



FMDA Journal Club

May 11, 2022

Diane Sanders-Cepeda, DO, CMD – Host



Long COVID – Clinical Deep Dive

Diane Sanders-Cepeda, DO CMD
FMDA President, Journal Club Chair



Let's start with a case



78 y/o woman admitted to SNF for Post-acute care

Patient has been in facility for 2 weeks, and is not progressing with therapy

Family informed of potential next steps – remain at facility as LTC resident or discharge home with in-home care.

Patient's daughter wants her mother transferred to an Acute Inpatient rehabilitation (AIR) facility because the SNF "is not treating her mother" and she is upset that this level of care was denied

78 y/o woman
not
progressing
with therapy

Patient's history includes – COVID diagnosis 5 months ago, patient with muscle weakness, multiple falls in the last 2 months

Pmhx: Osteoarthritis & HTN

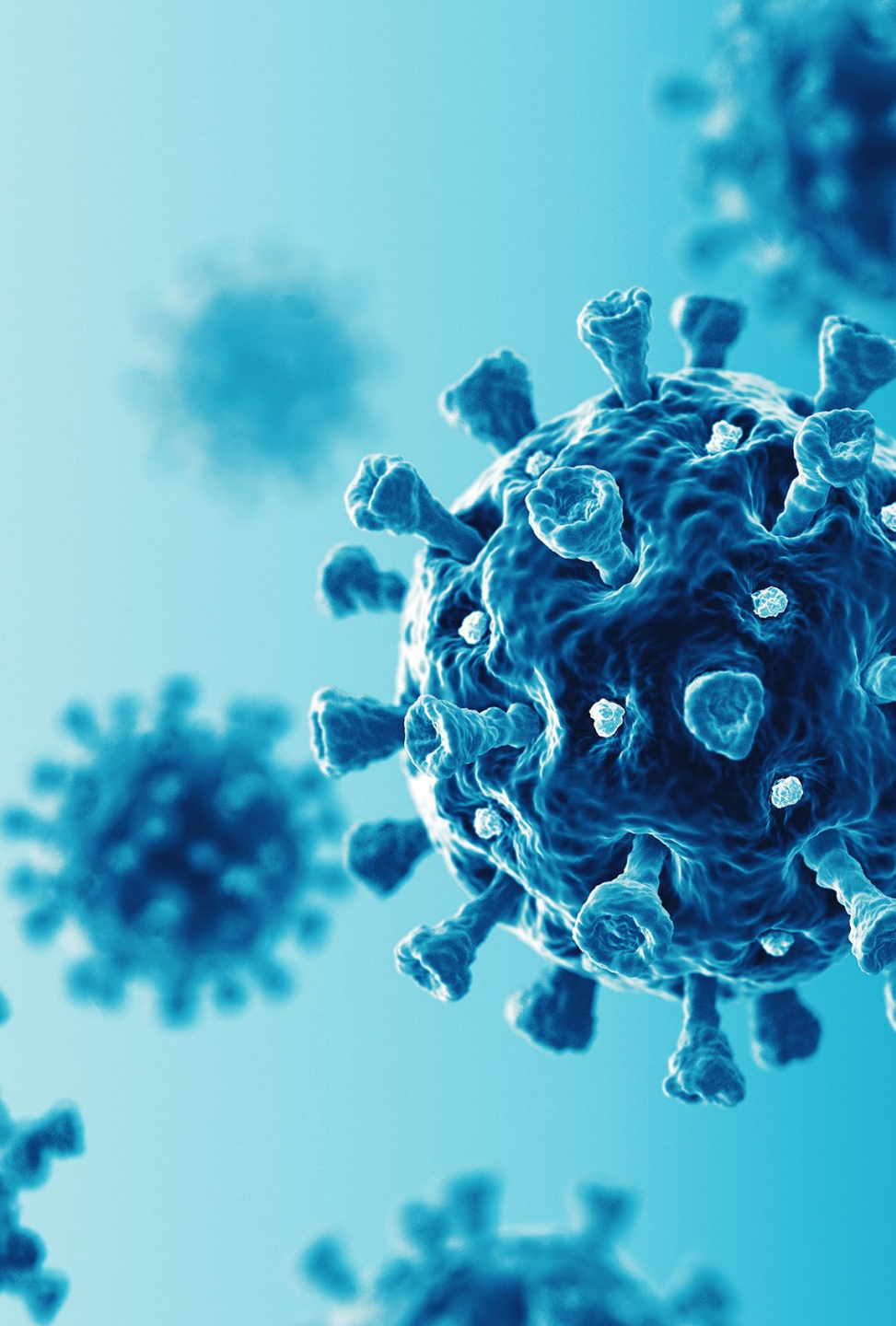
At Baseline – Per daughter she was very active. Activities included gardening, walking around the neighborhood, visiting with friends, watching her grandkids

What's going on?

Patient has complained of fatigue for the past 3 months, and has exertional dyspnea when attempting to complete certain activities

At the last hospitalization she was treated for UTI despite negative Urine Cultures

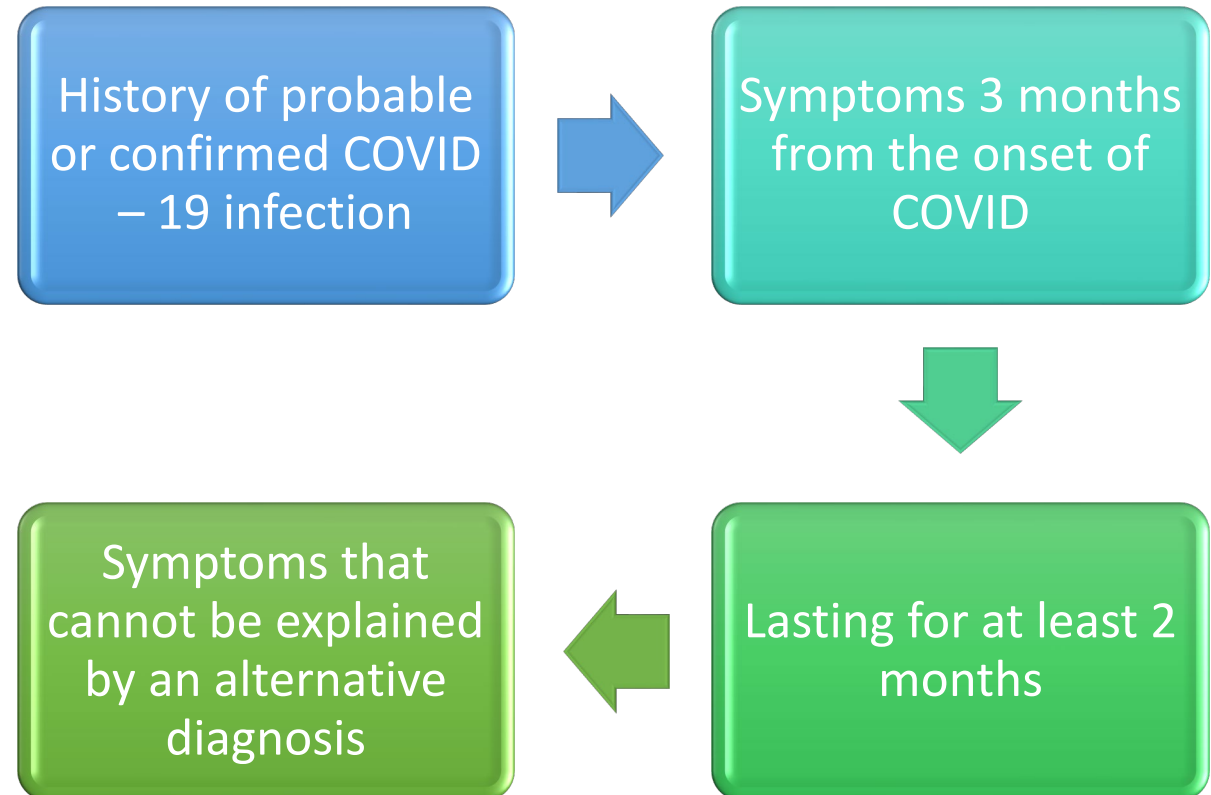
Upon review of her chart it was noted that Post-COVID condition was documented by physical and occupational therapist

