, Harvard Medical School, Boston, MA, USA.

Black and Hispanic populations had different odds of developing specific post-COVID-19 symptoms compared to white individuals.

ORIGINAL ARTICLE—CME



Race, ethnicity, and utilization of outpatient rehabilitation for treatment of post COVID-19 condition

```
Claudia B. Hentschel MD<sup>1</sup> | Benjamin A. Abramoff MD<sup>2</sup> | Timothy R. Dillingham MD<sup>2</sup> | Liliana E. Pezzin PhD JD<sup>3</sup>
```

Black population had a lower utilization of outpatient rehabilitation services despite similar incidence of post COVID-19 conditions.

# Post-COVID-19 Conditions After Reinfection?

## nature medicine



Article

https://doi.org/10.1038/s41591-022-02051-3

# Acute and postacute sequelae associated with SARS-CoV-2 reinfection

Received: 12 June 2022

Benjamin Bowe<sup>1,2</sup>, Yan Xie <sup>(1)</sup> & Ziyad Al-Aly <sup>(1)</sup> L<sup>2,3,4,5</sup>

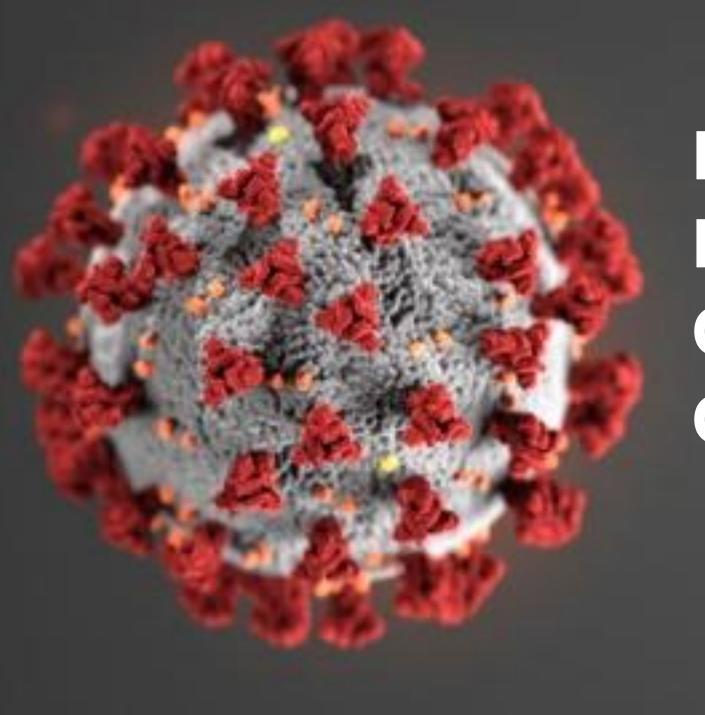
Accepted: 23 September 2022

## JAMA | Original Investigation

## Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection

Tanayott Thaweethai, PhD; Sarah E. Jolley, MD, MS; Elizabeth W. Karlson, MD, MS; Emily B. Levitan, ScD; Bruce Levy, MD; Grace A. McComsey, MD; Lisa McCorkell, MPP; Girish N. Nadkarni, MD, MPH; Sairam Parthasarathy, MD; Upinder Singh, MD; Tiffany A. Walker, MD; Caitlin A. Selvaggi, MS; Daniel J. Shinnick, MS; Carolin C. M. Schulte, PhD; Rachel Atchley-Challenner, PhD; RECOVER Consortium Authors; Leora I. Horwitz, MD; Andrea S. Foulkes. ScD; for the RECOVER Consortium

- SARS-CoV-2 reinfection associated with higher risk of sequelae
- Cumulative risk of post-COVID-19 conditions increases with the total number of infections



Reducing the Risk of Post-COVID-19 Conditions

Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study



Michela Antonelli, Rose S Penfold, Jordi Merino, Carole H Sudre, Erika Molteni, Sarah Berry, Liane S Canas, Mark S Graham, Kerstin Klaser, Marc Modat, Benjamin Murray, Eric Kerfoot, Liyuan Chen, Jie Deng, Marc F Österdahl, Nathan J Cheetham, David A Drew, Long H Nguyen, Joan Capdevila Pujol, Christina Hu, Somesh Selvachandran, Lorenzo Polidori, Anna May, Jonathan Wolf, Andrew T Chan, Alexander Hammers, Emma L Duncan, Tim D Spector, Sebastien Ourselin<sup>5</sup>, Claire J Steves\*



## **ARTICLES**

https://doi.org/10.1038/s41591-022-01840-0



#### **OPEN**

## Long COVID after breakthrough SARS-CoV-2 infection

Ziyad Al-Aly 10,1,2,3,4,5 , Benjamin Bowe<sup>1,2</sup> and Yan Xie 10,2,6</sup>

### JAMA | Original Investigation

## Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection

Tanayott Thaweethai, PhD; Sarah E. Jolley, MD, MS; Elizabeth W. Karlson, MD, MS; Emily B. Levitan, ScD; Bruce Levy, MD; Grace A. McComsey, MD; Lisa McCorkell, MPP; Girish N. Nadkarni, MD, MPH; Sairam Parthasarathy, MD; Upinder Singh, MD; Tiffany A. Walker, MD; Caitlin A. Selvaggi, MS; Daniel J. Shinnick, MS; Carolin C. M. Schulte, PhD; Rachel Atchley-Challenner, PhD; RECOVER Consortium Authors; Leora I. Horwitz, MD; Andrea S. Foulkes, ScD; for the RECOVER Consortium

Clinical Infectious Diseases







Prevalence of Post-Coronavirus Disease Condition 12 Weeks After Omicron Infection Compared With Negative Controls and Association With Vaccination Status

Mayssam Nehme, 1.0 Pauline Vetter, 2.3.4.0 François Chappuis, 5.6 Laurent Kaiser, 2.3.4 and Idris Guessous; 1.6.0 for the CoviCare Study Team

<sup>1</sup>Division of Primary Care Medicine of the Geneva University Hospitals, Geneva, Switzerland; <sup>2</sup>Division of Infectious Diseases, Geneva University Hospitals, Geneva, Switzerland; <sup>4</sup>Division of Laboratory Medicine, Laboratory of Virology, Geneva University Hospitals, Geneva, Switzerland; <sup>5</sup>Division of Tropical and Humanitarian Medicine, Geneva University Hospitals, Geneva, Switzerland; <sup>6</sup>Division of Tropical and Humanitarian Medicine, Geneva University Hospitals, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva, Geneva, Switzerland; and <sup>6</sup>Faculty of Medicine, University of Geneva, Geneva

## Association Between BNT162b2 Vaccination and Long COVID After Infections Not Requiring Hospitalization in Health Care Workers

Survivors of COVID-19 may present with long-lasting symptoms. Some factors have been associated with the development of post-COVID conditions (also referred to as "long"

+

Supplemental content

COVID"), 2 including hospitalization. 3 A study of older US veterans showed 15% reduction of long COVID after vaccina-

tion; however, study limitations included the low number of women and suboptimal vaccination schedules.<sup>4</sup>

## A Summary of the Findings:

- COVID-19 vaccination is associated with a reduction in risk of post-COVID-19 conditions in a dose response fashion.
- Proportion of individuals with post-COVID-19 conditions was lower among fully vaccinated than unvaccinated participants before and during Omicron circulation
- 3. To protect against post-COVID-19 conditions, a layered approach combining COVID-19 vaccination and non-pharmaceutical interventions to prevent SARS-CoV-2 infection in the first place is needed.



