Long Covid and Lasting Lung Problems

Lekshmi Santhosh, MD., M.A. Ed.
Shari Brosnahan, MD, M.S.

Allergy & Asthma NETWORK

May 25th, 2023

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The mission of

ALLERGY & ASTHMA NETWORK

Is to end the needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy and research.

2

This will be recorded

The recording will be posted on our website shortly

3

MEET OUR SPEAKERS

Lekshmi Santhosh, MD., M.A. Ed.

Associate Professor of Medicine
Pulmonary/Critical Care Medicine & Hospital Medicine

Faculty at Pulmonary Outpatient Practice UCSF-Parnassus

Medical Director Long Covid/post-ICU OPTIMAL Clinic at UCSF Health

Shari Barnett Brosnahan, MD, MS

Assistant Professor of Medicine, Pulmonary and Critical Care at NYU Langone Health

Assistant Program Director Fellowship Program at NYU

Co-Investigator for NIH RECOVER COVID Project

4

Conflicts of Interest

LS- I have no disclosures.

SBB- Receives funding for ACTIV-4c Study and RECOVER

5

"All the News That's Fit to Print"

The New York Times

Late Edition

VOL. CLXIX . . . No. 58,703 NEW YORK, SUNDAY, MAY 24, 2020 $6.00

U.S. DEATHS NEAR 100,000, AN INCALCULABLE LOSS

They Were Not Simply Names on a List. They Were Us.

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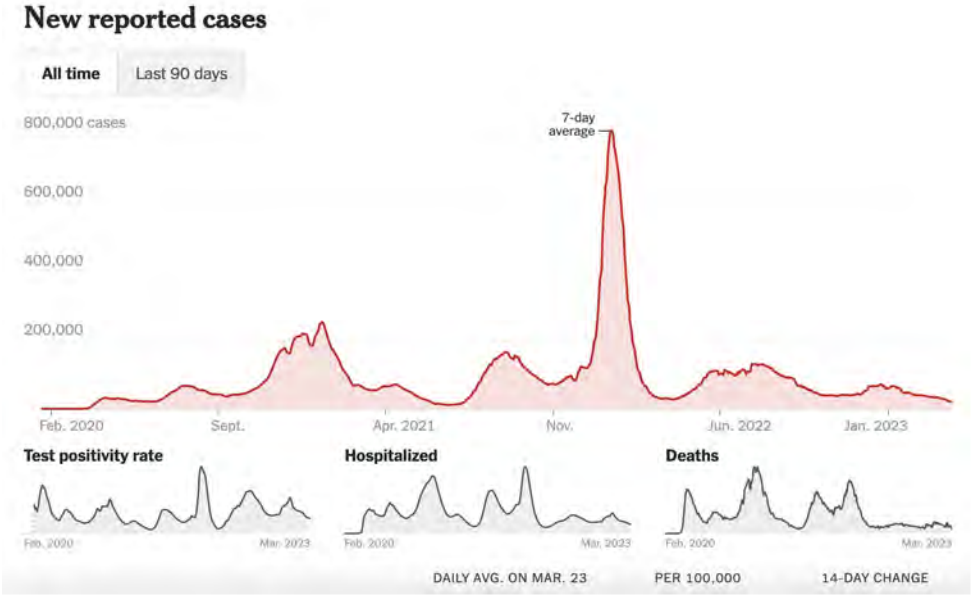
COVID-19 Is Still "Down, but Not Out"... Nationally



NYT COVID Tracker

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UCSF's Bob Wachter is still doing all he can to avoid COVID. Here's why

Aidin Vaziri

Sep. 9, 2022 | Updated: Sep. 11, 2022 12:11 p.m.