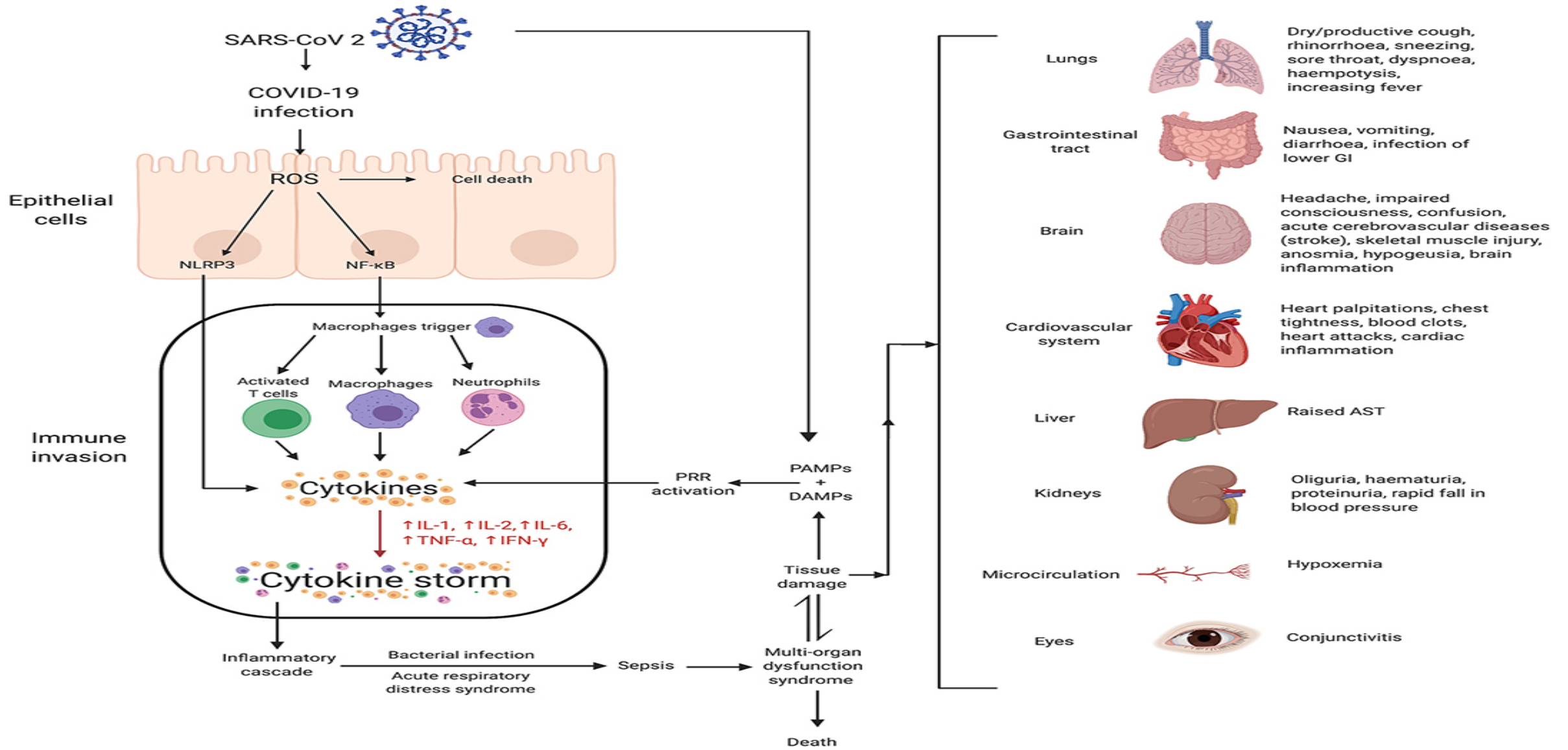


Defining Post-Acute Sequelae of COVID aka Long COVID

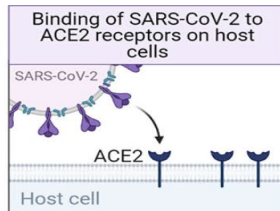
- Long COVID
- Long haulers COVID
- Post Acute Sequelae of COVID
- Post COVID Conditions

Post Acute Sequelae of COVID (PASC) WHO Definition



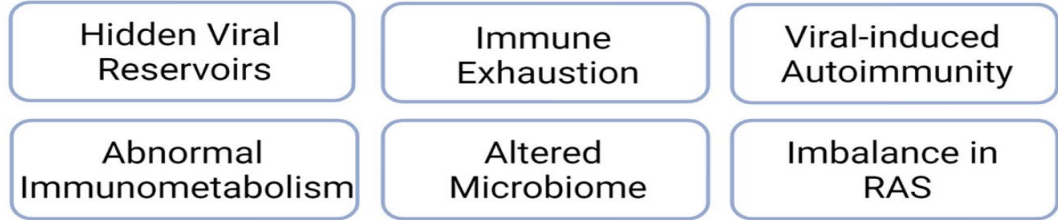


SARS-CoV-2 EXPOSURE

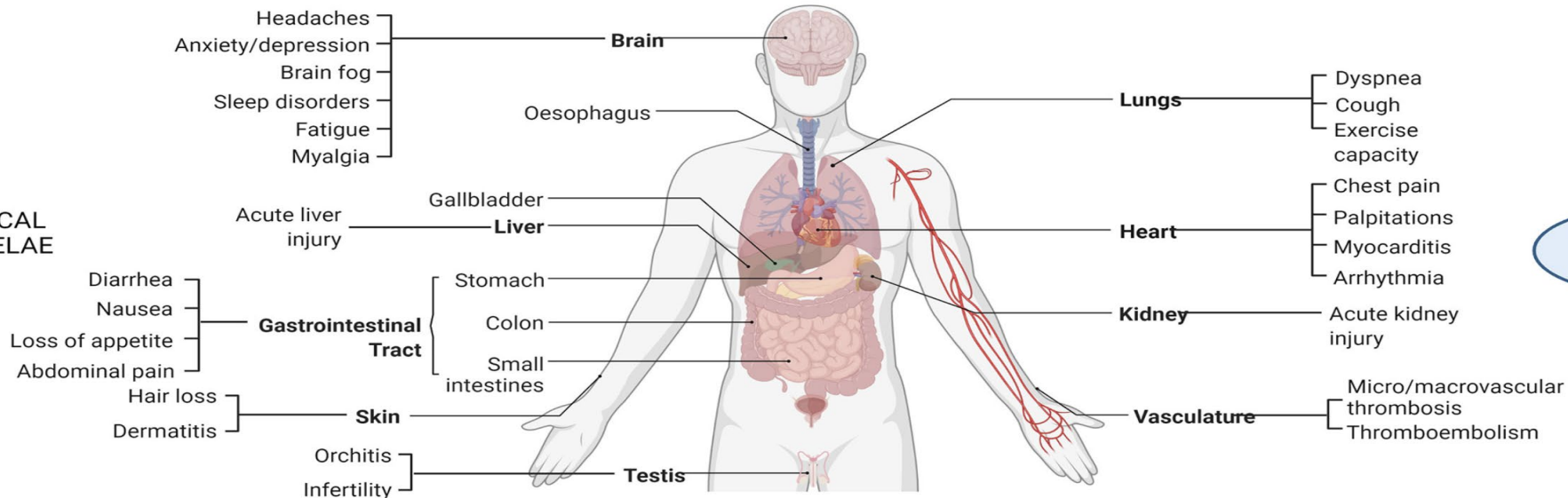


ACUTE COVID-19

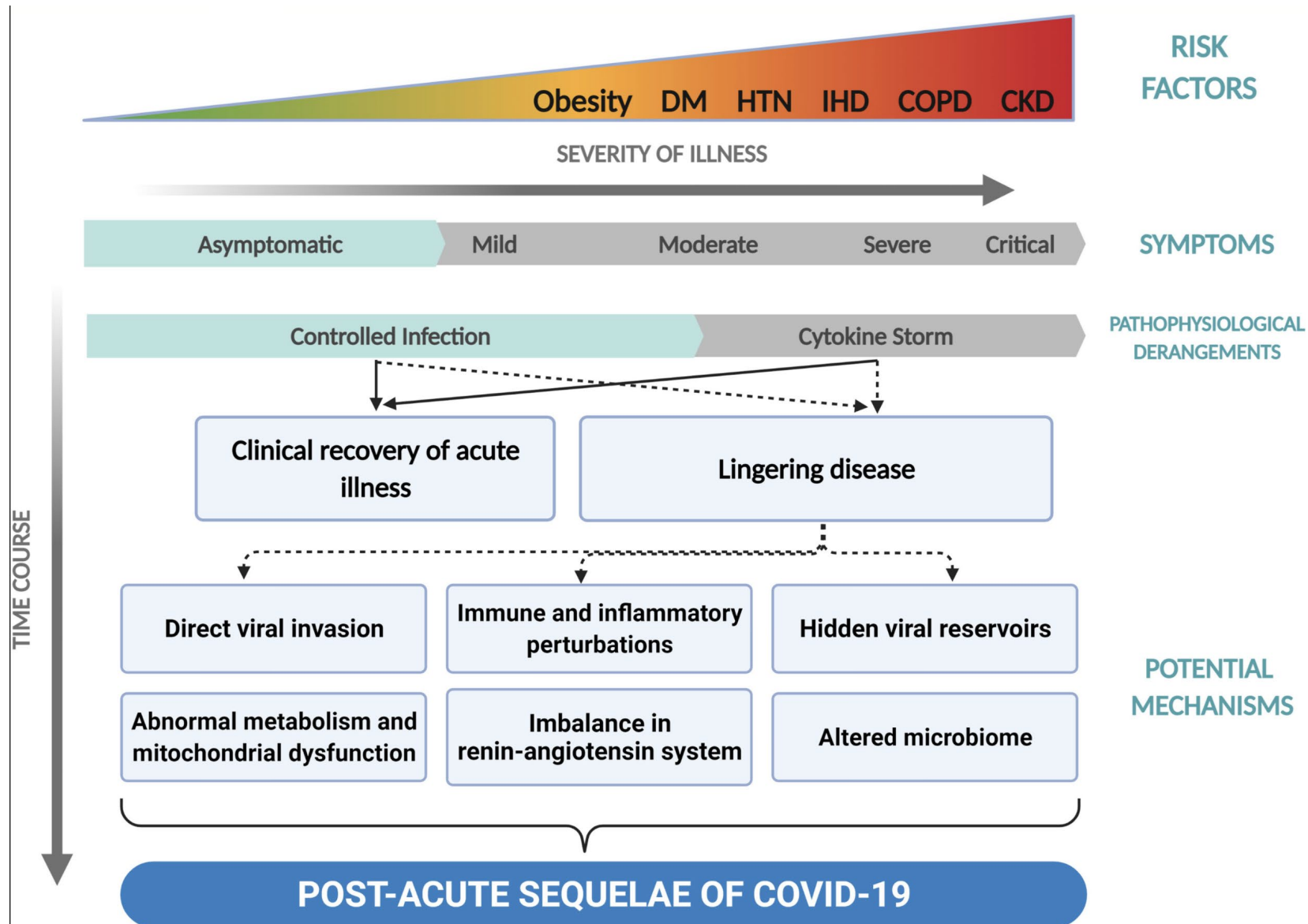
POTENTIAL IMMUNOPATHOLOGICAL MECHANISMS



CLINICAL SEQUELAE



POST-ACUTE COVID-19



Prevalence & Recognition

Are we seeing this in our care settings?