Research

JAMA Internal Medicine | Original Investigation

## Association of Treatment With Nirmatrelvir and the Risk of Post-COVID-19 Condition

Yan Xie, PhD; Taeyoung Choi, MPH; Ziyad Al-Aly, MD

## Original Research

#### **Annals of Internal Medicine**

## Effectiveness of Nirmatrelvir–Ritonavir Against the Development of Post–COVID-19 Conditions Among U.S. Veterans

#### A Target Trial Emulation

George N. Ioannou, BMBCh, MS; Kristin Berry, PhD; Nallakkandi Rajeevan, PhD; Yuli Li, MS; Pradeep Mutalik, MD; Lei Yan, PhD; David Bui, PhD; Francesca Cunningham, PharmD; Denise M. Hynes, MPH, PhD, RN; Mazhgan Rowneki, MPH; Amy Bohnert, PhD, MHS; Edward J. Boyko, MD, MPH; Theodore J. Iwashyna, MD, PhD; Matthew L. Maciejewski, PhD; Thomas F. Osborne, MD; Elizabeth M. Viglianti, MD, MPH, MSc; Mihaela Aslan, PhD; Grant D. Huang, MPH, PhD; and Kristina L. Bajema, MD, MSc





RESEARCH

Molnupiravir and risk of post-acute sequelae of covid-19: cohort study

Yan Xie, 1,2 Taeyoung Choi, 1,2 Ziyad Al-Aly 1,2,3,4,5

#### **Research Letter**

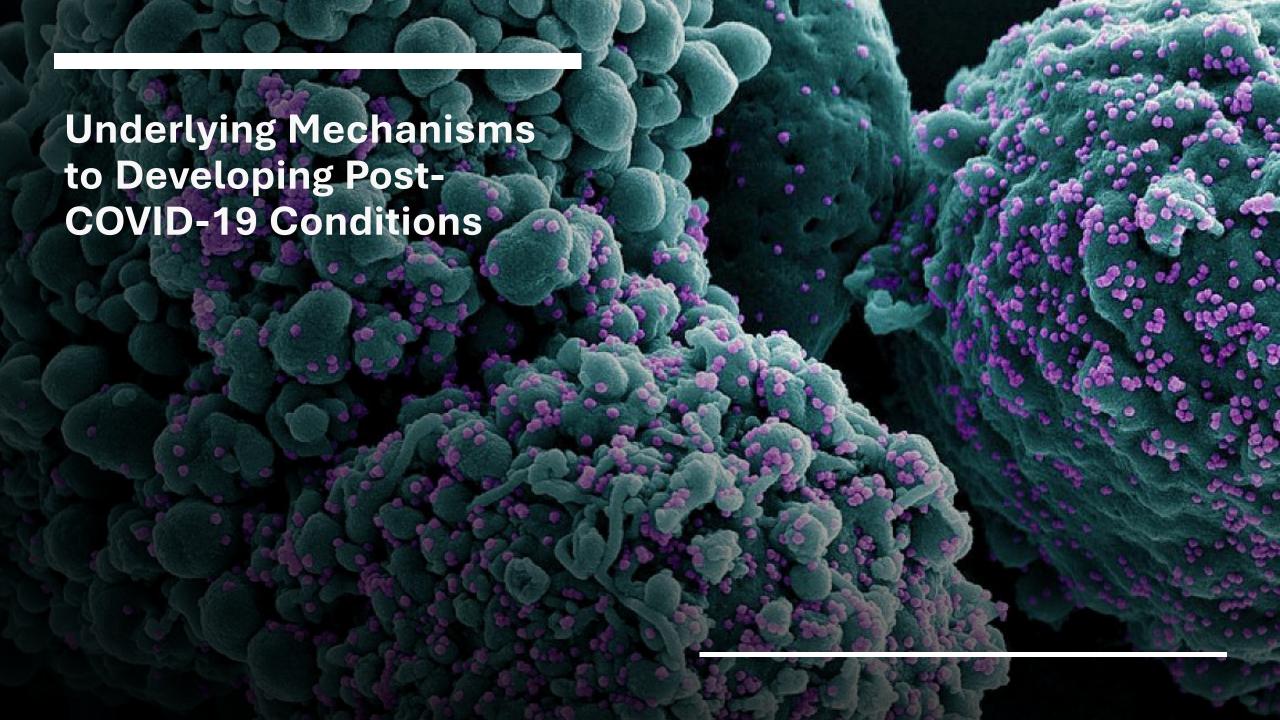
October 23, 2023

## Nirmatrelvir and Molnupiravir and Post-COVID-19 Condition in Older Patients

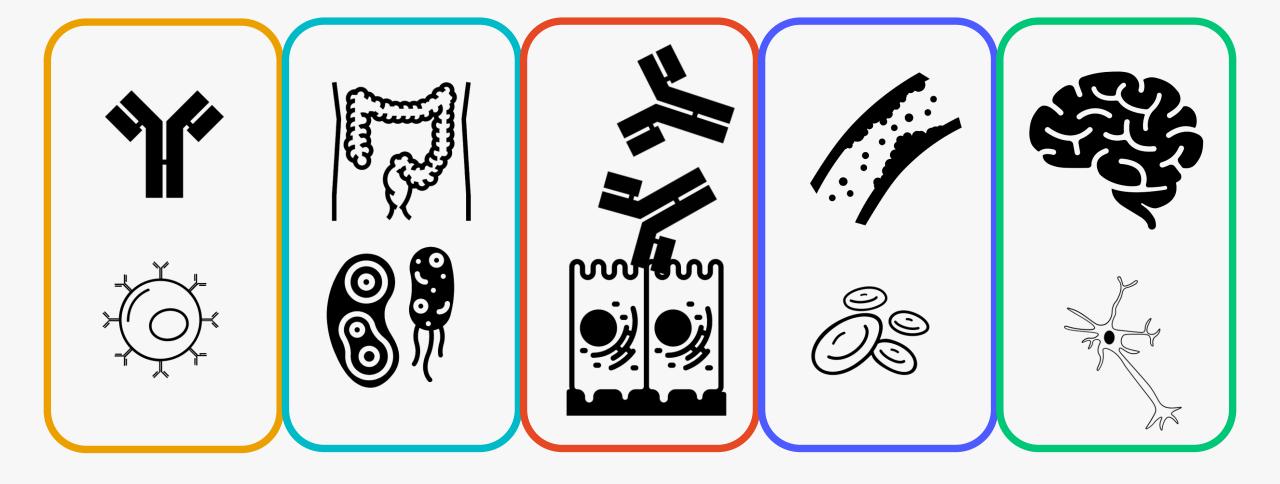
Kin Wah Fung, MD1; Fitsum Baye, MS1; Seo H. Baik, PhD1,2; et al.

» Author Affiliations | Article Information

JAMA Intern Med. 2023;183(12):1404-1406. doi:10.1001/jamainternmed.2023.5099



Reactivation Persistent **Impacts of** of underlying reservoirs of pathogens acute infection on SARS-CoV-2 microbiome in tissues Post-**Dysfunctional Immune** COVID-19 nerve or brain **Dysregulation Conditions** signaling Microvascular blood clotting **Autoimmunity** and endothelial dysfunction



