

Overview of Post acute COVID-19

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OVERVIEW OF COVID-19 DEFINITIONS

- Acute infection due (SARS-CoV-2) can present as a spectrum of illness and for it, the widely accepted categorization for disease severity that currently exists include asymptomatic, mild, moderate, severe, and critical disease.
 - Recently, clinicians have begun to observe **prolonged sequelae of acute COVID-19**.
- Currently, there is **no universally accepted time period** that defines the beginning of the postacute period.

LASTING LONG-TERM EFFECTS OF COVID-19:

Prolonged symptoms = "LONG COVID"

Those experiencing
symptoms:
"LONG HAULERS"



↳ a.k.a. "LONG-TERM COVID"
"CHRONIC COVID"
"POST COVID SYNDROME"



REMEMBER:

- * RESEARCH on COVID-19's PROLONGED EFFECTS HAVE ONLY JUST BEGUN
- * NO FIRM CONCLUSIONS
- * STUDIES REPRESENT ONLY INITIAL FINDINGS





**BRITISH NATIONAL INSTITUTE for
HEALTH and CARE EXCELLENCE**
(aka "NICE")

3 STAGES of COVID-19 RECOVERY:

ACUTE COVID-19

WITHIN 4 WEEKS AFTER DIAGNOSIS

ONGOING COVID-19

4 to 12 WEEKS AFTER DIAGNOSIS

LONG COVID-19

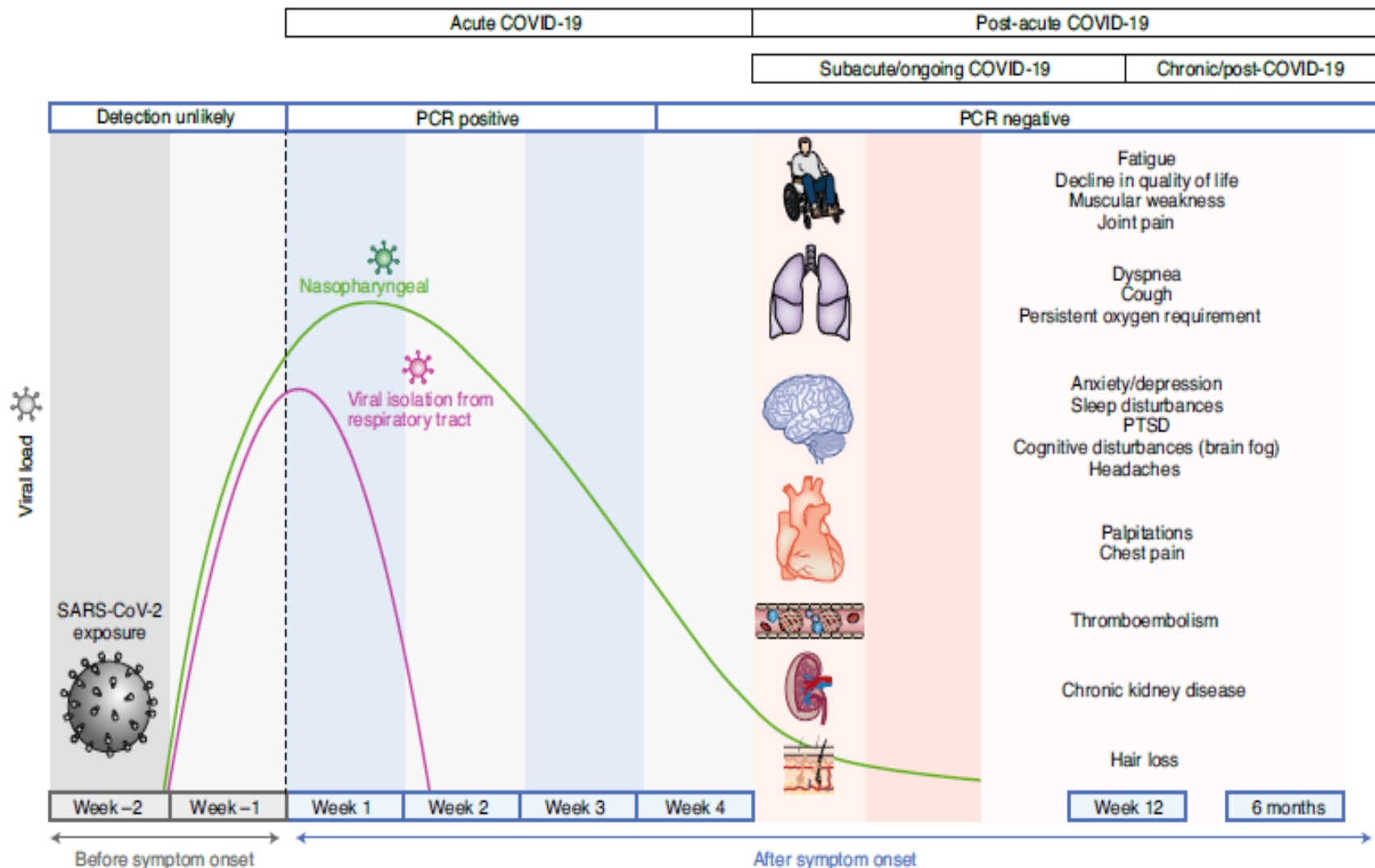
OVER 12 WEEKS AFTER DIAGNOSIS

Timeline of post-acute COVID-19

REVIEW ARTICLE | FOCUS

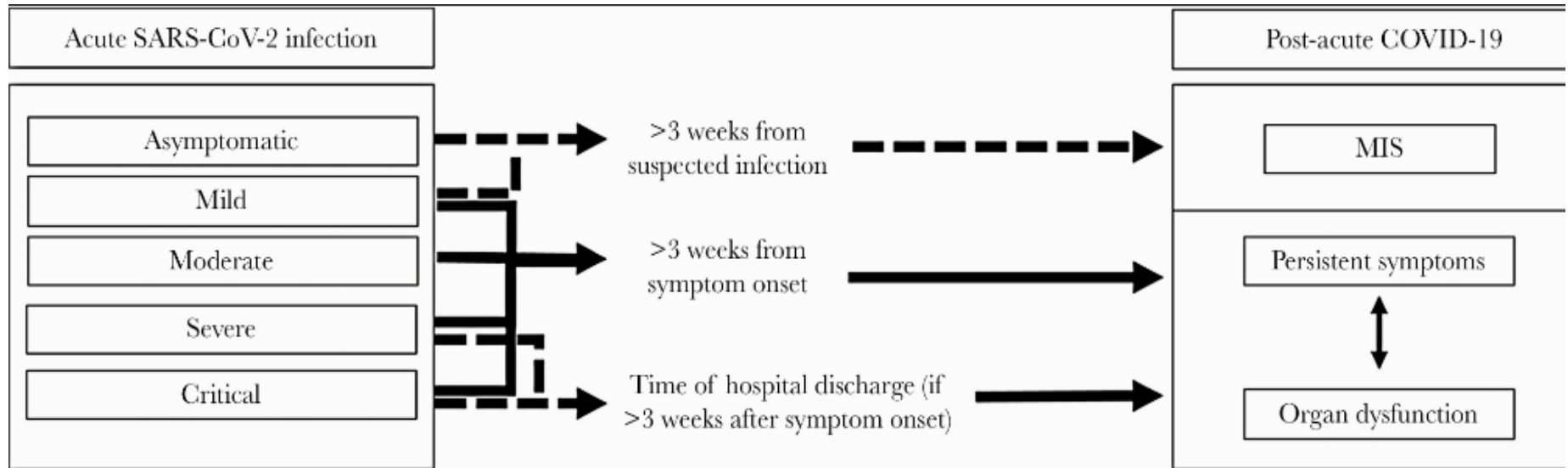
<https://doi.org/10.1038/s41591-021-01283-z>

NATURE MEDICINE



Postacute COVID-19: An Overview and Approach to Classification

- Studies propose that the postacute period for COVID-19 **starts 3 weeks after symptom onset**;
- And “**chronic COVID-19**” is defined as persistent symptomatology extending **beyond 12 weeks** after initial symptoms.



There is likely a relationship between **organ dysfunction and persistent symptoms** that is not yet completely understood.

practical and useful clinical definition

- 1) from a clinical perspective, because the majority of infections due to SARS-CoV-2 are asymptomatic or mild, **3 weeks** is a reasonable time frame to define **recovery from a viral respiratory illness**.
 - 2) **replication-competent virus** has not been recovered after **10 days** following symptom onset in mild to moderate cases or after **20 days** even in severe or critical.
 - 3) the median **duration of (PCR) positivity** in symptomatic patients is **24 days**, and the mean duration among asymptomatic patients is 24.5 days.
- ✓ One specific modification we propose to the definitions is that for patients who **remain hospitalized at 3 weeks after symptom onset**, the postacute period start **when the patient is discharged from inpatient acute care**.