Post-Acute Sequelae of SARS-CoV-2 Infections (PASC) Estimates and Insights

American Academy of Physical Medicine and Rehabilitation

Data as of 5/10/2022

[View Dashboard Assumptions, Methodology, and Sources](#)

SUMMARY | **BY STATE**

FILTERS

(reset to default)

Select Est. PASC %

30%

Select a State

All

Select a County

All

MODEL ASSUMPTIONS AND SOURCES

[\(see all\)](#)

1. Model assumes 30% of COVID-19 surviving cases in the U.S. result in PASC.
2. COVID-19 surviving cases are confirmed cases less deaths.
3. U.S. case data is pulled nightly from JHU CSSE COVID-19 Data. U.S. Census data uses 2019 1-year estimates.

Powered by
ASSOCIATION ANALYTICS

COVID-19 SURVIVING CASES (TOTAL)

80,860,658

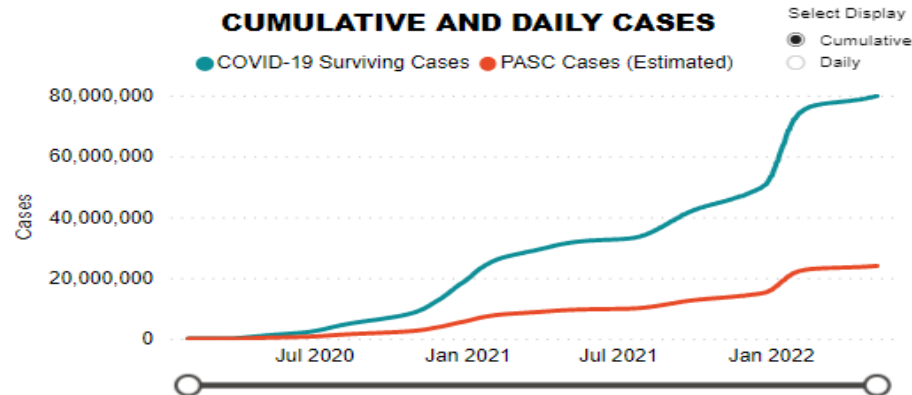
PASC CASES (ESTIMATED)

24,258,197

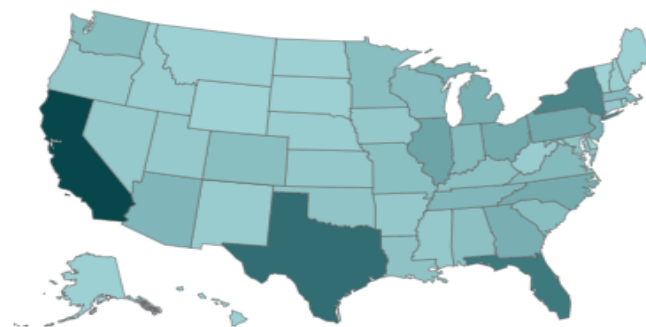
ESTIMATED PASC CASES PER STATE

State	PASC Cases (Estimated)
California	2,758,383
Texas	2,004,857
Florida	1,777,570
New York	1,548,140
Illinois	940,667
Pennsylvania	835,288
Ohio	800,875
North Carolina	794,625
Georgia	718,293
Michigan	709,322
New Jersey	674,683
Arizona	598,574
Tennessee	576,101
Virginia	506,841
Indiana	505,047
Massachusetts	482,760
Wisconsin	482,587

CUMULATIVE AND DAILY CASES



PASC CASES (ESTIMATED)



Post-Acute Sequelae of SARS-CoV-2 Infections (PASC) Estimates and Insights

American Academy of Physical Medicine and Rehabilitation

Data as of 5/10/2022

[View Dashboard Assumptions, Methodology, and Sources](#)

SUMMARY | **BY STATE**

FILTERS

(reset to default)
Select Est. PASC %

30%

Select a State

Florida

- Arizona
- Arkansas
- California
- Colorado
- Connecticut
- Delaware
- District of Columbia
- Florida
- Georgia
- Hawaii

MO

NS

1. Most COVID-19 survivors in PA have long-term health issues.

2. COVID-19 surviving cases are confirmed cases less deaths.

3. U.S. case data is pulled nightly from JHU CSSE COVID-19 Data. U.S. Census data uses 2019 1-year estimates.



COVID-19 SURVIVING CASES (TOTAL)

5,925,232

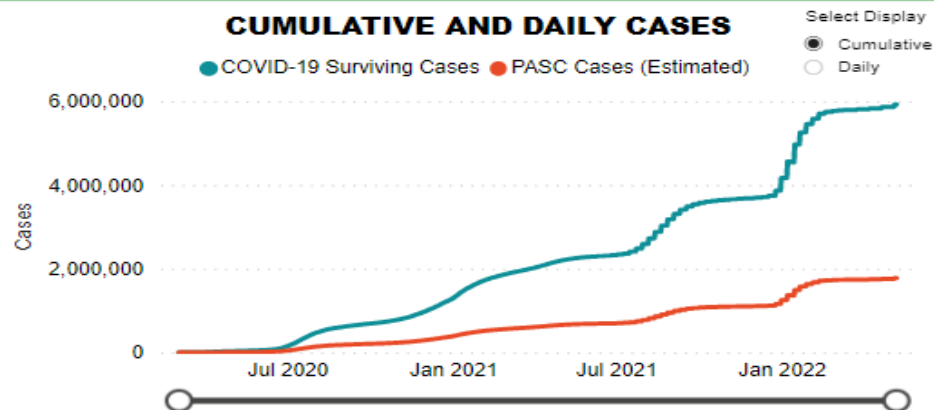
PASC CASES (ESTIMATED)

1,777,570

ESTIMATED PASC CASES PER STATE

State	PASC Cases (Estimated)
Florida	1,777,570

CUMULATIVE AND DAILY CASES



PASC CASES (ESTIMATED)



PASC Symptoms

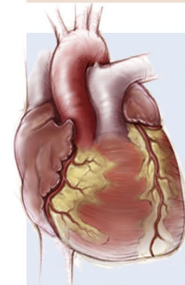


Neurologic

- Olfactory deficits
- Gustatory deficits
- Headache
- Cognitive impairment
- Hearing loss/earache/tinnitus
- Retinopathy (possible)

Psychiatric/mental health

- Insomnia
- Post traumatic stress disorder
- Depression
- Anxiety
- Obsessive compulsive syndromes
- Secondary emotional stresses (financial, social isolation, etc.)



Cardiac/cardiovascular

- Dyspnea
- Tachycardia/palpitations
- Myocarditis
- Cerebrovascular disease
- Postural tachycardia syndrome (POTS)

Pulmonary

- Dyspnea
- Cough
- Pulmonary fibrosis
- Impaired pulmonary function
- Pulmonary hypertension

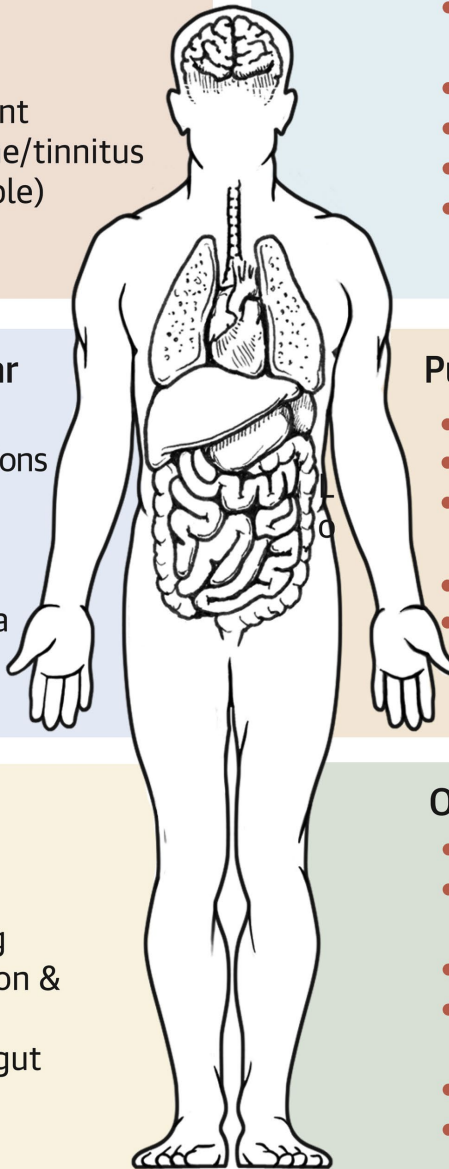


Gastrointestinal

- Loss of appetite
- Acid reflux
- Diarrhea & vomiting
- Abdominal distension & pain
- Possible change in gut microbiome