"There's still a fair amount of COVID around, and I still don't want to get it…The main reason is the data we see on long COVID is very concerning…Not just the chances that you're going to feel crummy a few months from now, which is a real number, but the chances that you're elevating your long-term risk of a heart attack or stroke, or diabetes or

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Roadmap for the Hour

- What: What is Long COVID? Pulmonary Symptoms?
- Why: What are the Biological Mechanisms?
- Who: Do Pulmonary Conditions increase Long COVID Risk?

www.sfpl.org/sfphoto

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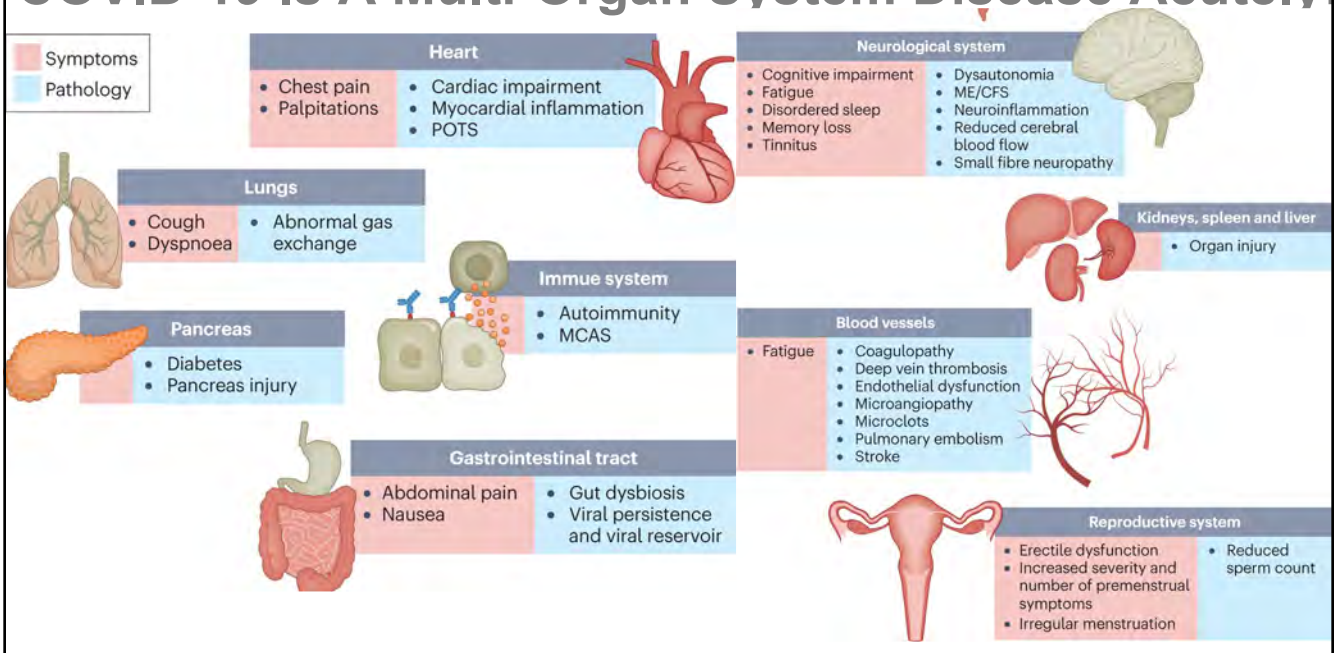
COVID-19 Is A Multi-Organ System Disease Acutely



Davis et al Nat Microbio 2023

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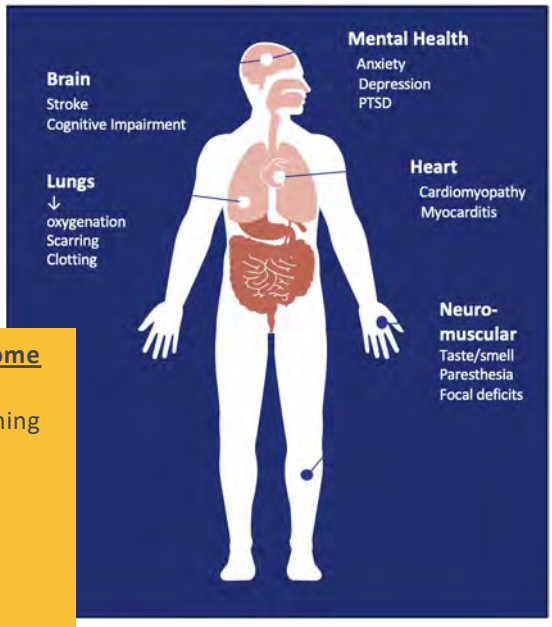
…And Long(er) Term Outcomes



