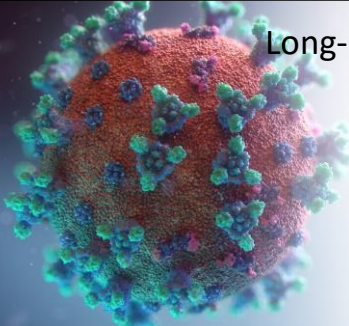
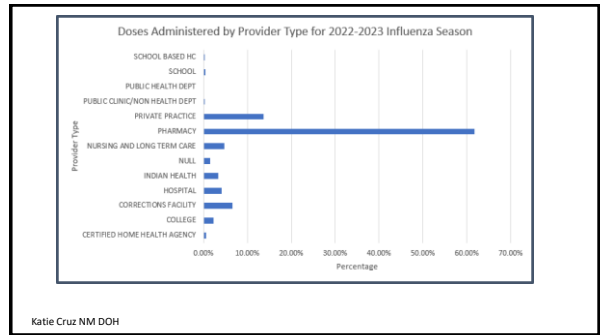


Long-Haul COVID



Melissa Martinez MD FAAFP
 Professor Emeritus
 Internal Medicine
 School of Medicine
 University of New Mexico

1



2

Objectives

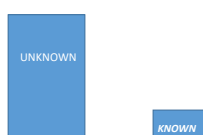
Pharmacist:
 Define Long Haul COVID
 Compare and contrast common symptom groups of long COVID
 Name three unapproved treatments for Long COVID

Pharmacy Clinicians:
 Define Long Haul COVID
 List 2 lifestyle approaches to address long COVID symptoms
 Explain the role of COVID vaccines in preventing long COVID

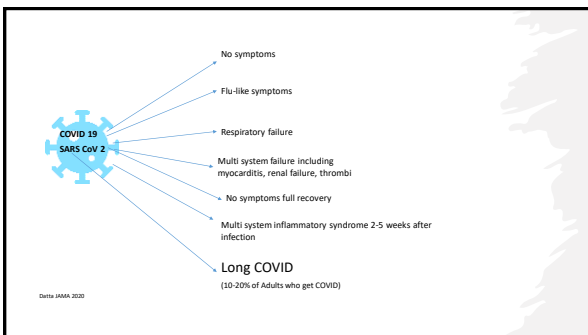
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Disclosures/Disclaimer

- Consultant Seqirus
- Off-label treatments for symptoms of Long COVID



4



5

How common is Long COVID


- 1 in 13 (7.5%) of US Adults
 - symptoms lasting three or more months after first contracting the virus
 - didn't have prior COVID-19 infection.
- 10-20% of adults who had COVID still experiencing symptoms

CDC
WHO

6

James


28-year-old sales representative. Married with one child.
 No tobacco
 Rare alcohol
 Healthy Diet
 Avid runner and works-out daily
 Elected not to get COVID Vaccination



7

James

June 22, 2021: Positive for COVID 19
 Fever, body aches, headache, loss of taste, cough, chest pain, diarrhea
 Progressive shortness of breath
 Temp 40°C, RR 30 BP 80/40 P 140 Room air O2 sat 65
 Admitted
 Remdesivir
 Not intubated
 Discharged 7 days later




8

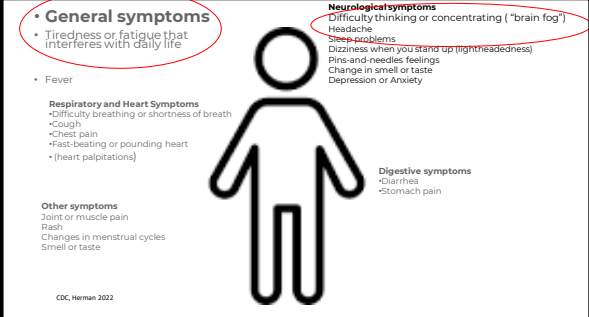
James

6 weeks after COVID 19 Diagnosis
 Fever and shortness of breath better
 Mild cough

Very tired
 "Brain Fog"
 Can't work
 Symptoms worse after exercise
 Is this long COVID?