Other complications

- Chronic fatigue
- Kidney injury/chronic kidney disease
- Hyperglycemia/diabetes
- Pediatric inflammatory multisystemic syndrome
- Skin rash
- Hair loss





Long-Term Effects of COVID-19

Shreeya Joshee, BS; Nikhil Vatti, MD; and Christopher Chang, MD, PhD, MBA

Immune-mediated damage to BBB & thromboembolism: viral mediated hypoxia and damage to PNS

- a) inflammatory markers increase leakage and allow leukocyte infiltration and basement membrane modification
- b) Megakaryocytes in the parenchyma of alveolar tissue which may travel into the brain tissue due to endothelial disruption
- c) Hypoxia due to hypercoagulable state → HIF-1 increase → increase in BBB permeability and prolonged cytokine release

Neuropsychiatric, cognitive and peripheral nerve pathologies

Viral mediated parenchyma damage; immune mediated microvascular damage

- a) Virus binds to ACE2 → cells release DAMPs/PAMPs
- b) Macrophages release IL1 and TNF-alpha → neutrophils attracted to site
- c) Neutrophils release chemokines → vascular permeability increased, differentiation of fibroblasts into myofibroblasts
- d) Release of protein-rich exudate to interstitial space
- e) Myofibroblasts release collagen, fibronectin, and ECM in response to TGF-beta → excess scar tissue deposition despite infection resolution

Dyspnea, hypoxia, fatigue, ground glass opacities and pulmonary fibrosis

Immune mediated endothelial dysfunction

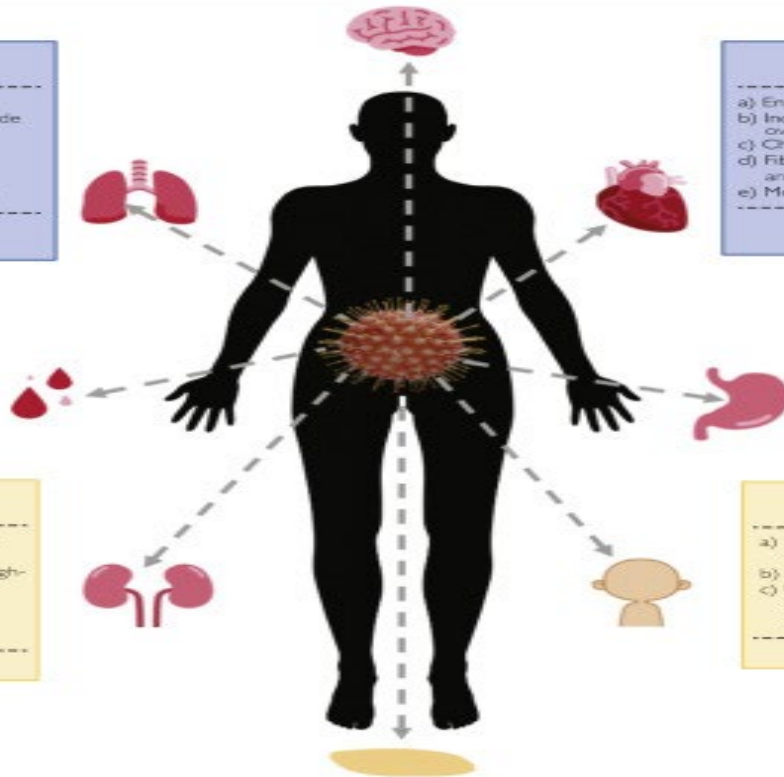
- a) Innate immune system activation of type I interferon → fuels pro-inflammatory and pro-coagulation processes through endothelial cell dysfunction, endothelitis, capillary leakage

Venous, arterial, pulmonary thromboembolisms

Viral mediated parenchyma damage; immune mediated microvascular damage

- a) ACE2 receptors in the proximal tubule apical brush border and podocytes
- b) "Second-hit phenomenon" where black patients with the high-risk APOL1 variant who also had COVID-19 are at an increased risk of collapsed glomerulopathy
- c) Indirect mechanisms such as fluid imbalance, mechanical ventilation, and organ crosstalk

AKI, glomerular and tubular diseases



Immune-mediated myocardial and microvascular destruction

- a) Endothelial cell disruption similar to pulmonary
- b) Increased cardiometabolic demand → myocardial injury via hypoxia and overuse
- c) Chronic myocarditis and IL6 → fibrofatty replacement
- d) Fibrofatty replacement → reentrant arrhythmias and sudden cardiac arrest and death
- e) Medications also induce cardiotoxicity and electrolyte imbalances

Chest pain, palpitations, pericarditis, myocarditis, fibrosis, arrhythmias/death

Viral mediated alterations in fecal microbiota

Mechanism is unknown

Loss of appetite, nausea, acid reflux, diarrhea, abdominal distension, belching, vomiting, and bloody stools

Immune-mediated microvascular dysfunction; viral mediated effects unknown; stress

- a) Microvascular vasculitis from complement system activation, protein deposition in dermal capillaries, or direct viral effects
- b) Hair loss due to COVID-19 has been attributed to telogen effluvium
- c) Urticaria or angioedema may include a combination of post infectious immune dysregulation, adverse drug reactions, interruptions in urticaria therapy (omalizumab or oral antihistamine) or pandemic related stress

Hair loss, skin rash, urticarial lesions, angioedema

Viral mediated insulin decreases and resistance; immune-mediated endocrine parenchymal destruction

- a) DKA development via downregulation of ACE2 receptors and damage of beta-islet during viral entry
- b) ACE2 absence → unopposed angiotensin II effects → impede insulin secretion
- c) Viral infections also induce insulin resistance to promote anti-viral effector CD8+ T-cells
- d) Thyroid effects due to ACE2/TMPSSR2 expression, secondary to HPA axis insult, or host inflammatory cytokine storm

New-onset diabetes, worsening preexisting diabetes, DKA, subacute thyroiditis, graves thyrotoxicosis

Is this LONG COVID?

Case Reviews

94 y/o Female LTC resident

PMHX – frailty, Dementia

Multiple Hospitalizations since COVID diagnosis in August 2021

Persistent cough, Worsening dysphagia now with PEG tube placement, progressively worse muscle weakness; treated twice for pneumonia in the past 6 months

Persistent abnormalities on bloodwork – leukocytosis, anemia, elevated BUN & Cr



63 y/o Female LTC resident

Pmhx of HIV, Frailty

Admitted several times to the hospital since COVID diagnosis – over 6 months ago

Now with significant functional decline, worsening renal function, refusal to eat, apathy, and anemia

ACP discussions ongoing, currently family does not want to consider hospice care

78 y/o male patient

Outpatient Care

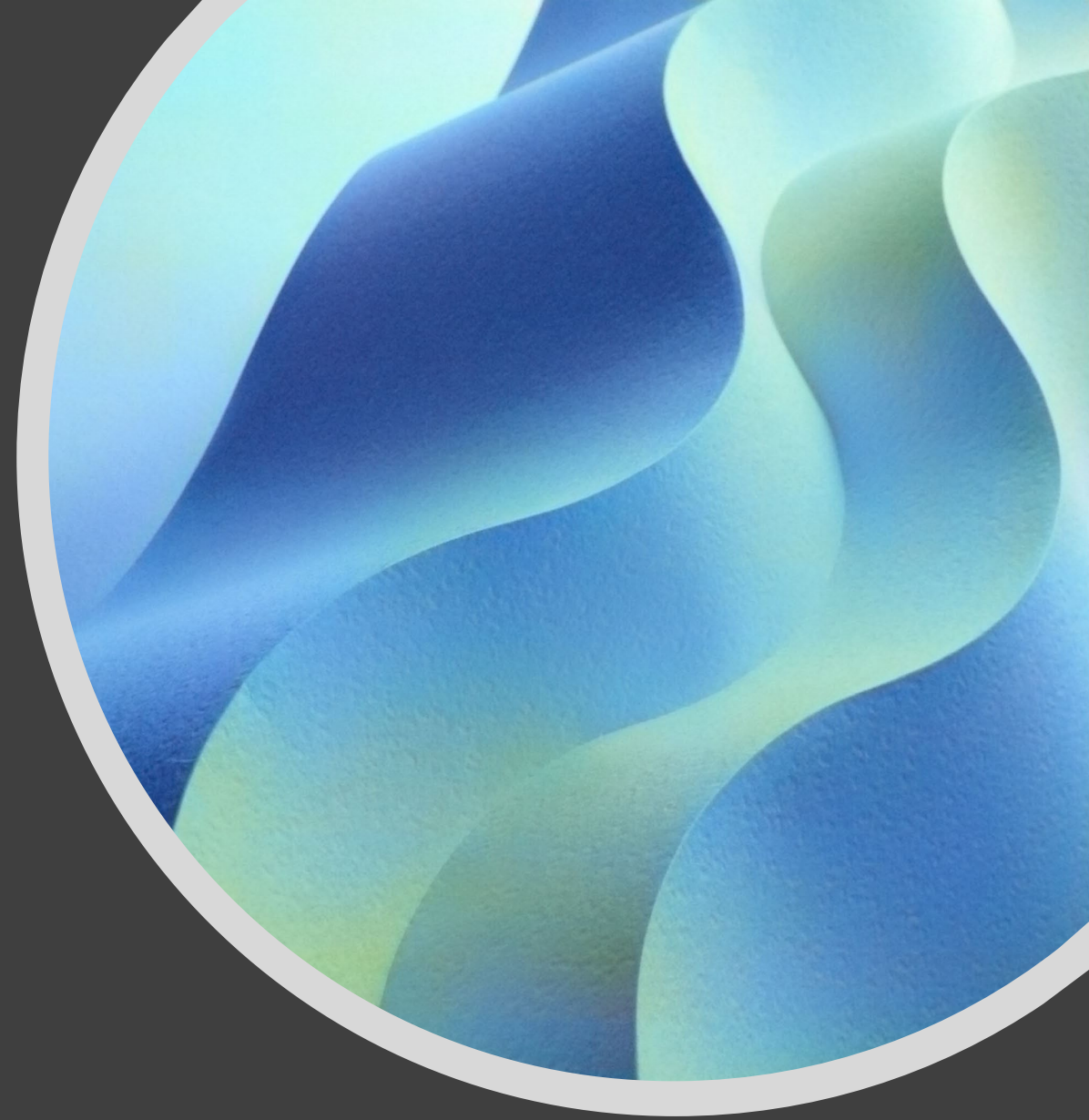
Patient with COVID infection 6 months ago; refused vaccination, treated with Monoclonal antibodies in first 72 hours