Post-COVID Syndrome
(Long-hauler)

- Waxing and waning
- Fatigue
- Paresthesia
- Cognitive impairment
- Dyspnea
- Palpitations

Figure courtesy of
Neeta Thakur MD

Huang Resp Research 2020
Puntmann JAMA 2020
Davis Nature Microbio 2023

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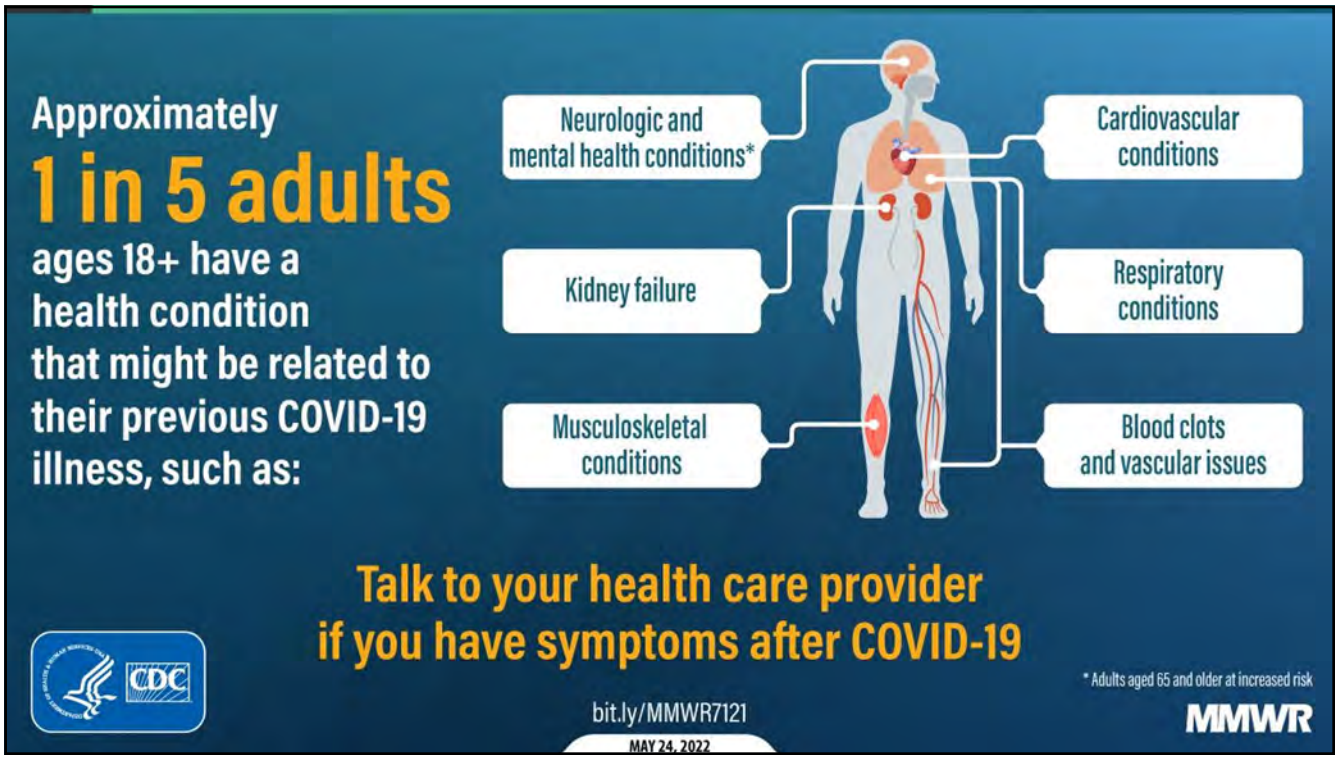