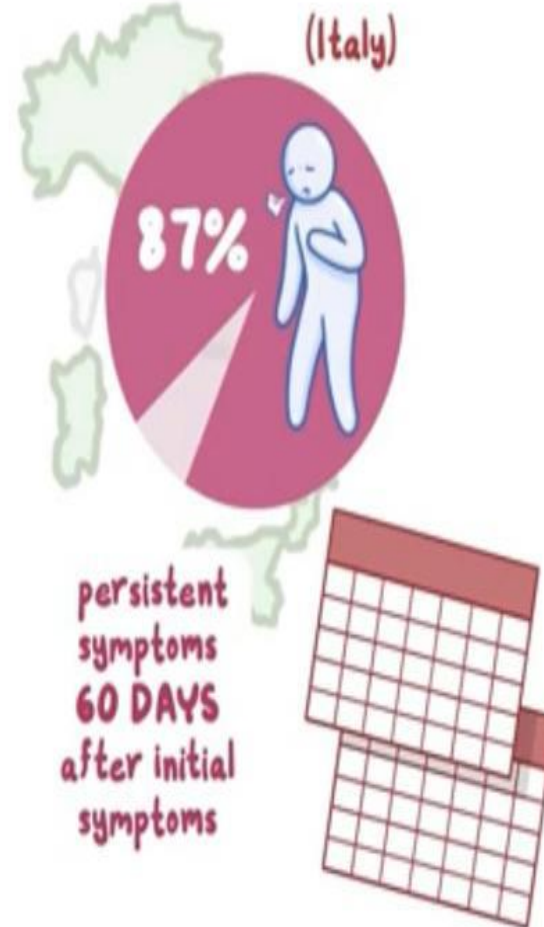
NICE guideline on long COVID

- **postacute manifestations is divided into 3 categories:**
 - (1) residual symptoms that persist after recovery from acute infection;
 - (2) organ dysfunction that persists after initial recovery;
 - (3) new symptoms or syndromes that develop after initial asymptomatic or mild infection.
-
- A recent US study found that only **65% of people had returned to their previous level of health 14-21 days** after a positive test.

www.thelancet.com/respiratory Vol 9 February 2021

* LONG-TERM COMPLICATIONS ARE FAIRLY COMMON

(OCT 2020, United Kingdom)
**NATIONAL INSTITUTE
for HEALTH RESEARCH:**



CAUSES of CONTINUED SYMPTOMS:

CONTINUATION
OF THE INITIAL
COVID-19
INFECTION?

OR

ENTIRELY NEW
YET SEPARATE
POST-COVID-19
SYNDROME?



There are a few hypotheses proposed which could be contributing to the prolongation of COVID-19 symptoms.

POTENTIAL MECHANISMS OF POSTACUTE COVID-19

- the etiology of postacute COVID-19 symptoms is likely multifactorial.
- ✓ the virus's potential for **direct neuro-invasion**: lead to persistent neuropsychiatric sequelae.
- ✓ The well-described virus-induced "**cytokine storm**" and dysregulated immune response.
- ✓ Additionally, replication-competent virus is rarely recovered beyond 20 days after symptom onset; this suggests that persistent symptoms are driven primarily **by immunological phenomena**.

Ackermann M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in

Coivd-19. *NEJM* 2020; 383:120–128

POTENTIAL MECHANISMS OF POSTACUTE COVID-19

- ✓ **lingering virus continues** to be present in immunologically privileged sites within the body, where it can be difficult for the immune system to eradicate
- ✓ **Persistent viraemia** due to weak or absent antibody response
- ✓ **relapse or reinfection**
- ✓ Finally, in a postmortem study of histologic features of peripheral lung tissue, features of **severe endothelial injury along with diffuse thrombosis with microangiopathy** were observed. Therefore, endothelial injury and ongoing dysfunction might also play a role in postacute organ dysfunction



Social and cultural considerations

- Covid-19 is **more common and has a worse prognosis** in the acute phase in people who are **poor, elderly**, and from certain minority **ethnic groups** (notably black, south Asian, and Jewish).
- **It is too early to say whether these sociodemographic patterns persist in post-acute covid-19.**
- Many have **comorbidities** including diabetes, hypertension, kidney disease, or ischemic heart disease. Some have experienced **family bereavements** as well as job losses and consequent financial stress and food poverty.