Pmhx: s/p Renal transplant, h/o spinal stenosis

Prior to COVID at baseline – walked 1 to 2 miles daily

Currently – has exertional dyspnea with exercise intolerance, muscle weakness, and low back pain

Now – receiving in-home physical therapy with incremental improvement



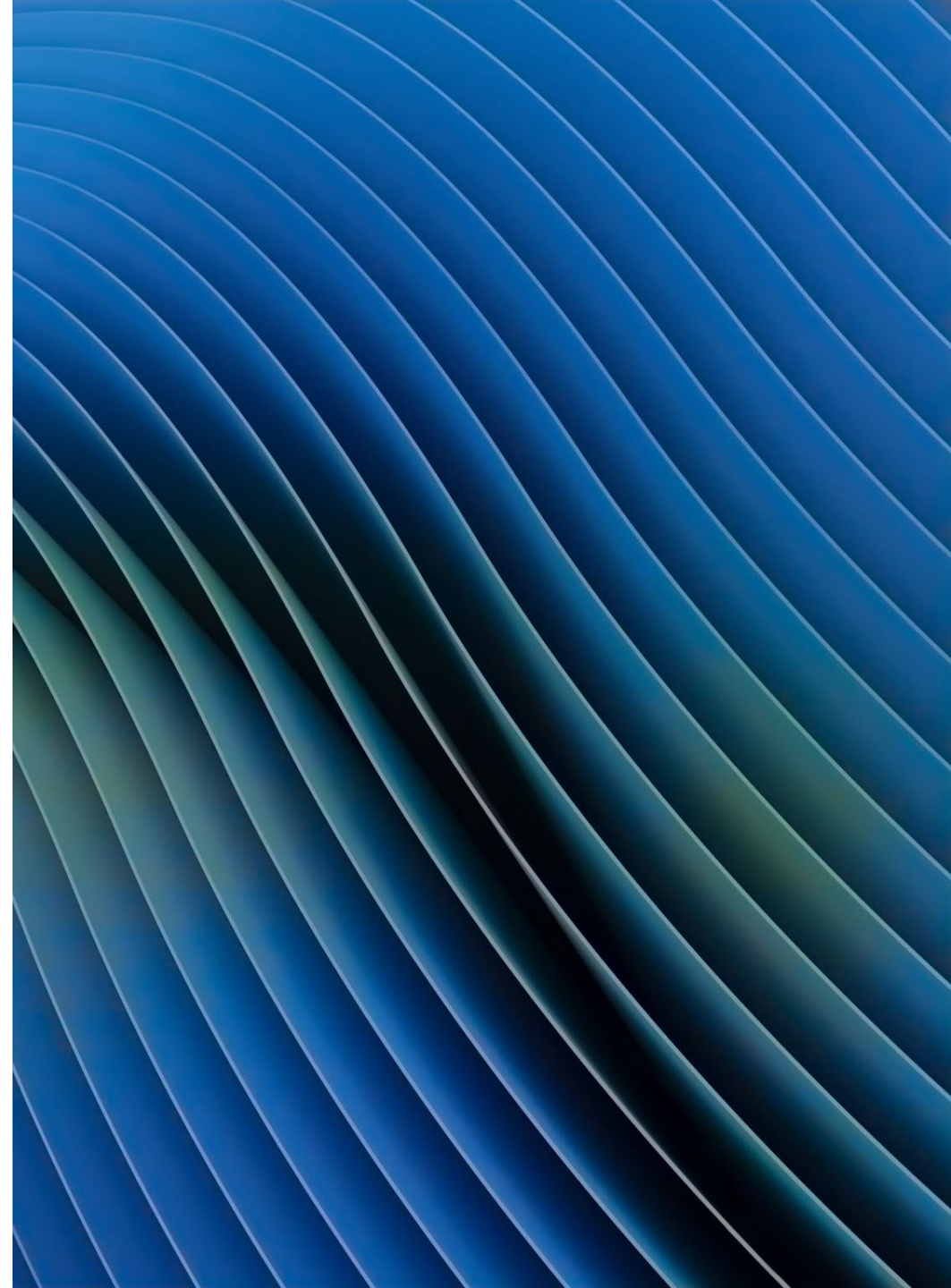
62 y/o Female LTC Resident

Pmhx of Diabetes, CVA, CKD 3, Morbid Obesity, HTN, Heart Failure, COPD, RA

Initially, was treated on COVID unit in facility until Acute Respiratory Failure

Upon discharge back to the facility she continued to have SOB, worsening renal function, and muscle weakness

Hospitalized Multiple times in the months following her initial COVID diagnosis



81 y/o Female LTC Resident

Pmhx COPD, CHF, AFIB, HTN, s/p Stroke, Diabetes, PAD

At baseline – mild cognitive impairments, normal PO intake

Diagnosed with COVID – 19 with mild symptoms – mild SOB, no fever, no chest pain

1 month later – significant mental and functional decline, worsening renal function and poor oral intake





71 y/o Male Homebound Patient

Pmhx: COPD, Chronic respiratory failure on Home O2,
Morbid Obesity, Heart Failure, OSA, B/L LE
Lymphedema with wounds

Fully vaccinated through home vaccine program, not
boosted

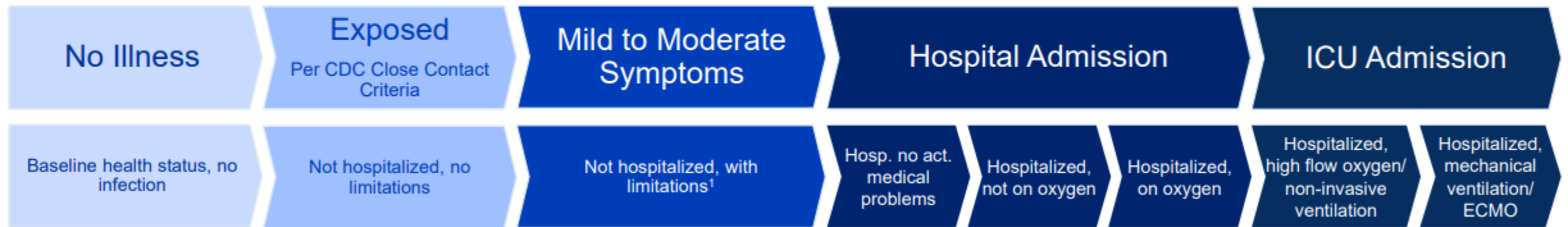
Never diagnosed with COVID, had several rapid test
that were negative during Omicron wave – despite
his family testing positive

3 months later – Muscle weakness, sacral wound
development, Bilateral LE wounds worsening, severe
diarrhea requiring hospitalization for dehydration.

What about
Treatment??



Summary of COVID-19 Preventative Agents & Therapeutics



Veklury® (remdesivir, Gilead)²

COVID-19 VACCINES

Monoclonal Antibodies for PrEP

- Evusheld (tixagevimab + cilgavimab, AZ)

None currently authorized for use in any US state or territory.

Oral Antivirals

- Paxlovid (nirmatrelvir + ritonavir, Pfizer)
- Lagevrio (molnupiravir, Merck)

Monoclonal Antibodies for Treatment

- Bebtelovimab (Lilly)

Please see [NIH Current Inpatient Therapies](https://www.covid19treatmentguidelines.nih.gov/therapies/) (https://www.covid19treatmentguidelines.nih.gov/therapies/)

¹ [Therapeutic Management of Nonhospitalized Adults With COVID-19](https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/) https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/

² [Therapeutic Management of Hospitalized Adults With COVID-19](https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/) https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/

Impact of Monoclonal Antibody Treatment on Post-Acute COVID-19 Syndrome (MAbPACs)