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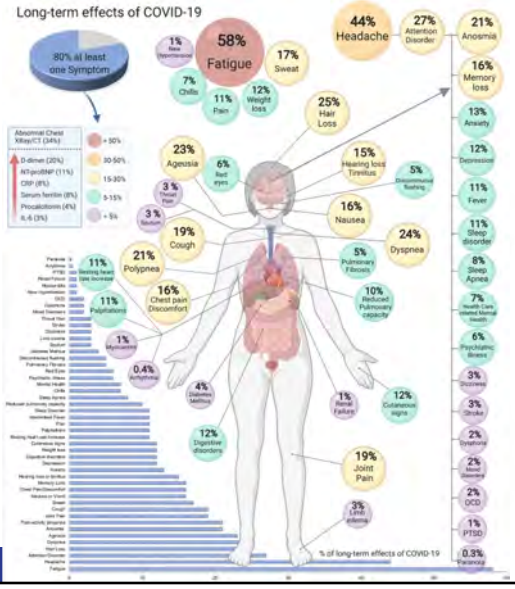
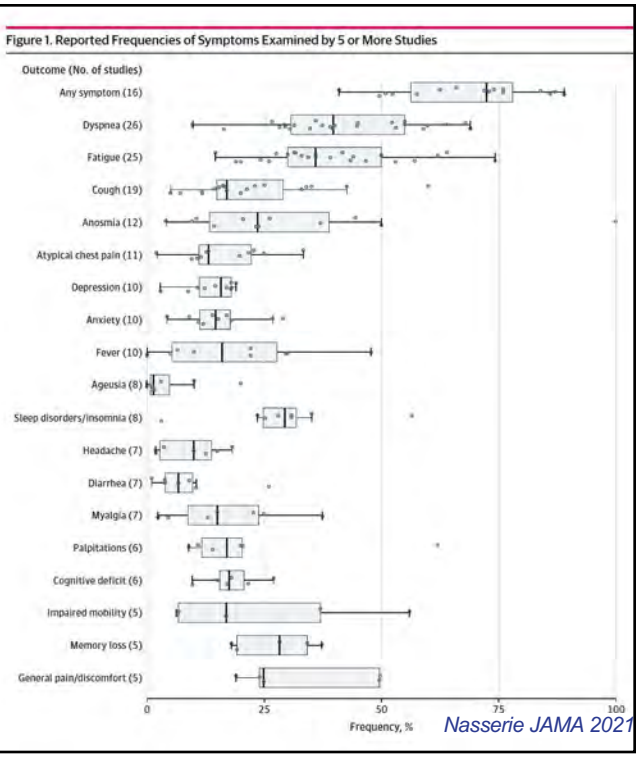
Newer Data Reaffirming



Lopez-Leon 2021



Nasserie JAMA 2021

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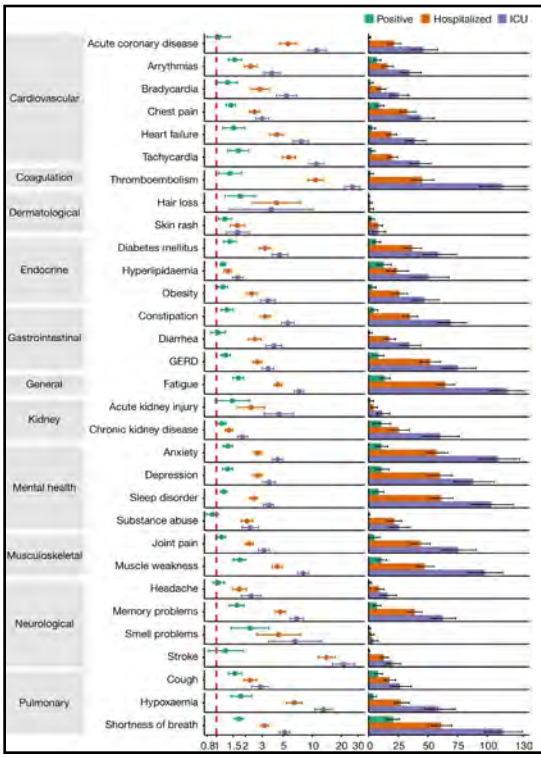

Newer & Larger Studies Corroborate This – Even Compared to Influenza

Al-Aly Nature 2021
(Al-Aly JAMA in press)