Immune dysregulation

Microbial flora disruption

**Autoimmunity and immune priming** 

Coagulation and endothelial dysfunction

Dysfunctional neurological signaling

### Gut microbiota



Original research

Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19

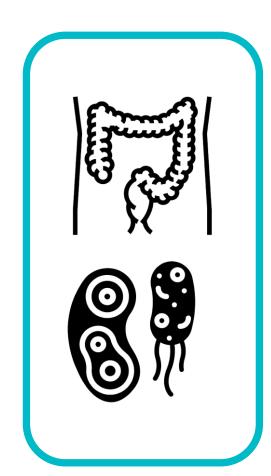
Yun Kit Yeoh , <sup>1,2</sup> Tao Zuo , <sup>2,3,4</sup> Grace Chung-Yan Lui, <sup>3,5</sup> Fen Zhang, <sup>2,3,4</sup> Qin Liu, <sup>2,3,4</sup> Amy YL Li, Arthur CK Chung, <sup>2,3,4</sup> Chun Pan Cheung, <sup>2,3,4</sup> Eugene YK Tso, Kitty SC Fung, Veronica Chan, Lowell Ling, Gavin Joynt, David Shu-Cheong Hui, <sup>3,5</sup> Kai Ming Chow , <sup>3</sup> Susanna So Shan Ng, <sup>3,5</sup> Timothy Chun-Man Li, <sup>3,5</sup> Rita WY Ng, Terry CF Yip, <sup>3,4</sup> Grace Lai-Hung Wong , <sup>3,4</sup> Francis KL Chan , <sup>2,3,4</sup> Chun Kwok Wong, Paul KS Chan, <sup>1,2,10</sup> Siew C Ng , <sup>2,3,4</sup>

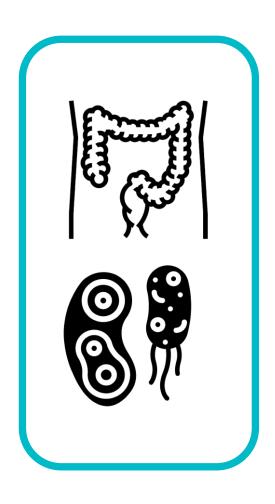
## COVID-19



Original research

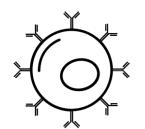
Gut microbiota dynamics in a prospective cohort of patients with post-acute COVID-19 syndrome





- Studies show that gut microbiome composition is significantly altered comparing those with COVID-19 and those without COVID-19.
- Commensals associated with immunomodulating potential were underrepresented in those with COVID-19.
- Disruption was associated with elevated inflammatory markers.
- Continued dysbiosis after infection resolution suggest possible pathway for lingering symptoms.







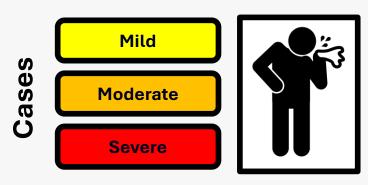
## Cell

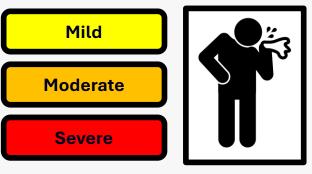


### **Article**

## Multiple early factors anticipate post-acute COVID-19 sequelae

Yapeng Su,<sup>1,2,3,28,\*</sup> Dan Yuan,<sup>1,4,28</sup> Daniel G. Chen,<sup>1,5,28</sup> Rachel H. Ng,<sup>1,4</sup> Kai Wang,<sup>1</sup> Jongchan Choi,<sup>1</sup> Sarah Li,<sup>1</sup> Sunga Hong,<sup>1</sup> Rongyu Zhang,<sup>1,4</sup> Jingyi Xie,<sup>1,6</sup> Sergey A. Kornilov,<sup>1</sup> Kelsey Scherler,<sup>1</sup> Ana Jimena Pavlovitch-Bedzyk,<sup>7</sup> Shen Dong,<sup>8</sup> Christopher Lausted,<sup>1</sup> Inyoul Lee,<sup>1</sup> Shannon Fallen,<sup>1</sup> Chengzhen L. Dai,<sup>1</sup> Priyanka Baloni,<sup>1</sup> Brett Smith,<sup>1</sup> Venkata R. Duvvuri,<sup>1</sup> Kristin G. Anderson,<sup>3,9</sup> Jing Li,<sup>7</sup> Fan Yang,<sup>10</sup> Caroline J. Duncombe,<sup>11</sup> Denise J. McCulloch,<sup>12</sup> Clifford Rostomily,<sup>1</sup> Pamela Troisch,<sup>1</sup> Jing Zhou,<sup>13</sup> Sean Mackay,<sup>13</sup> Quinn DeGottardi,<sup>14</sup> Damon H. May,<sup>14</sup> Ruth Taniguchi,<sup>14</sup> Rachel M. Gittelman,<sup>14</sup> Mark Klinger,<sup>14</sup> Thomas M. Snyder,<sup>14</sup> Ryan Roper,<sup>1</sup> Gladys Wojciechowska,<sup>1,15</sup>