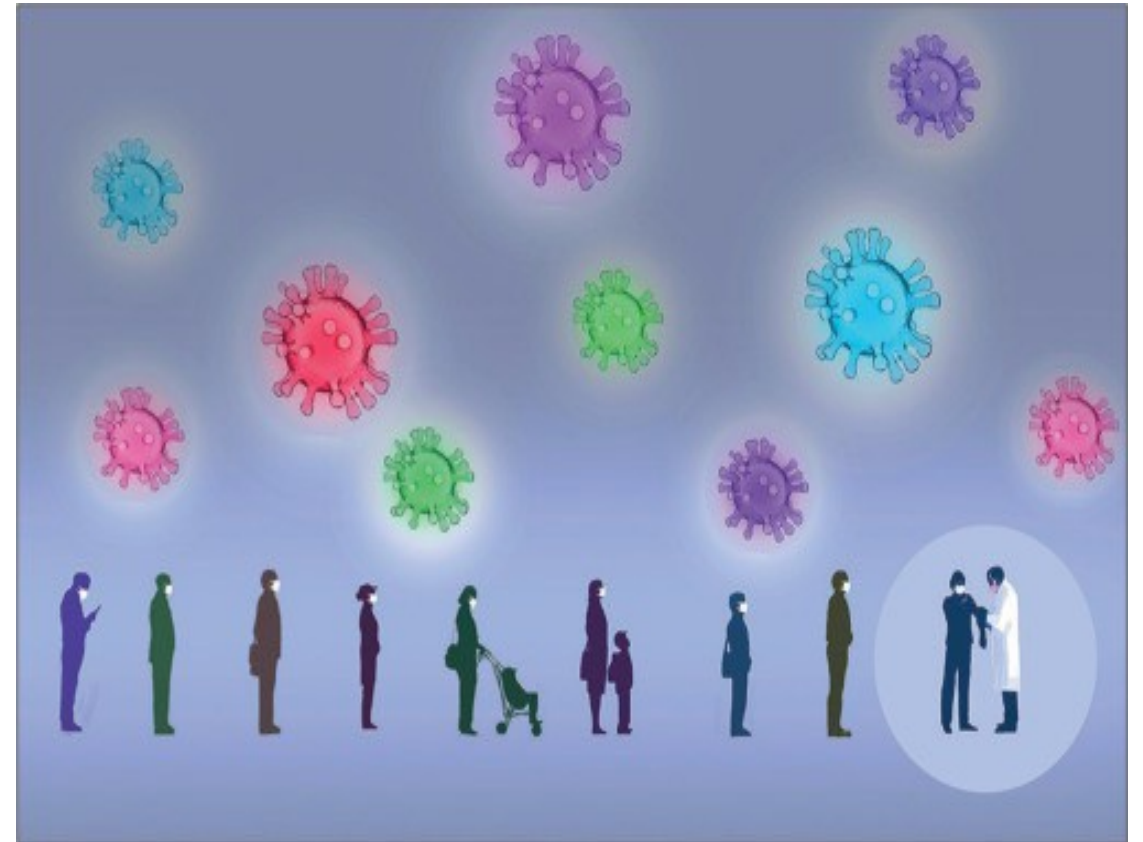
THE LANCET
Respiratory Medicine

NEWS | ONLINE FIRST

Do vaccines protect from long COVID?

Priya Venkatesan

Published: January 20, 2022 • DOI: [https://doi.org/10.1016/S2213-2600\(22\)00020-0](https://doi.org/10.1016/S2213-2600(22)00020-0)



medRxiv

THE PREPRINT SERVER FOR HEALTH SCIENCES



Cold
Spring
Harbor
Laboratory

BMJ Yale

HOME | ABOUT

Search

[Comment on this paper](#)

Reduced Incidence of Long-COVID Symptoms Related to Administration of COVID-19 Vaccines Both Before COVID-19 Diagnosis and Up to 12 Weeks After

Michael A. Simon, Ryan D. Luginbuhl, Richard Parker



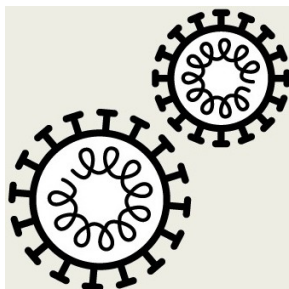
What about Vitamins?



RCT: Effect of High-Dose Zinc and Ascorbic Acid Supplementation on Symptom Length Among Ambulatory Patients With SARS-CoV-2 Infection

POPULATION

82 Men, 132 Women



Adult patients with SARS-CoV-2 infection confirmed with a PCR-based assay as outpatients

Mean (SD) age, 45.2 (14.6) y

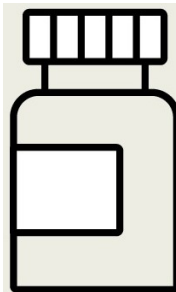
SETTINGS/ LOCATIONS



Hospitals in a single health system with sites in Ohio and Florida

INTERVENTION

214 Patients randomized and analyzed



50 Standard of care

Standard outpatient prescription for viral illness

48 Ascorbic acid

8 000 mg Ascorbic acid

58 Zinc gluconate

50 mg Zinc

58 Zinc and ascorbic acid

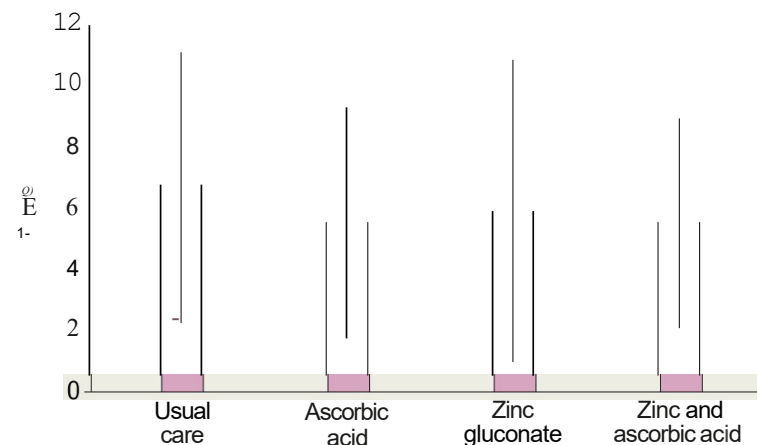
50 mg Zinc and 8 000 mg of ascorbic acid

PRIMARY OUTCOME

The primary end point was the number of days required to reach a 50% reduction of symptoms, such as severity of fever, cough, shortness of breath, and fatigue

FINDINGS

The study was stopped for a low conditional power for benefit with no significant difference among the 4 groups for the primary end point, a 50% reduction in symptoms



Time to 50% symptom reduction

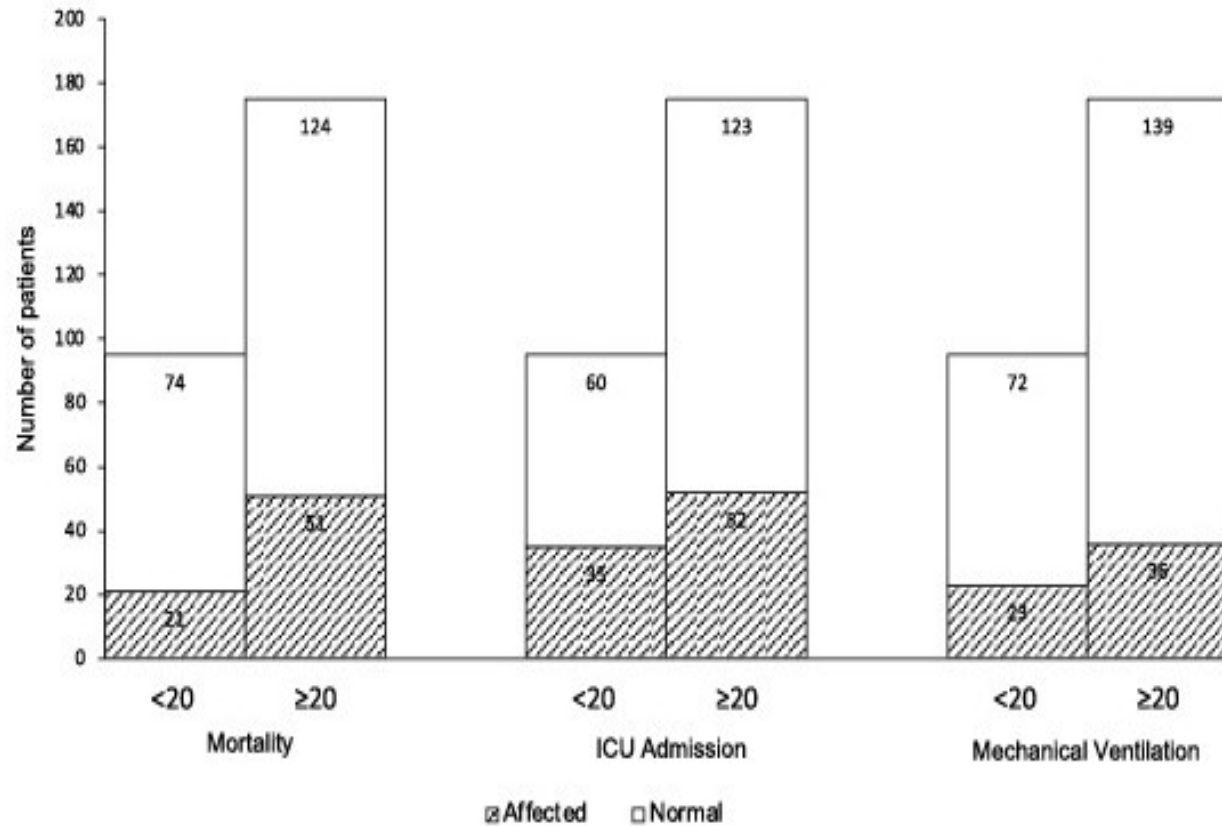
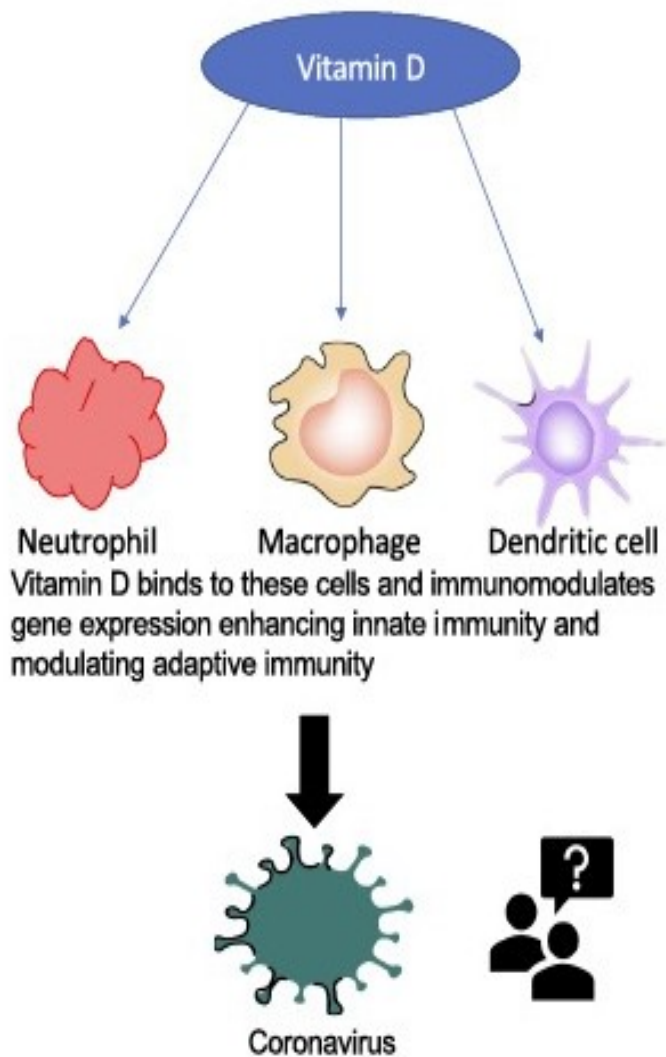
Usual care: Mean (SD). 6.7 (4.4) d