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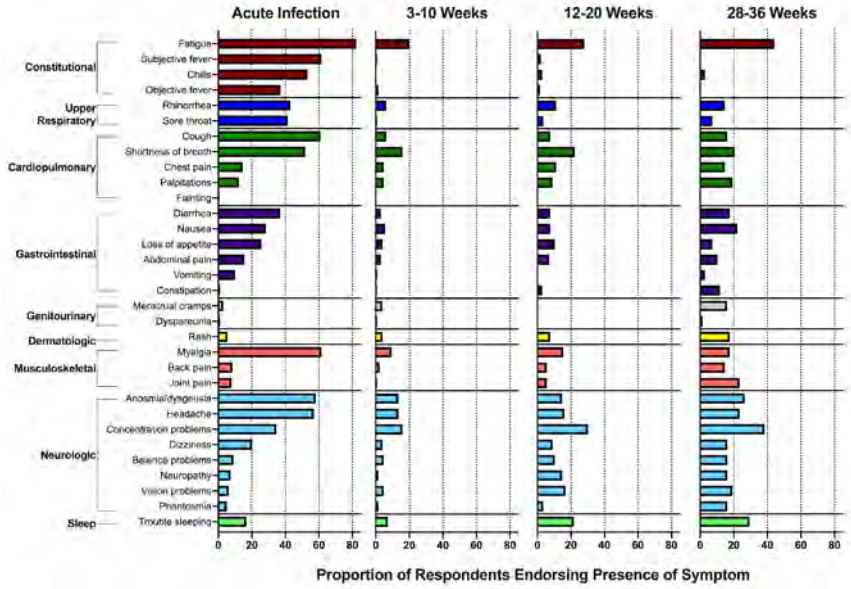
Newer & Larger Studies Corroborate This – Even in the Bay Area (LIINC Study)



Peluso OFID 2022

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Persistent Pulmonary Sx

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ARDS Survivors Have Persistent PFT Abnormalities

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 7, 2011 VOL. 364 NO. 14

Functional Disability 5 Years after Acute Respiratory Distress Syndrome

Margaret S. Herridge, M.D., M.P.H., Catherine M. Tansey, M.Sc., Andrea Matté, B.Sc., George Tomlinson, Ph.D., Natalia Diaz-Granados, M.Sc., Andrew Cooper, M.D., Cameron B. Guest, M.D., C. David Mazer, M.D., Sangeeta Mehta, M.D., Thomas E. Stewart, M.D., Paul Kudlow, B.Sc., Deborah Cook, M.D., Arthur S. Slutsky, M.D., and Angela M. Cheung, M.D., Ph.D., for the Canadian Critical Care Trials Group

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Differential – Persistent Dyspnea

1. Post-viral reactive airways disease
2. Deconditioning
3. Organizing pneumonia
4. Post-ARDS fibrosis
5. PVD

Other: Reflux-associated cough, Pleuritis, NM disease, Vocal cord dysfunction, Tracheal stenosis, Tracheomalacia

David Geffen School of Medicine

Slide Credit: Dr. Kristin Schwab, UCLA

UCLA Health

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ACPOHE
PHYSIOS FOR WORK AND HEALTH

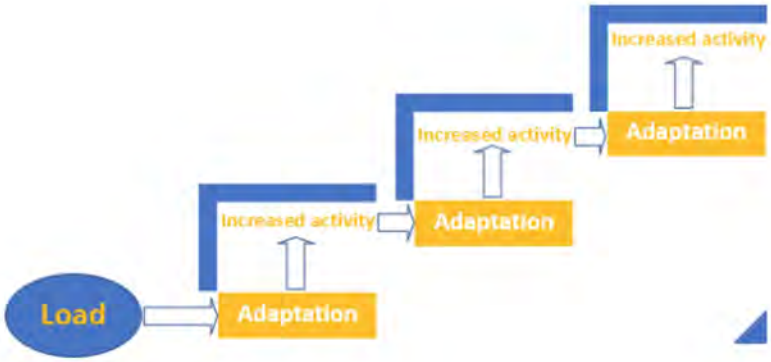

Figure 3: Progressive or graded increase in activity to increase functional capacity

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Critical Care Original Research

CHEST

Fatigue Symptoms During the First Year Following ARDS

Kerri J. Neufeld, MD, MPH; Jeannie-Marie S. Leoutsakos, PhD, MHS; Haijun Yan, PhD; Shihong Lin, MS; Jeffrey E. Zabinski, MD; Victor D. Dinglas, MPH; Megan M. Hosey, PhD; Ann M. Parker, MD; Ramona O. Hopkins, PhD, and Dale M. Needham, MD, PhD

BACKGROUND: Fatigue is commonly reported by ARDS survivors, but empirical data are scarce.