9



• **General symptoms**
 • Tiredness or fatigue that interferes with daily life
 • Fever

Respiratory and Heart Symptoms
 • Difficulty breathing or shortness of breath
 • Cough
 • Chest pain
 • Fast-beating or pounding heart
 • (heart palpitations)

Other symptoms
 Joint or muscle pain
 Rash
 Changes in menstrual cycles
 Smell or taste

Neurological symptoms
 Difficulty thinking or concentrating ("brain fog")
 Headache
 Sleep problems
 Dizziness when you stand up (lightheadedness)
 Pins-and-needles feelings
 Change in smell or taste
 Depression or Anxiety

Digestive symptoms
 • Diarrhea
 • Stomach pain

CDC, Herman 2022

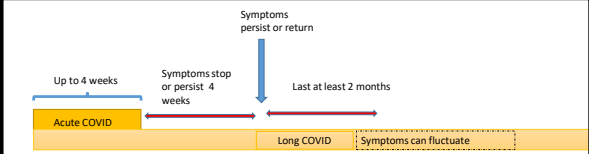
10

Long COVID Definitions

- CDC: New, returning, or ongoing symptoms associated with acute COVID-19 that persist beyond 28 days
- World Health Organization: Symptoms that last for at least two months.

CDC
WHO

11



Up to 4 weeks
 Symptoms stop or persist 4 weeks
 Last at least 2 months

Acute COVID
 Long COVID
 Symptoms can fluctuate

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

Department of Health and Human Services <https://www.covid.gov/longcovid/definitions>

12

Differential Diagnosis

- Previous comorbidities
- Unmasking of preexisting health conditions
- Reinfection
- Prolonged acute COVID 19
- Complications of prolonged illness, hospitalization, or isolation

13

James

- History and Physical exam
- Blood work
- Reassurance “this is not all in your head”
- Follow up 1 month
- Note for work



14

James

- 10 weeks later
 - Most symptoms better
- Fatigue all the time
Good and bad days
Exhausted if he exerts himself
Brain fog- “I just can’t think straight”



15

Post Exertional Malaise and Brain Fog

- Very common in long COVID
- Disabling exhaustion
- Disproportionate to the effort exerted
- Triggered by routine physical activities (e.g., bathing), cognitive activities, and emotional stress
- Often delayed (12 to 72 hours after activity)



Herrea PM R 2021

16

Chronic Fatigue Syndrome = Myalgia Encephalomyelitis

- Post COVID similar symptoms
- Unclear if pathology is the same

17

Risk factors for long COVID

- Conditions
 - Diabetes mellitus, hypertension, obesity, immunosuppression
- Age older than 50 years
- Female sex
- More severe acute infection
- More than five symptoms in the first week of acute infection
- No COVID Vaccine

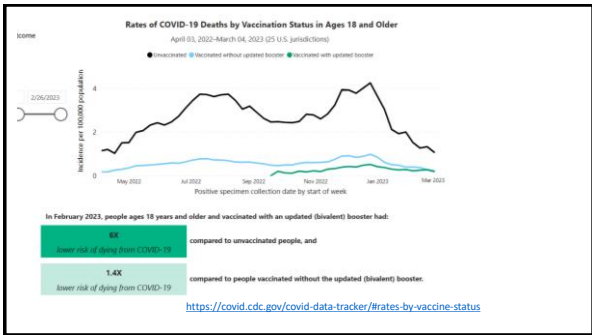
Tenforde MMWR 2020

18

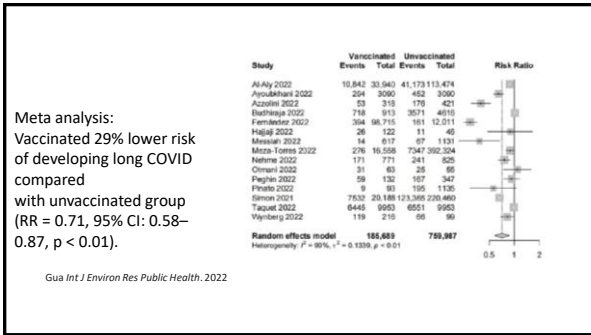
COVID Vaccine and preventing Long Covid

- Prevent Long COVID by
 - Preventing COVID 19 Infections
 - Decreasing severity of COVID
 - Treatment post COVID
- No RCT

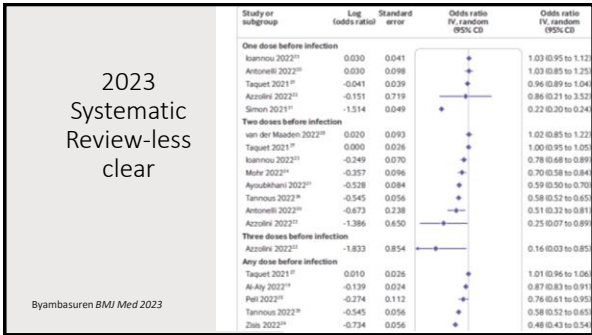
19



20



21



22

Antivirals to Prevent Long COVID

246, 076 received no COVID-19 antiviral
35, 717 received oral nirmatrelvir within 5 days