Ascorbic acid: Mean (SD). 5.5 (3.7) d

Zinc gluconate: Mean (SD). 5.9 (4.9) d

Zinc and ascorbic acid: Mean (SD). 5.5 (3.4) d


Exploring the link between Vitamin D and clinical outcomes in COVID-19



Severe disease outcomes in relation to Vitamin D Levels

Question- Does Vitamin D help decrease the severity of clinical outcomes in COVID-19?

Conclusion- No significant association found between Vitamin D levels and clinical outcomes in COVID-19.



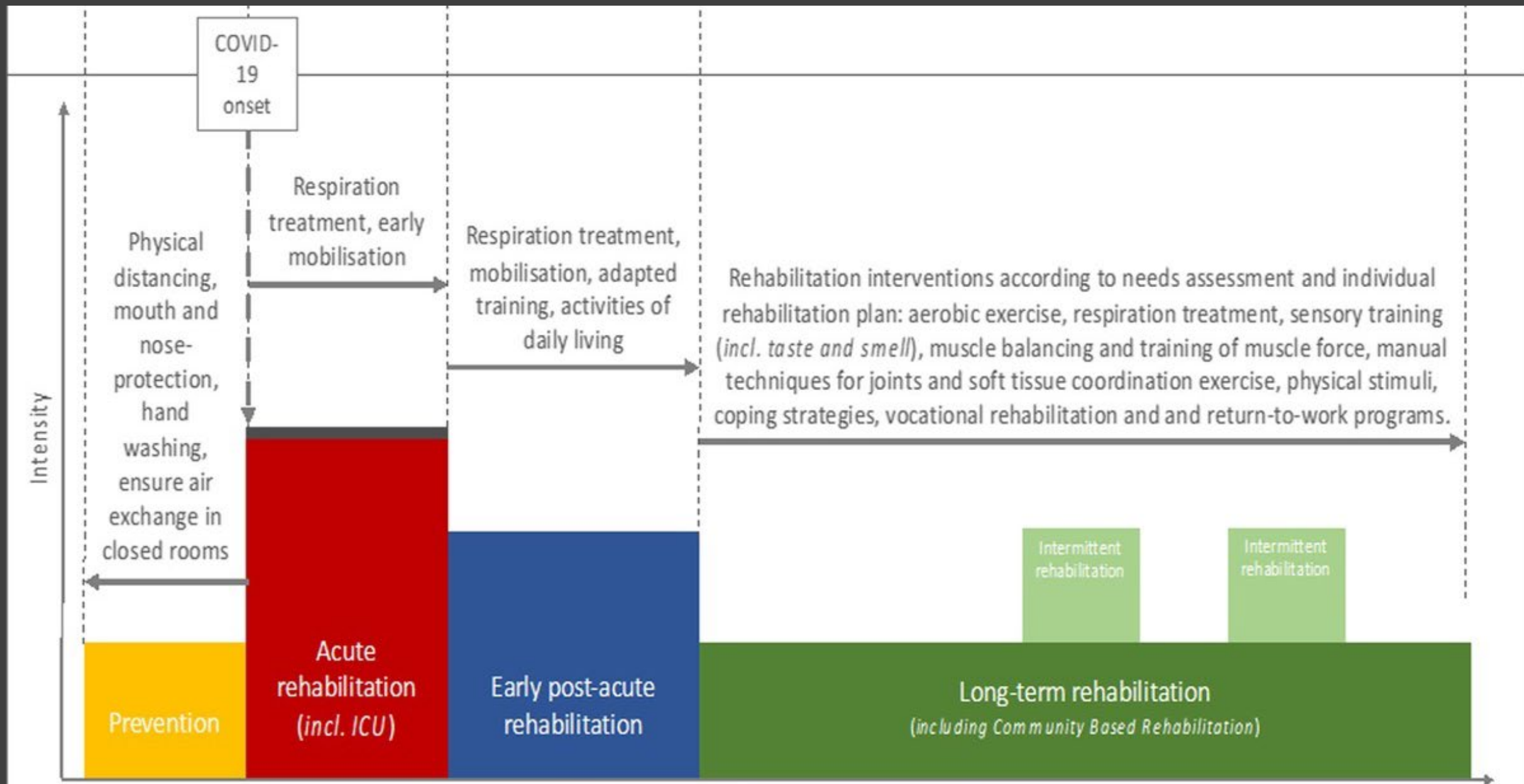
Managing Post Acute Sequelae of COVID

- Multidisciplinary Team approach
- Individualized care plans
- Ongoing Support

EDUCATION & ADMINISTRATION

Phase-Adapted Rehabilitation for Acute Coronavirus Disease-19 Patients and Patient With Long-term Sequelae of Coronavirus Disease-19




Christoph Gutenbrunner, MD, PhD, FRCP, Boya Nugraha, MS, PhD, and Lidia Teixido Martin, MD

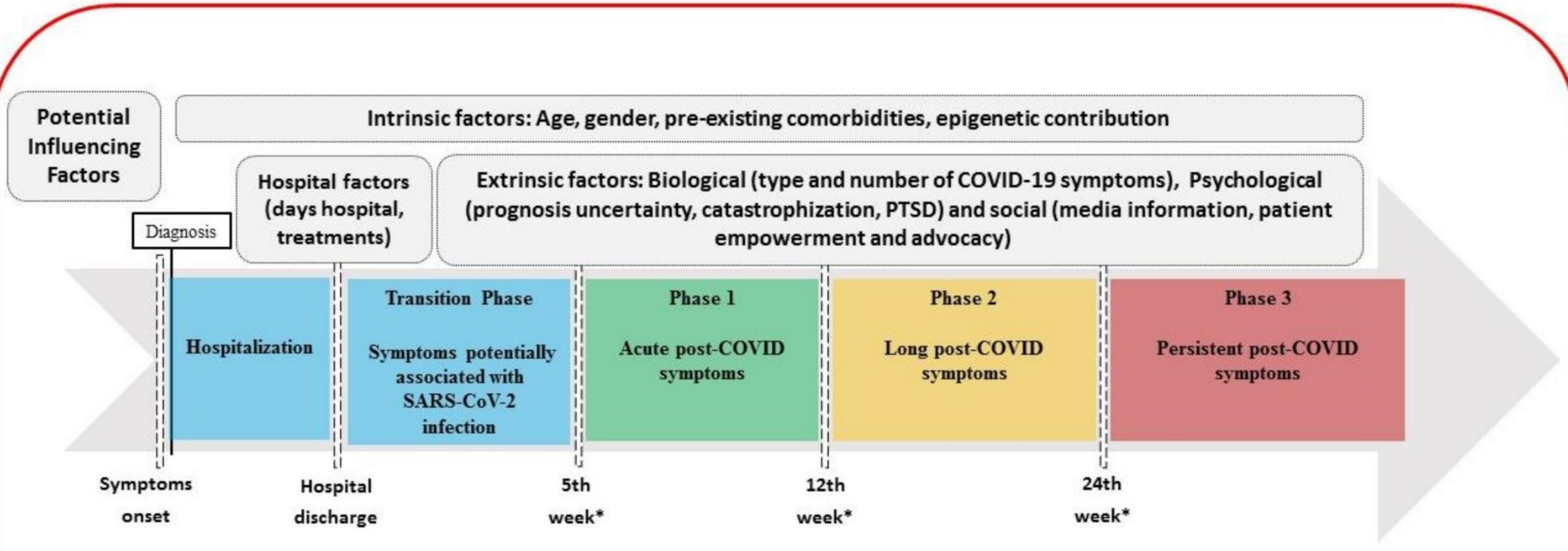




Communication

Defining Post-COVID Symptoms (Post-Acute COVID, Long COVID, Persistent Post-COVID): An Integrative Classification