Acute Complications of COVID-19

Neuropsychiatric

- Cerebrovascular accident
- Large vessel disease
- Encephalopathy, delirium
- Anosmia, ageusia

Respiratory

- Pneumonia
- Hypoxemic respiratory failure, ARDS

Cardiovascular

- Arrhythmia
- Myocarditis

Hematologic, Vascular

- Coagulopathy
- Thrombotic events

Renal

- Acute kidney injury

Gastrointestinal, Hepatobiliary

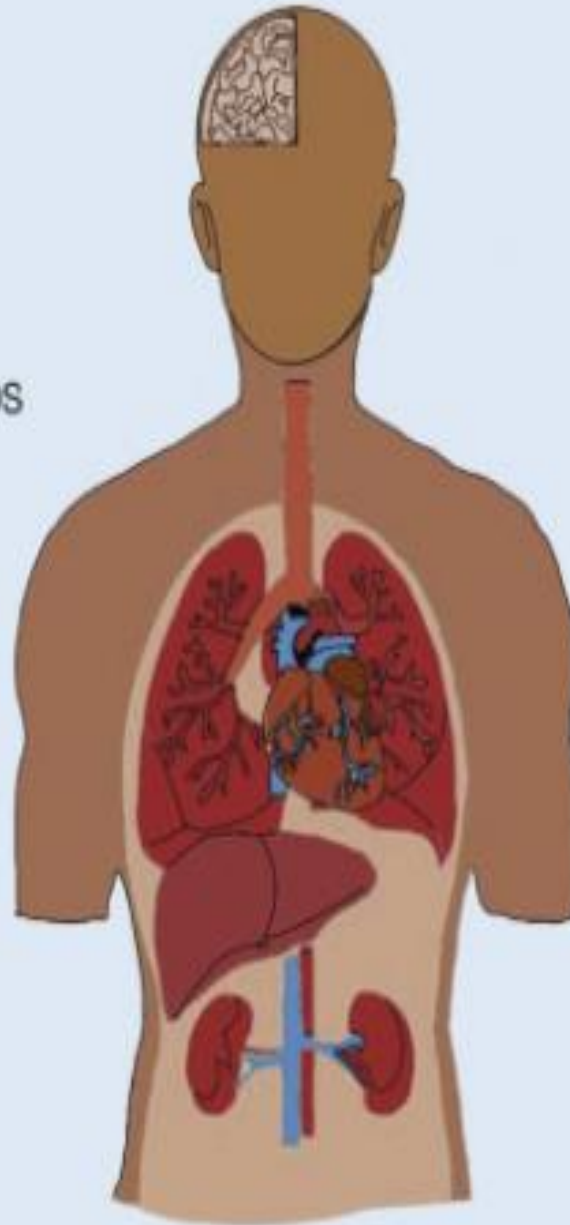
- Diarrhea
- Acute liver injury

Musculoskeletal

- Rhabdomyolysis

Dermatologic

- Livedo reticularis
- Maculopapular or urticarial rash



Post-COVID Symptoms, Sequelae

Neuropsychiatric

- Neurocognitive deficits
- Mood changes
- Sensory & motor deficits
- Chronic fatigue and sleep disruption

Respiratory

- Persistent dyspnea
- Chronic cough

Cardiovascular

- Chest pain
- Palpitations

Hematologic, Vascular

- Persistent or recurrent thrombosis

Renal

- Chronic kidney disease

Gastrointestinal, Hepatobiliary

- Persistent liver dysfunction

Musculoskeletal

- Muscle wasting
- Weakness
- Deconditioning

Dermatologic

- Hair loss

PROLONGED SYMPTOMS:

CARDIOPULMONARY:

- * SHORTNESS of BREATH
- * COUGH
- * CHEST PAIN



(United Kingdom)



GENERAL
MEDICINE
PATIENTS



INTENSIVE
CARE
PATIENTS



shortness of breath
4-8 WEEKS
after discharge

(China)



OVER 50% performed
worse on **SPIROMETRY**
pulmonary function tests
30 DAYS after discharge

78%

(Germany, using MRI)



CARDIAC ISSUE
(potentially from COVID)
2-3 MONTHS
after diagnosis



60%

**MYOCARDIAL
INFLAMMATION**

PROLONGED SYMPTOMS:

COMMON NEUROLOGICAL ISSUES 3 MONTHS AFTER DIAGNOSIS:

- * HEADACHES
- * MOBILITY CHALLENGES
- * SENSORY LOSS
 - ↳ vision
 - ↳ hearing
 - ↳ taste
 - ↳ smell
 - ↳ numbness
- * MEMORY LOSS
- * TREMORS
- * COGNITIVE IMPAIRMENT



More than 50 Long-term effects of COVID-19: a systematic review and meta-analysis

- In a Systematic Reviewers and Meta-analysis, from a total of 18,251 publications, The prevalence of **55 long-term effects** was estimated, and 47,910 patients were included. The follow-up time ranged from **14 to 110 days** post-viral infection.
- It was estimated that **80% of the patients** that were infected with SARS-CoV-2 developed **one or more long-term symptoms**. The five most common symptoms were **fatigue** (58%), **headache** (44%), **attention disorder** (27%), **hair loss** (25%), and **dyspnea** (24%).

doi: <https://doi.org/10.1101/2021.01.27.21250617>; January 30, 2021.