Nirmatrelvir was associated with 26% reduced risk of Long COVID
RR, 0.74 (95%CI, 0.72-0.77) ARR 4.51% (95%CI, 4.01-4.99)

Xie JAMA Internal Med 2023

23

James: Summary


- Symptoms that do not resolve in 2-3 months'
- Fatigue and brain fog most common symptoms
- Certain risk factors but anyone can get long COVID
- Look for other causes
- Vaccines are probably protective against Long COVID
- Careful about calling this anxiety

24

Ellen

60-year-old farmer. History of hypertension. Got primary COVID vaccines.
November 13, 2021 COVID. Not hospitalized.
 12 weeks later:

- Fatigue
- Abdominal Pain
- Nausea
- Frequent fainting, light-headed, dizzy
- Constipation and diarrhea
- Heat and cold intolerance
- BP drops when she stand up ----elevated when she lies down
- Pules 70 lying down 110 standing



25

Postural Orthostatic Tachycardia Syndrome (POTS)

- Autonomic dysfunction (dysautonomia)

Autonomic Nervous System

PARASYMPATHETIC	SYMPATHETIC
<ul style="list-style-type: none"> Parit Constriction Stimulation Saliva Constrict Bronchi Slow Heart rate Stimulate Production of Bile Stimulate Digestion Stimulate Digestion Causes an Erection 	<ul style="list-style-type: none"> Dilate Pupils inhibit Salivation Relaxes Bronchi Increases HeartBeat Slows Down Digestion Stimulate Glucose release Reduces Intestinal Muscles Adrenaline Production Reduces Blood Flow

Raj Clin Auto Res 2021

26

• General symptoms

- Tiredness or fatigue that interferes with daily life
- Fever

Respiratory and Heart Symptoms

- Difficulty breathing or shortness of breath
- Cough
- Chest pain
- Fast-beating or pounding heart
- (heart palpitations)

Other symptoms


- Joint or muscle pain
- Rash
- Changes in menstrual cycles
- Smell or taste

Neurological symptoms

- Difficulty thinking or concentrating ("brain fog")
- Headache
- Sleep problems
- Coziness when you stand up (lightheadedness)
- Pins-and-needles feelings
- Change in smell or taste
- Depression or Anxiety

Digestive symptoms

- Diarrhea
- Stomach pain




CDC, Hernan 2022

27

Ellen Summary

- Dysautonomia and POTS less common
- Very debilitating



28

Tony

55-year-old construction worker.


Did not get COVID vaccines.

Thinks he may have had COVID a few months ago when he had URI symptoms.

Now with sensation of shortness of breath, chest discomfort with exertion has lasted greater than 2 months

Hard to sleep

Has not been able to do vigorous work



29

• General symptoms

- Tiredness or fatigue that interferes with daily life
- Fever

Respiratory and Heart Symptoms

- Difficulty breathing or shortness of breath
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- Pins-and-needles feelings
- Change in smell or taste
- Depression or Anxiety

Digestive symptoms


- Diarrhea
- Stomach pain



CDC, Hernan 2022

30

Tony




Healthy 55-year-old construction worker.
Exam normal (except for cough)
EKG normal
Chest X ray normal
D dimer negative
Treated with Albuterol without improvement
Echocardiogram and stress test pending

DDX
Reactive airways
Pulmonary emboli
Coronary disease
Congestive heart failure
Deconditioning
Anxiety

31

Tony summary



- Persistent respiratory problems common
- Rule out other causes

32

Proposed explanations for Long COVID

- Residual virus
- Autoimmune
- Unmasking preexisting conditions
- Microthrombi

Crook *BMJ* 2021

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Treatment

- No randomized control trials
- Vaccination Observational studies
- Supportive care

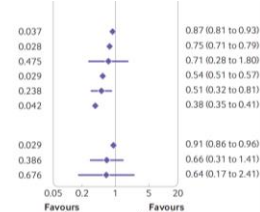
Davis *Nat Rev Microbiol.* 2023;21(3)