Cases

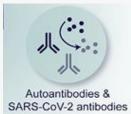


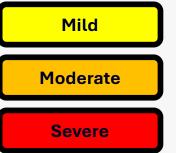










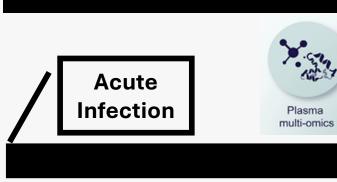




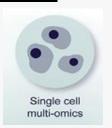




Cases

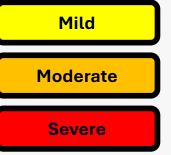
























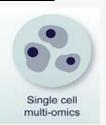




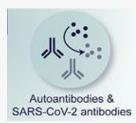


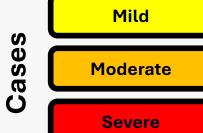








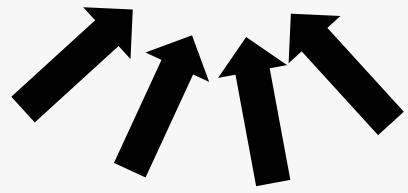




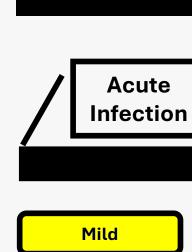




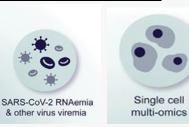








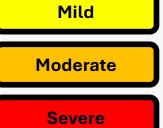








2-3 months after symptom onset



Cases

**Healthy Controls** 









**Pre-existing Type** 2 Diabetes

> SARS-CoV-2 **RNAemia at Acute** Infection

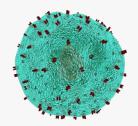


Autoantibodies **During** Acute Infection

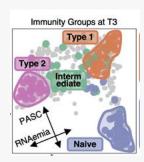
## **Additional Findings**



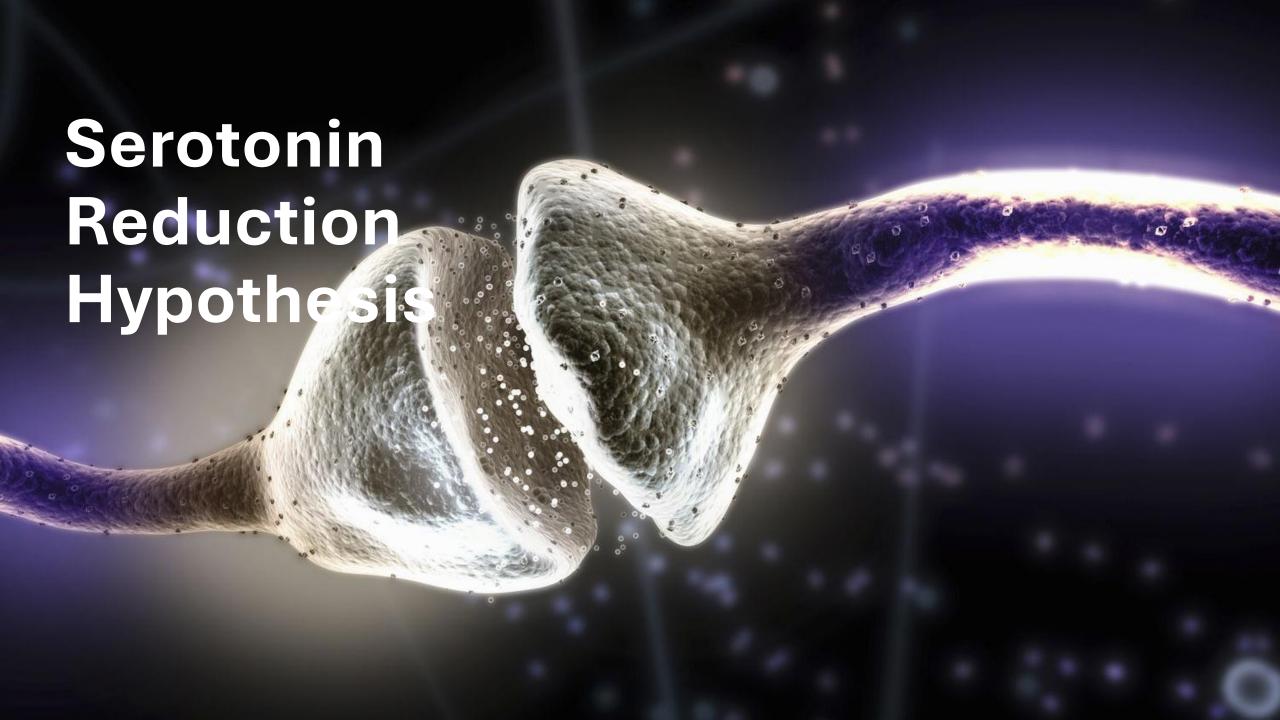
 Markers of post-COVID-19 conditions are mostly present at time of acute infection and many are no longer detectable at the time of diagnosis.



 Specific T-cell subpopulations are associated with specific post-COVID-19 conditions (e.g. gastrointestinal symptoms).

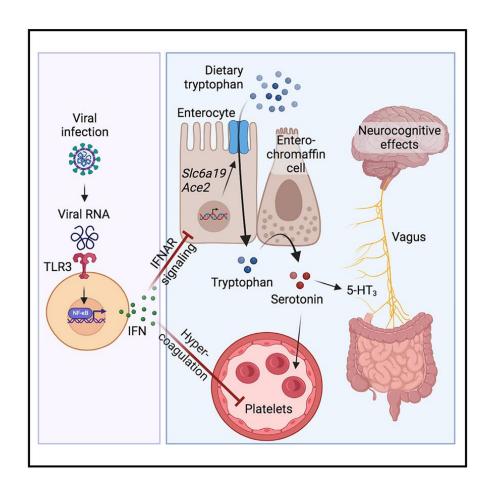


 Distinct immune endotypes or "signatures" at the time of post-COVID-19 condition were present with various expressions of immune cell sub-types.





# Serotonin reduction in post-acute sequelae of viral infection



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#### In brief

Post-viral syndromes are associated with serotonin reduction, which may contribute to the neurological and cognitive symptoms seen in individuals with Long COVID.

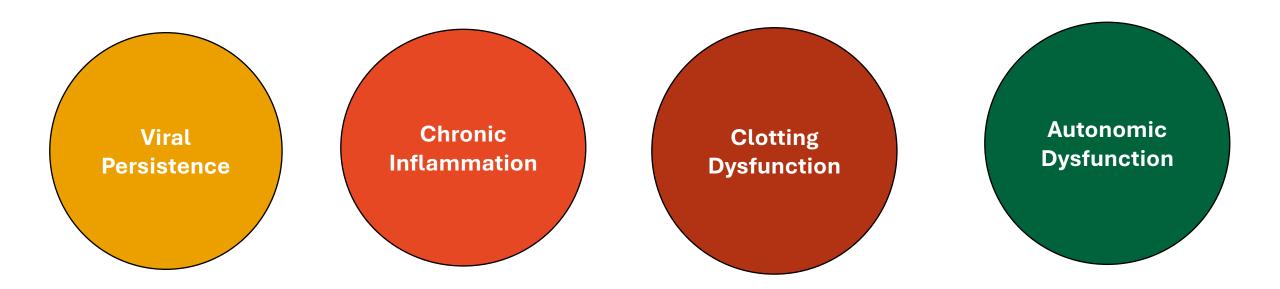
Reactivation Persistent **Impacts of** of underlying reservoirs of pathogens acute infection on SARS-CoV-2 microbiome in tissues Post-**Dysfunctional Immune** COVID-19 nerve or brain **Dysregulation Conditions** signaling Microvascular blood clotting **Autoimmunity** and endothelial dysfunction

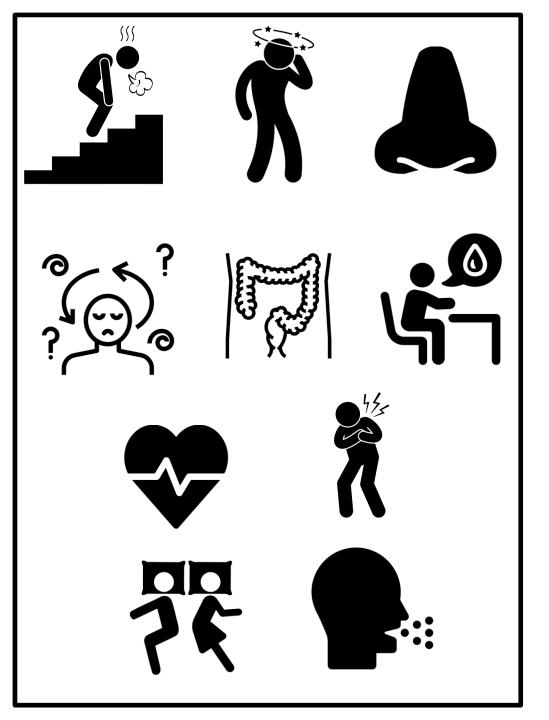
Persistent reservoirs of SARS-CoV-2 in tissues

Immune Dysregulation

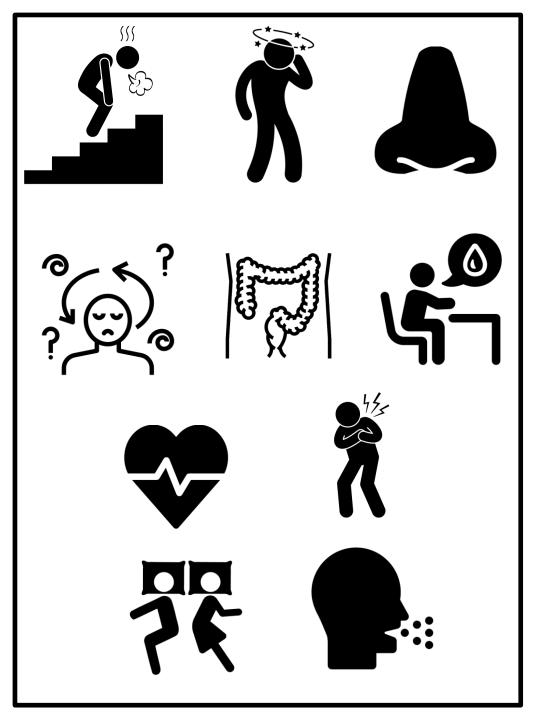
Microvascular blood clotting and endothelial dysfunction

Dysfunctional nerve or brain signaling





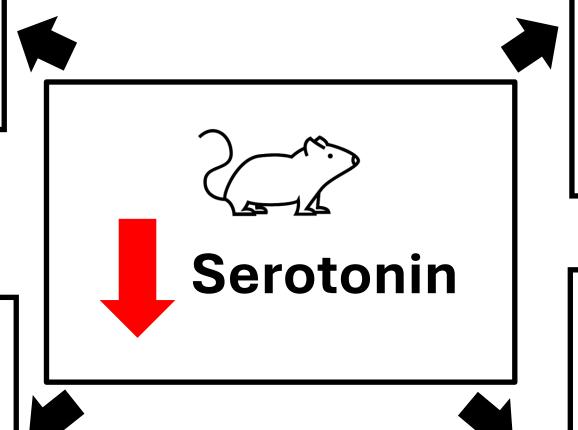
- Performed plasma
   metabolomics among
   patients with long COVID.
- 2. Metabolite profile distinct from those who recovered symptom-free.
- 3. Serotonin levels most notably depleted in acute and post-acute COVID-19.