Another survey study from the **U.K** evaluated **100** patients at a mean of **48 days** after hospital discharge.

Out of them, 32 had required admission to the (ICU).

- **New fatigue was more common** among patients admitted to the ICU (72%) than ward patients (60%).
- Although mild in severity, **new or worsened breathlessness** was more common among ICU patients (66%) versus (43%).
- **Almost half of patients** admitted to the ICU also reported symptoms of **(PTSD)**.
- Finally, **new or worsened concentration problems** were reported by 16% of ward patients and 34% of ICU patients.



PROLONGED SYMPTOMS:

FATIGUE

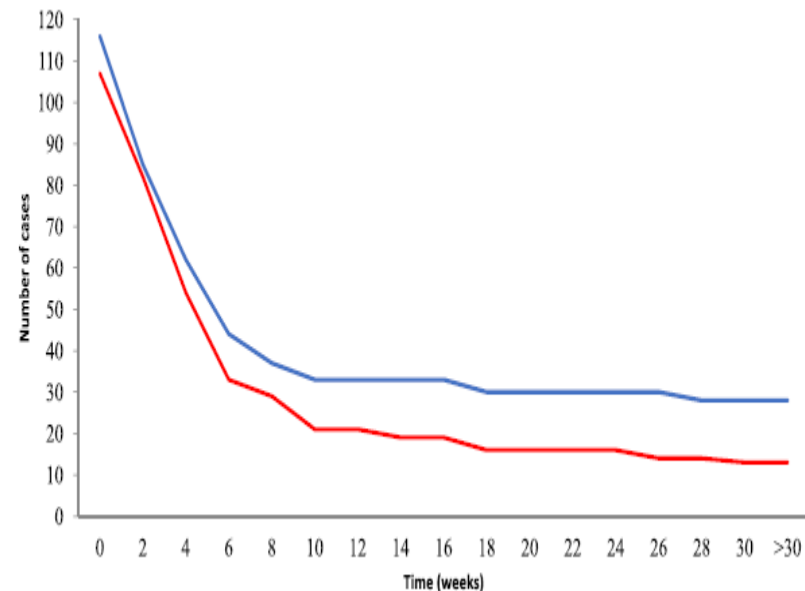
* most common symptom that persists after COVID-19 infection

PERSISTENT SYMPTOMS IN MILD COVID-19

- A report published by the **(CDC)** described persistent symptoms in patients with mild COVID-19.
- Out of 270 patients from around the United States, the most commonly reported persistent symptoms were **cough** (43%), **fatigue** (35%), and **dyspnea** (29%).
- (35%) patients reported not having returned to their baseline state of health.
- There was also a statistically significant **association between the presence of underlying chronic medical conditions and not returning to baseline state of health**, with **28% of those with 0 to 1** chronic condition, **46% with 2**, and **57% with 3 or more** chronic conditions. Other risk factors included **obesity** and presence of an **underlying psychiatric condition**.

Tenforde MW, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 United States, June 2020. *Morbidity and Mortality Weekly Report* 2020; 69:993

- From 3737 COVID-19 patients, 39.2% reported anosmia and 37.8% ageusia.
- Of the patients, 68.1% recovered their sense of smell and 73.0% their sense of taste during **the first 6 weeks** following the onset of symptoms.
- Anosmia tended to take more time to resolve than ageusia.
- 24% reported persistent taste and smell disorders 7 months after onset of symptoms.
- Female patients were more likely to report persistent symptoms than male patients. Age, comorbidities and severity of disease at admission did not associated with persistence of symptoms.