César Fernández-de-las-Peñas ^{1,*} , Domingo Palacios-Ceña ^{1,*} , Víctor Gómez-Mayordomo ² ,
María L. Cuadrado ^{2,3} and Lidiane L. Florencio ¹



INTEGRATIVE POST-COVID SYMPTOMS MODEL
Hospitalized patients with COVID-19

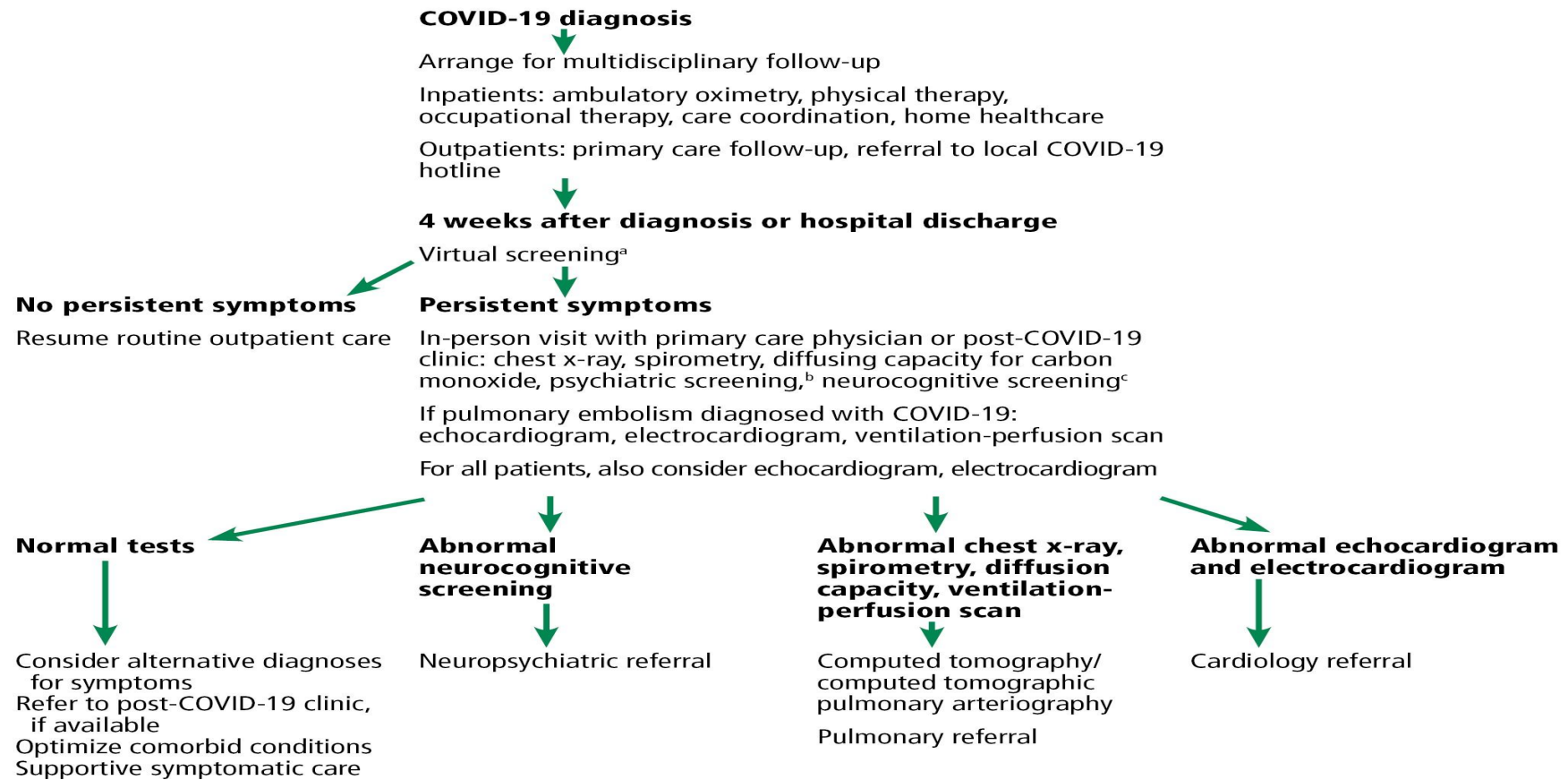
COVID-19 Curbside Consults

Update to post-acute sequelae of SARS-CoV-2 infection: Caring for the 'long-haulers'

Susan Vehar, MD, Marina Boushra, MD, Prince Ntiamoah, MD and Michelle Biehl, MD, MS

Cleveland Clinic Journal of Medicine October 2021, DOI: <https://doi.org/10.3949/ccjm.88a.21010-up>





^aScreening tools to consider: Post-COVID-19 Functional Status Scale, COVID-19 Yorkshire Rehabilitation Screen, University of Pennsylvania Post-COVID Screening Measures.

^bAvailable psychiatric screening tools: General Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9; for depression screening), PTSD Checklist for DSM-5 (PCL-5), Impact of Event Scale-6 (IES-R; for PTSD screening), Hospital Anxiety and Depression Score (HADS).

^cAvailable neurocognitive screening tools: Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE), Cognitive Assessment Tool Rapid Version (CAT-rapid).

Figure 1. Care pathway for patients with the post-acute sequelae of SARS-CoV-2 infection.



Coding Post COVID Syndrome

```
... object to mirror...  
mirror_mod.mirror_object  
...operation == "MIRROR_X":  
mirror_mod.use_x = True  
mirror_mod.use_y = False  
mirror_mod.use_z = False  
...operation == "MIRROR_Y":  
mirror_mod.use_x = False  
mirror_mod.use_y = True  
mirror_mod.use_z = False  
...operation == "MIRROR_Z":  
mirror_mod.use_x = False  
mirror_mod.use_y = False  
mirror_mod.use_z = True
```

```
...selection at the end -add  
...mirror_ob.select= 1  
...modifier_ob.select=1  
...context.scene.objects.active  
...("Selected" + str(modifier_ob...  
...mirror_ob.select = 0  
...= bpy.context.selected_object...  
...data.objects[one.name].select...  
...print("please select exactly
```

OPERATOR CLASSES -----

```
...types.Operator):  
...X mirror to the selected  
...object.mirror_mirror_x"  
...mirror X"
```

```
...context):  
...context.active_object is not
```


Post COVID – 19 Condition ICD-10 U09.9

WHO added new code to ICD-10



Proposal to add to ICD-10 CM made at the March 2021 Meeting

Implementation date – October 1, 2021

POST COVID Syndrome Symptoms

- **Fatigue**
- **Difficulty thinking or concentrating**
 - *sometimes referred to as “brain fog”*
- **Difficulty breathing**
 - *with and without abnormal imaging and pulmonary function testing*
- **Cough**
- **Painful joints or muscles**
- **Chest pain**
- **Depression or anxiety**
- **Headache**
- **Fever**
- **Palpitations**
- **Loss of smell or taste**
- **Dizziness on standing**
- *Rashes*
- *Hair Loss*
- *Lesions on Toes “ COVID TOES”*

Code presenting symptom first, then code Post COVID condition

Example: Coding Post COVID Condition

CODE The Presenting Condition first

**Patient with Fatigue 2 months after
COVID infection**

You will code R53.8 first



Then add Post COVID Condition code

Then, You will code U09.9

Example: Coding Post COVID Condition

Add **U09 Post COVID-19 condition**

Add **U09.9 Post COVID-19 condition, unspecified**

Add **Note:** This code enables establishment of a link with COVID-19.

Add This code is not to be used in cases that are still presenting with active COVID-19. However, an exception is made in cases of re-infection with COVID-19, occurring with a condition related to prior COVID-19.

Add Post-acute sequela of COVID-19

Add **Code first** the specific condition related to COVID-19 if known, such as:

Add chronic respiratory failure (J96.1-)

Add loss of smell (R43.8)

Add loss of taste (R43.8)

Add multisystem inflammatory syndrome (M35.81)

Add pulmonary embolism (I26.-)

Add pulmonary fibrosis (J84.10)



Practical Takeaways – PALTC CALL TO ACTION


DOI: 10.1111/jgs.17760

Journal of the
American Geriatrics Society

COMMENTARY

Post-acute sequelae of SARS-CoV-2 infection in nursing homes: Do not forget the most vulnerable

Himali Weerahandi MD, MPH^{1,2}  | Mana Rao MD^{3,4} |

Kenneth S. Boockvar MD, MS^{5,6} 

What should we be doing now?



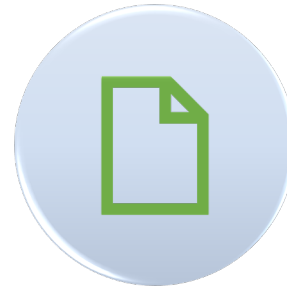
Know your resident's
baseline



High suspicion for Post
COVID conditions



Document and capture
coding appropriately



Write it up - ***Future case reports and studies are needed for PALTC***

Open Discussion



THE FLORIDA SOCIETY
FOR POST-ACUTE AND
LONG-TERM
CARE MEDICINE

**400 Executive Center Drive, Suite 208
West Palm Beach, FL 33401**

www.fmda.org; www.bestcarepractices.org



This meeting has been recorded and will be available at www.fmda.org/journalclub.php