# Associated with Lower Serotonin Levels



Serotonin decreases was seen in SARS-CoV-2 and other systemic virus models.





Persistent viral infection was associated with higher levels of interferon-stimulated genes also seen in long COVID patients.

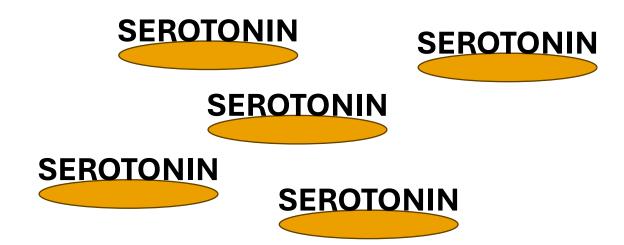


Most serotonin in our bodies is produced in the GI tract from dietary tryptophan; people with acute COVID-19 and long COVID have reduce plasma tryptophan levels.



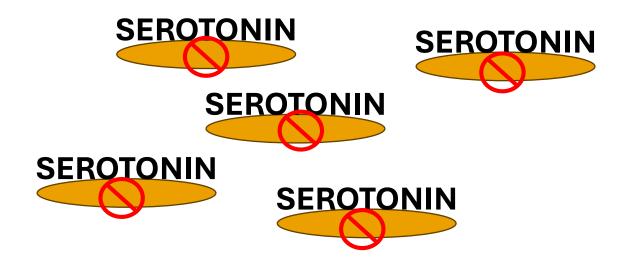
Serotonin levels recovered in those that cleared infection but not those with chronic infection or persistent inflammation.





Viral inflammation drives platelet hyperactivation and consumption.







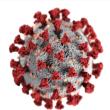


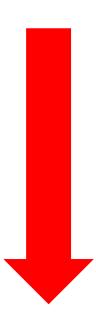




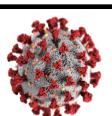


Viral inflammation drives platelet hyperactivation.





Viral inflammation drives platelet hyperactivation.







# Serotonin

- Hippocampus responsible for shortterm memories and requires serotonin as a key player for its function.
- Serotonin in the brain is unaffected by viral inflammation so peripheral serotonin levels associated with cognitive impairment.
- Reductions of serotonin impact vagal neuros and then go on to affect the hippocampus.







### The NEW ENGLAND JOURNAL of MEDICINE

# Perspective october 12, 2023

#### Do Pandemics Ever End?

Joelle M. Abi-Rached, M.D., Ph.D., and Allan M. Brandt, Ph.D.

"The declaration of the end of a pandemic therefore marks a critical point when the value of a human life becomes a variable of actuarial significance – in other words, when a government determines that the social, economic, and political costs of saving a life exceed the benefits of doing so....

It is neither epidemiology nor any political declaration that determines the end of a pandemic, but the normalization of mortality and morbidity by means of a disease's routinization and endemicization – what in the context of the COVID-19 pandemic has been called 'living with the virus.' "

~ Joelle M. Abi-Rached, MD, PhD and Allan M. Brandt, PhD





#### **Acute COVID-19**

Asymptomatic

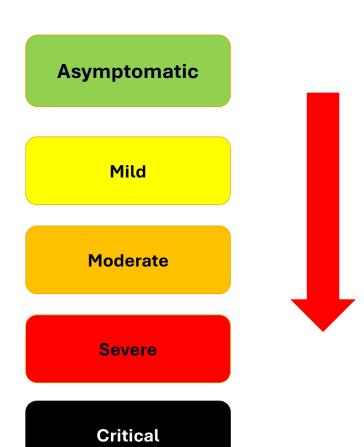
Mild

Moderate

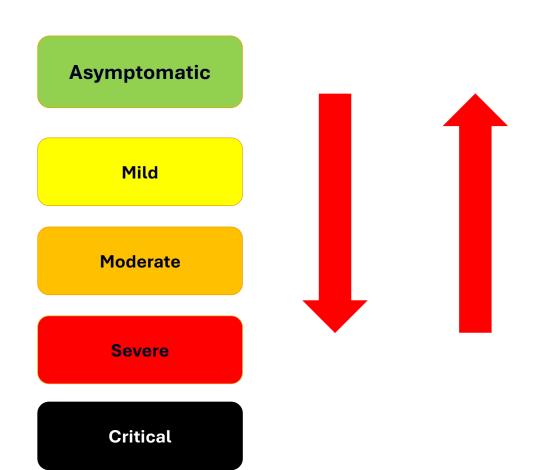
Severe

Critical

#### **Acute COVID-19**



#### **Acute COVID-19**



# Post COVID-19 conditions become more common.

# Risk of infection and severe acute COVID-19



# Risk of post-COVID-19 conditions

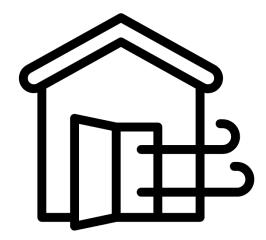


Stay up to date with recommended vaccinations



Stay up to date with recommended vaccinations









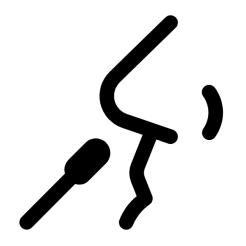
Stay up to date with recommended vaccinations







Get treated early if eligible



## Questions?

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## Acknowledgements - Noun Project

- United States by Joel Wisneski
- Exhaustion by Gan Khoon Lay
- Headache by b farias
- Dizzy by Gan Khoon Lay
- Cough by Asep Yopie Hardi Noer
- Shortness of breath by Gan Khoon Lay
- Chest pain by Gan Khoon Lay
- Nose by Xinh Studio
- Insomnia by Ayub Irawan
- Depression by Narakorn Chanchittakarn
- Globe by Nick Novell
- Heart by Academic Technologies
- Lungs by Karina
- Kidney by Mello
- Red blood cells by Lucas Helle
- Colon by Turkkub

- Joint by Vectors Market
- Brain by Cedric Villain
- Pancreas by Suncheli Project
- Group of people Oksana Latysheva
- Disorientation by Nithinan Tatah,
   TH
- Couple in bed by Alvaro Cabrera
- Heart by AmruID
- Thirst by Adrien Coquet
- Step by Step by Adrien Coquet
- Family by TukTuk Design
- Gender by Three Six Five
- Antibody by Lea Lortal
- Immune Cell by Ims.icon
- Bacteria by myiconfinder
- Epithelium by dDara

- Clogged Artery by Peter Van Driel
- Neuron by Lea Lortal
- Sneeze by Akhmad Taufiq
- Adult by Alexander Gruzdev
- Mouse by Iconic
- DNA by pictranoosa
- Stomach by Podgornaia Elena
- Swab by The Iconz
- Face Mask by Milinda Courey
- Ventilation by Andre Buand
- Pills by Verrena