34

Vaccination for Long COVID treatment

30-40% improve after vaccination


Study	OR	95% CI
One dose after infection or after diagnosis of long covid		
Ayoubkhani 2022 ²⁸	-0.139	0.037
Simon 2021 (8-12 weeks) ³¹	-0.288	0.028
Witwivitsky 2022 ³²	-0.343	0.475
Simon 2021 (4-8 weeks) ³¹	-0.616	0.029
Tran 2021 ³³	-0.673	0.238
Simon 2021 (0-4 weeks) ³¹	-0.968	0.042
Two doses after infection or after diagnosis of long covid		
Ayoubkhani 2022 ²⁸	-0.094	0.029
Witwivitsky 2022 ³²	-0.416	0.386
Wynberg 2022 ²⁴	-0.446	0.676



Byambasuren *BMJ Med* 2023

35

Treatment: James



Fatigue: Lifestyle changes
Frequent rests
Listen to your body
Avoid triggers

Brain Fog:
Neurophysiologist
Stop medications that impair cognition
Off label/untested:
modafinil (Provigil), methylphenidate (Ritalin), and amantadine

Herman *AFP* 2023

36

Off Label/Untested

I am not
recommending these
medications

- Modafinil (Provigil)-Central Nervous System (CNS) Stimulant
- Methylphenidate (Ritalin)- Central Nervous System (CNS) Stimulant
- Amantadine ? Antiviral, Dopamine agonist, antiinflammatory

Herman AFP 2023

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Treatment: James



- **Plan** your activities for the day and week ahead of time as much as possible. Set up your work area so you don't have to use extra energy trying to complete something. Plan rest times throughout the activity.
- **Pace** yourself. Break larger tasks into smaller, easier steps. Try to rest for five to 10 minutes each hour.
- **Prioritize** the most challenging activities of the day so that they are done when you have the most energy.
- **Position and posture** are important. Sit down to work when you can. Practice deep breathing exercises while you work to help you stay relaxed and get more air into your lungs.

Herman AFP 2023

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Treatment: Ellen



Autonomic dysfunction and Postural Orthostatic Tachycardia

Push Fluids
Salt repletion
Compression garments
Isometric exercises
Frequent small meals
Avoid triggers: warm environment, alcohol

Medications that have been used:

Propranolol
Fludrocortisone
Pyridostigmine
Midodrine

Herman AFP 2023

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Off Label

Propranolol Beta blocker

Fludrocortisone Mineralocorticoid promoting sodium retention
Used in POTS

Pyridostigmine blocks breakdown of acetylcholine
Used for myasthenia gravis

Midodrine alpha-adrenergic agonists
Used for Orthostatic Hypotension

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Treatment: Tony



Shortness of breath

Lifestyle changes

Breathing exercises
Optimal body position and posture
Pulmonary rehabilitation
Phased return to activity program.

Herman AFP 2023

41

Breathing exercises

- **Belly breathing:** Lie flat on your back. Place one hand on your stomach and the other on your chest. Expand (push out) your stomach, but not your chest, while breathing in for four counts. Breathe out for four counts (you will feel your stomach go back down).
- **Pursed-lip breathing:** Sit down and relax. Breathe in through your nose for two counts. Form a tight circle with your lips, and blow out slowly for four counts.
- **Boxed breathing:** Breathe in for four counts, hold your breath for four counts, breathe out for four counts, and hold your breath again for four counts.

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Off label

- Guaifenesin
- Albuterol-often not helpful

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Prognosis

- Most patients can expect gradual improvement in functional status.
- Relapsing and remitting course
- The ultimate long-term prognosis of long COVID is unclear
- One study found a progressive decline in the average number of symptoms after seven months; however, 65.2% of patients still had symptoms after six months.
- Most individuals with long-term breathing difficulties do not develop permanent or chronic lung injury
- Most people will gradually recover from cognitive impairment after a severe illness.

Herman AFP 2023

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Support Groups

- Body Politic: <https://www.wearebodypolitic.com/covid-19>
- Survivor Corps: <https://www.survivorcorps.com>
- Long COVID Alliance: <https://longcovidalliance.org>
- Long COVID Kids: <https://www.longcovidkids.org>

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Summary: Long COVID


- Symptoms persist or reoccur 2-3 months after acute COVID 19
- Symptoms can wax and wane
- Symptoms can vary
- Many different mechanisms proposed
- Vaccines offer some protection
- Treatment based on symptoms

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Summary: Long COVID

- There is a lot we don't know
- Prognosis is unclear
- Dose long COVID change with variants?
- Many clinical trials

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Thank You

MLMartinez@salud.unm.edu

Questions

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