Renal Sequelae

- **Acute kidney injury** (AKI) has been well described as a potential complication in patients hospitalized due to severe COVID-19, with rates as high as **37%–40%**.
- Less is known regarding long-term recovery of kidney function after the acute period.
- report outcomes in 9657 patients admitted with COVID-19, **AKI**, both with and without need for renal replacement therapy (RRT), was significantly associated **with risk of death**.
- among patients who did require **RRT,(31%) remained on dialysis** at the time of discharge, suggesting prolonged kidney dysfunction despite resolution of acute COVID-19 infection. Among patients with **AKI who did not require RRT**, a substantial proportion (**36.9%) continued to have kidney dysfunction** at the time of hospital discharge.

Bucaloiu ID, et al. Increased risk of death and de novo chronic kidney disease following reversible acute kidney injury. *Kidney Int* 2021; 81:477–85

Endocrine sequelae

- new or worsening control of existing DM , subacute thyroiditis with clinical thyrotoxicosis and bone demineralization has been observed in patients weeks to months after resolution of COVID-19 symptoms.
- COVID- 19 may also potentiate latent thyroid autoimmunity manifesting as new-onset Hashimoto's thyroiditis or Graves' disease.
- Endocrine manifestations may be consequences of direct viral injury, immunological and inflammatory damage, as well as iatrogenic complications.
- There is no concrete evidence of lasting damage to pancreatic β cells. Although some surveys have shown ACE2 expression in β cells.
- So far, there is no evidence that COVID-19-associated diabetes can be reversed after the acute phase, nor that its outcomes differ in COVID-19 long haulers.

Gastrointestinal and hepatobiliary sequelae

- Significant gastrointestinal and hepatobiliary sequelae have not been reported in COVID-19 survivors.
- **Prolonged viral fecal shedding** occurs in COVID-19 for a **mean duration of 28 d** after the onset of SARS-CoV-2 infection symptoms and persisting for a mean of 11 d after negative respiratory samples.
- COVID-19 has the potential to **alter the gut microbiome**, including enrichment of opportunistic infectious organisms and depletion of beneficial commensals. **The ability of the gut microbiota to alter the course of respiratory infections** (gut–lung axis) has been recognized previously in influenza and other respiratory infections.
- Studies are currently evaluating the long-term consequences of COVID-19 on the gastrointestinal system, including post-infectious **IBS and dyspepsia**.

Multisystem Inflammatory Syndrome in Children (MIS-C)

- A unique aspect of SARS-CoV-2 infection
- Initially described in children and adolescents,
- **overlap with KD**
- occur **many weeks after initial mild or asymptomatic** SARS-CoV-2 infection

- **CDC definition for MIS-C has multiple components:**
- (1) age <21 years with fever, laboratory findings of inflammation,
- and severe illness affecting multiple organ systems;
- (2) no alternative diagnosis;
- (3) evidence of SARS-CoV-2 infection or exposure to a suspected or confirmed COVID-19 case within the 4 weeks before presentation)

MIS-C

- **Clinical presentations** of MIS-C include fever, abdominal pain, vomiting, diarrhea, skin rash, mucocutaneous lesions, hypotension and cardiovascular and neurologic complications.
- A meta-analysis of MIS-C studies reported **recovery in 91.1%** and death in 3.5% of patients.
- **Possible mechanisms** of injury related to **immune complexes**, complement activation, **autoantibody** formation, and massive **cytokine release** related to superantigen stimulation of T cells.



- Since June 2020, several case reports and series have been published reporting a similar MIS in adult.
- Like children, **adults who have been infected with the virus can develop symptoms of MIS-A, days to weeks after getting sick**, with problems can occur in different parts of the body like the heart, gastrointestinal tract, skin, or brain.
- Adults with MIS-A may have various signs and symptoms including:
 - Fever, Low BP, Abdominal pain, Vomiting, Diarrhea, Neck pain, Rash, chest pain, Feeling very tired
- we do not know why some adults have gotten sick with MIS-A and others have not. We **also do not know if adults with certain health conditions are more likely to develop MIS-A.**

Can the vaccine be effective in reducing the symptoms in long-haulers?

- As many as **30 to 40%** of those who get the vaccine have reported **improvements to their symptoms**: 'brain fog,' gastrointestinal problems shortness of breath.
- It's possible that the vaccine is helping the immune system **fight off residual virus** lingering in their bodies and clearing these remnants away, Or the vaccine could be stopping a **harmful immune response**. Or it might serve to **reset the immune system**. At this point, **researchers can only hypothesize**.
- reports show about 10-15% percent of long-haulers feel worse after vaccination, and there are a number who don't notice any change at all

*Even if the vaccine isn't helping everyone with long-term symptoms, vaccines will protect long-haulers from **reinfection by the virus**.*



Thanks for your
attention!