#### **Additional Resources**

- CDC timeline of COVID-19 events: <a href="https://www.cdc.gov/museum/timeline/covid19.html">https://www.cdc.gov/museum/timeline/covid19.html</a>
- World Health Organization clinical case definition of post COVID-19 condition by Delphi
  Consensus: <a href="https://www.who.int/publications/i/item/WHO-2019-nCoV-Post\_COVID-19\_condition-Clinical\_case\_definition-2021.1">https://www.who.int/publications/i/item/WHO-2019-nCoV-Post\_COVID-19\_condition-Clinical\_case\_definition-2021.1</a>
- National Institute for Health and Care Excellence (NICE) Long COVID-19 Guidelines:
   https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-51035515742
- European Centre for Disease Prevention and Control systematic review of post COVID-19 condition prevalence: <a href="https://www.ecdc.europa.eu/sites/default/files/documents/Prevalence-post-COVID-19-condition-symptoms.pdf">https://www.ecdc.europa.eu/sites/default/files/documents/Prevalence-post-COVID-19-condition-symptoms.pdf</a>
- Department of Health and Human Services: Services and Supports for Longer-Term Impacts of COVID-19: <a href="https://www.covid.gov/assets/files/Services-and-Supports-for-Longer-Term-Impacts-of-COVID-19-08012022.pdf">https://www.covid.gov/assets/files/Services-and-Supports-for-Longer-Term-Impacts-of-COVID-19-08012022.pdf</a>
- Department of Health and Human Services: National Research Action Plan on Long COVID: <a href="https://www.covid.gov/assets/files/National-Research-Action-Plan-on-Long-COVID-08012022.pdf">https://www.covid.gov/assets/files/National-Research-Action-Plan-on-Long-COVID-08012022.pdf</a>
- COVID.gov: What is Long COVID?: <a href="https://www.covid.gov/longcovid/definitions">https://www.covid.gov/longcovid/definitions</a>
- Infectious Disease Society of America: Post-COVID Conditions: <a href="https://www.idsociety.org/covid-19-real-time-learning-network/disease-manifestations--complications/post-covid-syndrome">https://www.idsociety.org/covid-19-real-time-learning-network/disease-manifestations--complications/post-covid-syndrome</a>

#### **Additional Resources**

- CDC: Post-COVID Conditions: Information for Healthcare Providers: <a href="https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html">https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html</a>
- CDC: Post-COVID Conditions: CDC Science: <a href="https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-science.html">https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-science.html</a>
- CDC Datasets: Post-COVID Conditions: <a href="https://data.cdc.gov/NCHS/Post-COVID-Conditions/gsea-w83">https://data.cdc.gov/NCHS/Post-COVID-Conditions/gsea-w83</a>
- Kaiser Family Foundation: Long COVID: What do the Latest Data Show? <a href="https://www.kff.org/policy-watch/long-covid-what-do-latest-data-show/#:~:text=As%20of%20January%2016%2C%202023%2C%2015%25%20of%20all%20adults">https://www.kff.org/policy-watch/long-covid-what-do-latest-data-show/#:~:text=As%20of%20January%2016%2C%202023%2C%2015%25%20of%20all%20adults</a>, are%20no%20longer%20reporting%20symptoms.
- CDC COCA Call: Evaluating and Supporting Children and Adolescents Presenting with Post-COVID Conditions: <a href="https://emergency.cdc.gov/coca/calls/2023/callinfo\_022323.asp">https://emergency.cdc.gov/coca/calls/2023/callinfo\_022323.asp</a>
- CDC COCA Call: Evaluating and Supporting Patients Presenting with Cardiovascular Symptoms
   Following COVID: <a href="https://emergency.cdc.gov/coca/calls/2022/callinfo\_092022.asp">https://emergency.cdc.gov/coca/calls/2022/callinfo\_092022.asp</a>
- CDC COCA Call: What Clinicians Need to Know about Multisystem Inflammatory Syndrome in Children: <a href="https://emergency.cdc.gov/coca/calls/2022/callinfo\_021022.asp">https://emergency.cdc.gov/coca/calls/2022/callinfo\_021022.asp</a>
- CDC COCA Call: Updates on Multisystem Inflammatory Syndrome in Children (MIS-C): Epidemiology, Case Definition, and COVID-19 Vaccination: <a href="https://emergency.cdc.gov/coca/calls/2022/callinfo\_120822.asp">https://emergency.cdc.gov/coca/calls/2022/callinfo\_120822.asp</a>

#### **Additional Resources**

- CDC COCA Call: Evaluating and Supporting Patients Presenting with Cognitive Symptoms Following COVID: <a href="https://emergency.cdc.gov/coca/calls/2022/callinfo\_050522.asp">https://emergency.cdc.gov/coca/calls/2022/callinfo\_050522.asp</a>
- CDC COCA Call: Evaluating and Supporting Patients Presenting with Fatigue Following COVID-19: <a href="https://emergency.cdc.gov/coca/calls/2021/callinfo\_093021.asp">https://emergency.cdc.gov/coca/calls/2021/callinfo\_093021.asp</a>
- CDC COCA Call: Evaluating and Caring for Patients with Post-COVID Conditions: <a href="https://emergency.cdc.gov/coca/calls/2021/callinfo\_061721.asp">https://emergency.cdc.gov/coca/calls/2021/callinfo\_061721.asp</a>
- CDC COCA Call: Treating Long COVID: Clinician Experience with Post-Acute COVID-19 Care: <a href="https://emergency.cdc.gov/coca/calls/2021/callinfo\_012821.asp">https://emergency.cdc.gov/coca/calls/2021/callinfo\_012821.asp</a>
- CDC COCA Call: Evaluating and Supporting Patients with Long COVID in Returning to Work: https://emergency.cdc.gov/coca/calls/2023/callinfo\_061523.asp

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#### **Extra Slides**



#### Original research



# Long COVID (post-COVID-19 condition) in children: a modified Delphi process

Terence Stephenson , <sup>1</sup> Benjamin Allin, <sup>2</sup> Manjula D Nugawela, <sup>1</sup> Natalia Rojas, <sup>1</sup> Emma Dalrymple, <sup>1</sup> Snehal Pinto Pereira , <sup>3</sup> Manas Soni, <sup>4</sup> Marian Knight , <sup>2</sup> Emily Y Cheung, <sup>1</sup> Isobel Heyman , <sup>1</sup> CLoCk Consortium, Roz Shafran

#### Original research



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#### History of confirmed SARS-CoV-2 infection



One or more persisting physical symptoms for at least 12 weeks from onset of COVID-19; may continue or develop after infection



Cannot be explained by an alternative diagnosis



Symptoms impact everyday functioning

>335,000,000

US Population (as of July 2023)



>103,000,000

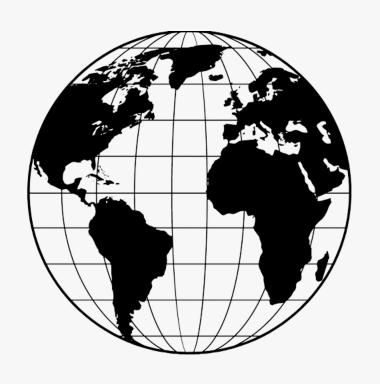
confirmed cases of COVID-19 (as of February 2023)



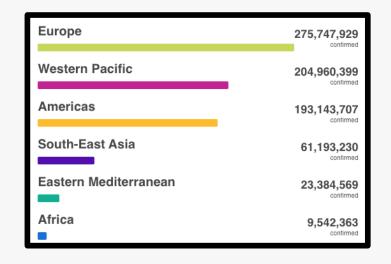
- Case counts are not an accurate assessment of community burden
- Changes in testing behavior and decreased access to testing

 Ending of WHO and US federal government PHE changed reporting requirements

 CDC seroprevalence study suggest that 78% of adults and older adolescents have had infection by December 2022

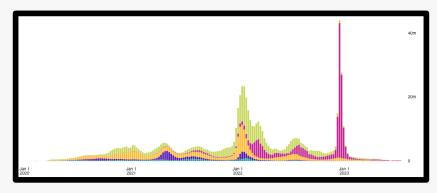


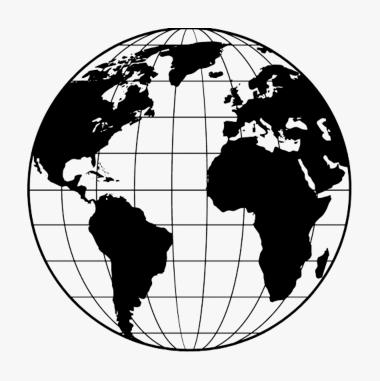
• Higher prevalence of post-COVID-19 conditions in Asia (51%) than in Europe (44%) or USA (31%)



 Higher prevalence of post-COVID-19 conditions in Asia (51%) than in Europe (44%) or USA (31%)\*

\*This may be due, in part, to reporting and testing biases.





- Higher prevalence of post-COVID-19 conditions in Asia (51%) than in Europe (44%) or USA (31%)
- Symptoms reported for post-COVID-19 conditions appears similar among studies done outside of the US

### A clinical case definition of post-COVID-19 condition by a Delphi consensus

Joan B Soriano, Srinivas Murthy, John C Marshall, Pryanka Relan, Janet V Diaz, on behalf of the WHO Clinical Case Definition Working Group on Post-COVID-19 Condition



Multispecialty Clinicians



**COVID-19 Survivors** 



Researchers



**Policymakers** 



Representation From All WHO Regions and World Bank Income Levels

#### Definition of a post-COVID-19 condition:



History of probable or confirmed SARS-CoV-2 infection



Symptoms usually present at 3 months from onset of COVID-19 lasting at least 2 months



Cannot be explained by an alternative diagnosis

Impact the everyday function of the individual

- Impact the everyday function of the individual
- Can be new following recovery from acute COVID-19 or carry over from the initial infection

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- Impact the everyday function of the individual
- Can be new following recovery from acute COVID-19 or carry over from the initial infection
- May fluctuate or relapse over time
- No minimum number of symptoms required for the diagnosis
- A separate definition for children has been developed

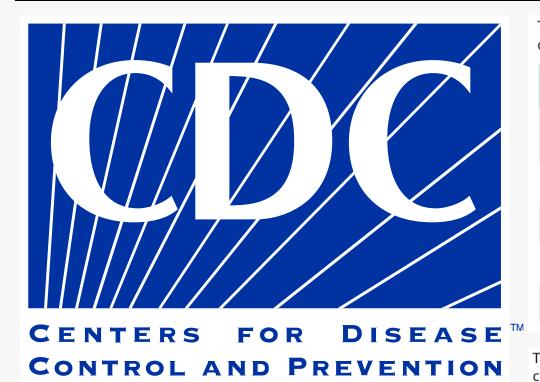


Table 1a. Basic diagnostic laboratory testing to consider for patients with post-COVID conditions

Category	Laboratory Tests
Blood count, electrolytes, and renal function	Complete blood count with possible iron studies to follow, basic metabolic panel, urinalysis
Liver function	Liver function tests or complete metabolic panel
Inflammatory markers	C-reactive protein, erythrocyte sedimentation rate, ferritin
Thyroid function	TSH and free T4
Vitamin deficiencies	Vitamin D, vitamin B12

Table 1b. Specialized diagnostic laboratory testing to consider for patients with post-COVID conditions

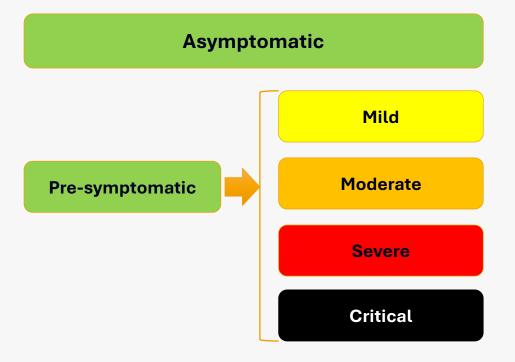
Category	Laboratory Tests
Rheumatological conditions	Antinuclear antibody, rheumatoid factor, anti-cyclic citrullinated peptide, anti-cardiolipin, and creatine phosphokinase
Coagulation disorders	D-dimer, fibrinogen
Myocardial injury	Troponin
Differentiate symptoms of cardiac versus pulmonary origin	B-type natriuretic peptide

https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html

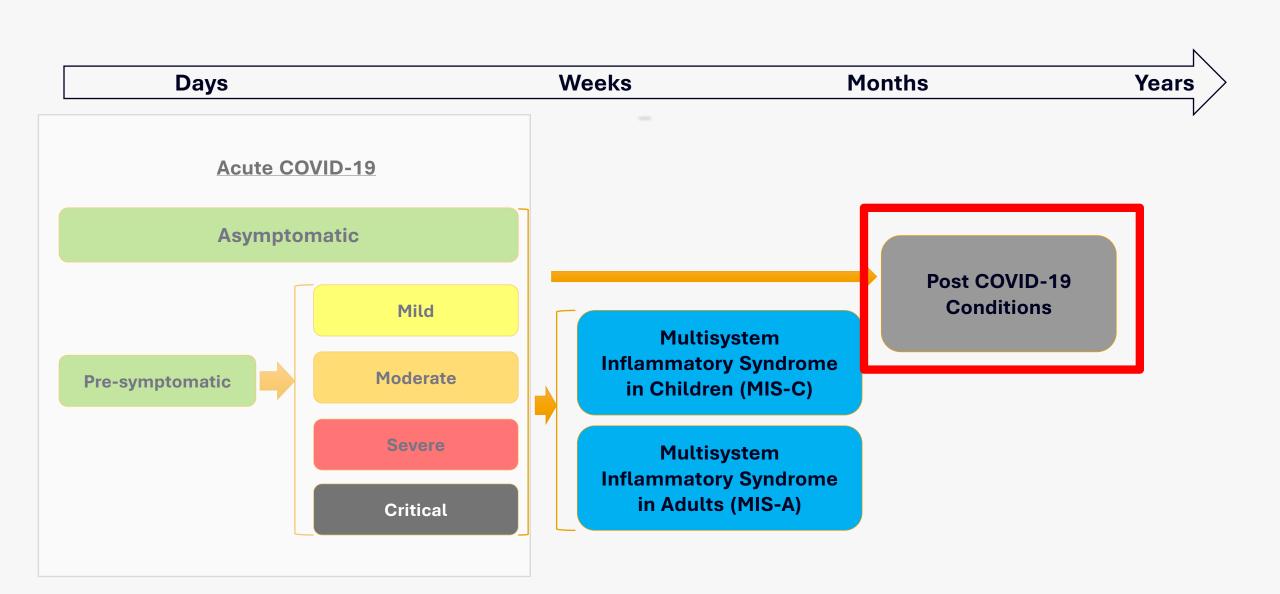


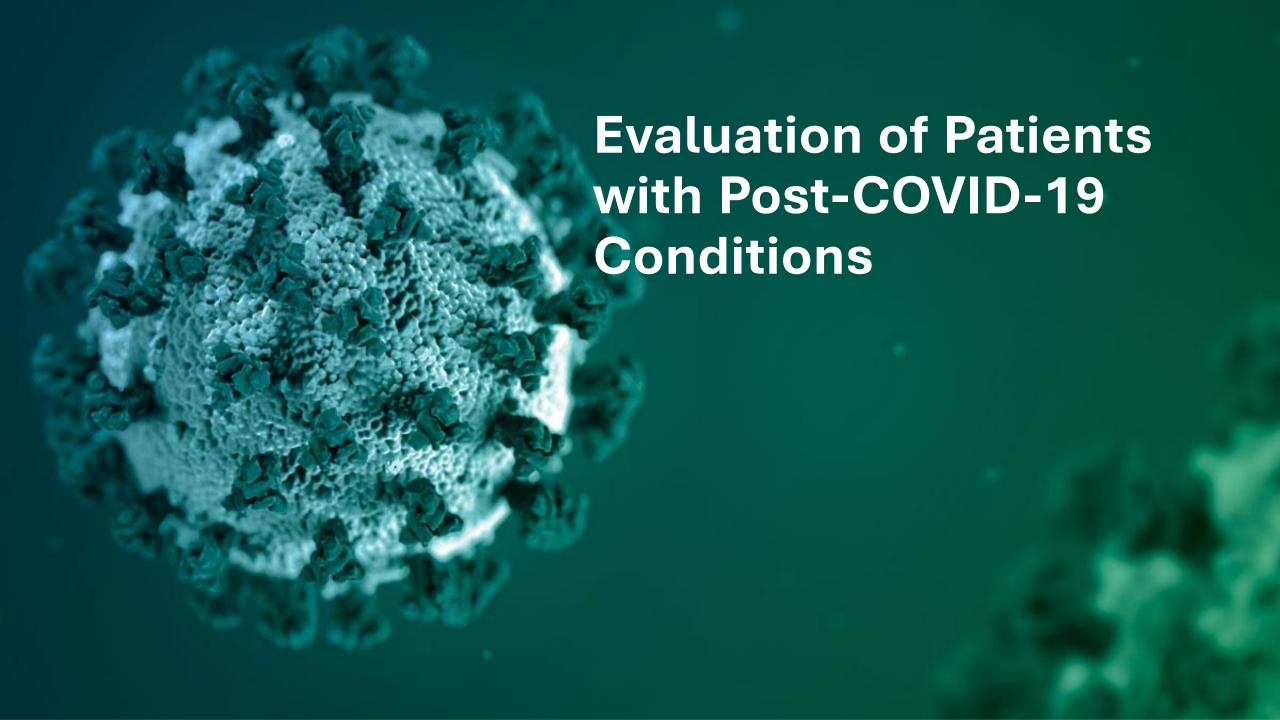
Days Weeks Months Years

#### **Acute COVID-19**



**Years** Days Weeks **Months Acute COVID-19 Asymptomatic Post COVID-19** Conditions Mild Multisystem **Inflammatory Syndrome** Moderate **Pre-symptomatic** in Children (MIS-C) Severe Multisystem **Inflammatory Syndrome** in Adults (MIS-A) Critical





# When evaluating a patient in clinic for a post-COVID-19 condition...





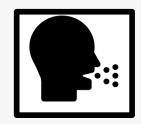
# determining where to start can feel daunting.











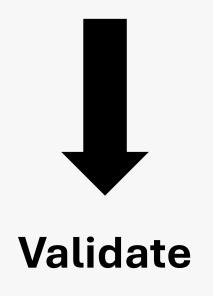








## There is currently no gold standard approach to evaluation.



Targeted Evaluations

Evaluate for life threatening conditions

**Validate** 



Targeted Evaluations

Evaluate for life threatening conditions

**Validate** 

Targeted Evaluations

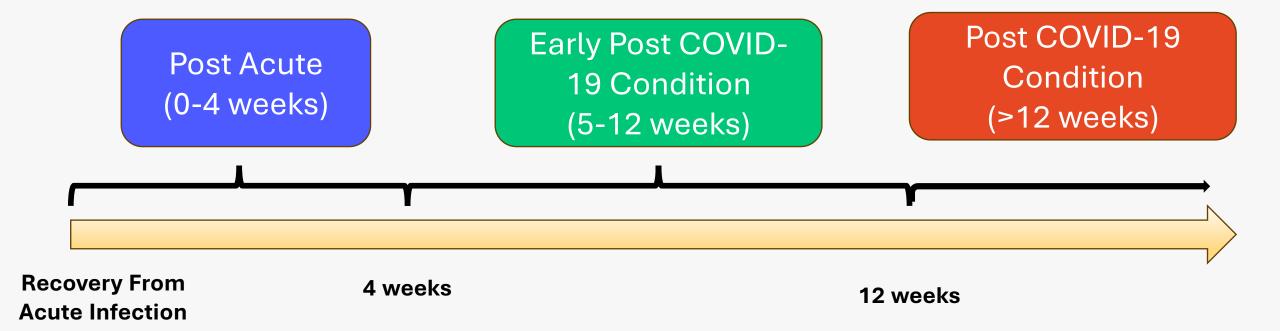
Evaluate for life threatening conditions

**Validate** 

Targeted Evaluations

Evaluate for life threatening conditions

Thinking about acute infection recovery in phases.



#### 60-day Outcomes Among Patients Hospitalized with COVID-19

- Early in the pandemic before vaccines and current subvariants
- 12.6% were discharged to skilled nursing or rehabilitation facility
- 6.7% died within 60 days (10.4% of those requiring ICU)
- 15.1% were re-hospitalized

### Invite patients to tell their story.

#### Important history details:

- 1. Acute COVID-19 history
- 2. Symptom onset and duration
- 3. Impact on daily activities



Evaluate for life threatening conditions and common actionable diagnoses.



#### Understanding the implications of broad testing

- Increased risk of incidental findings
- Patient anxiety about abnormal results without clinical significance
- Risk/harm associated with invasive or radiologic procedures
- Cost and time to the patient for appointments and workup

 There is no definitive single or collective tests to diagnose post-COVID-19 conditions

• SARS-CoV-2 testing may be warranted to rule out re-infection.

May consider expanded testing for those with symptoms beyond 12 weeks



Decision to not do additional testing or the absence of abnormal findings should not lead to dismissal of patient's symptoms.



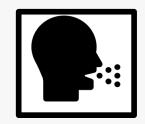
## Symptom and Diagnosis Focused Management















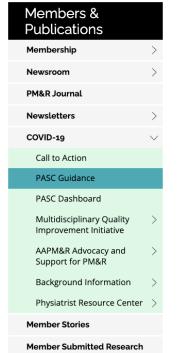






Home / Members & Publications / COVID-19 / PASC Guidance

#### **PASC Consensus Guidance**



The Academy has undertaken comprehensive efforts to support our call for a national plan to address Post-Acute Sequelae of SARS-CoV-2 infection (PASC or Long COVID) and the 3 to 10 million Americans it is affecting.

AAPM&R understands the need for focused, meaningful, and ongoing clinical exchange between the medical community to assess and implement appropriate clinical practice for treating and following all long-term COVID issues, not just those issues requiring PM&R intervention, is necessary. Therefore, AAPM&R has gathered a multidisciplinary collaborative with goals to foster engagement and share experiences to propel the health system towards defining standards of care for persons experiencing Long COVID-19/PASC.

#### **Published Guidance**

The collaborative is working to publish guidance on a rolling basis. Writing groups are working within a consensus process with 3 waves. All published guidance will be linked here as it becomes available.



- Neurological Symptoms
- Automatic Dysfunction
- Fatigue
- Cognitive Symptoms
- Cardiovascular
   Complications
- Breathing Discomfort
- Pediatrics

## Evaluating and Supporting Patients with Long COVID in Returning to Work

Print





### Evaluating and Supporting Patients with Long COVID in Returning to Work

Clinician Outreach and Communication Activity (COCA) Call Thursday, June 15, 2023



Low and slow

Gradual increases

Titrated work hours

• Holistic support and validation of symptoms is a key aspect of care; this can include referral to patient support services such as social work where needed

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  - Individuals with disabilities
  - People experiencing homelessness or people in correctional facilities
  - Individuals with substance use disorders

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- Removing barriers to accessing care including the availability of telehealth visits to those with internet access

### Thank you for joining us and being part of the Power of Providers!

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