RESEARCH QUESTION: This study evaluated fatigue prevalence and associated variables in a prospective study of ARDS survivors.

STUDY DESIGN AND METHODS: This analysis is part of the ARDSNet Long-Term Outcomes Study (ALTOS) conducted at 38 US hospitals. Using age- and sex-adjusted, time-averaged random effects regression models, we evaluated associations between the validated Functional Assessment of Chronic Illness Therapy–Fatigue Scale with patient and critical illness variables, and with physical, cognitive, and mental health status at 6 and 12 months following ARDS.

RESULTS: Among ARDS survivors, 501 of 711 (70%) and 436 of 659 (66%) reported clinically significant symptoms of fatigue at 6 and 12 months, respectively, with 41% and 28% reporting clinically important improvement and worsening (n = 638). At 6 months, the prevalence of fatigue (70%) was greater than that of impaired physical functioning (50%), anxiety (42%), and depression (36%); 46% reported both impaired physical function and fatigue, and 27% reported co-existing anxiety, depression, and fatigue. Fatigue was less severe in men and in those employed prior to ARDS. Critical illness variables (eg, illness severity, length of stay) had little association with fatigue symptoms. Worse physical, cognitive, and mental health symptoms were associated with greater fatigue at both the 6- and 12-month follow-up.

INTERPRETATION: During the first year following ARDS, more than two-thirds of survivors reported clinically significant fatigue symptoms. Due to frequent co-occurrence, clinicians should evaluate and manage survivors' physical, cognitive, and mental health status when fatigue is endorsed.

CHEST 2020; 158(3):999-1007

KEY WORDS: acute lung injury; cognitive function; depression; disability; rehabilitation

FOR EDITORIAL COMMENT, SEE PAGE 868

ABBREVIATIONS: APACHE III = Acute Physiology and Chronic Health Evaluation III; FACIT-F = Functional Assessment of Chronic Illness Therapy–Fatigue Scale; SF-36v2 = Short Form-36 Version 2

AFFILIATIONS: From the Department of Psychiatry and Behavioral Sciences (Drs Neufeld, Leoutsakos, Yan, and Zabinski and Mr Lin), Division of Pulmonary and Pulmonary and Critical Care Medicine (Ms Dinglas and Drs Parker and Needham), Department of Physical Medicine and Rehabilitation (Drs Dinglas and Needham), and, Outcomes After Critical Illness and Surgery (OACIS) Group, (Drs Neufeld, Leoutsakos, Hosey, Parker, and Needham, and Ms Dinglas) Johns Hopkins University School of Medicine, Baltimore, MD; Neuroscience Center and Psychology Department (Dr Hopkins), Brigham Young University, Provo, UT; and Pulmonary and Critical Care Medicine (Dr Hopkins), Intermountain Healthcare, and Center for Humanizing Critical Care (Dr Hopkins), Intermountain Medical Center, Murray, UT.

FUNDING/SUPPORT: This research was supported by the National Heart, Lung, and Blood Institute [Grants R24 HL111895, R01HL091760, and R01HL091760-02S1], the Johns Hopkins Institute for Clinical and Translational Research [Grant UL1 TR 000424-06], and the Alliance for Treatment of Acute Lung Injury Trial [ALTA]; Early Versus Delayed Enteral Nutrition Trial [EDEN], Omega Nutrition Supplement Trial [OMEGA], and Statins for Acutely Injured Lungs from Sepsis Trial [SAILS] [National Heart, Lung, and Blood Institute contracts HHSN268200953416C to HHSN268200953419C and HHSN268200953417C].

CORRESPONDENCE TO: Kerri J. Neufeld, MD, MPH, AdCentra, Ste 457, Johns Hopkins Bayview Medical Center, 4940 Eastern Ave, Baltimore, MD 21224; e-mail: kneufel@jhmi.edu

DOI: https://doi.org/10.1016/j.chest.2020.03.044

More than 2/3rds of ARDS survivors reported clinically significant fatigue symptoms 1 year after discharge.

Neufeld CHEST 2020

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The Why?

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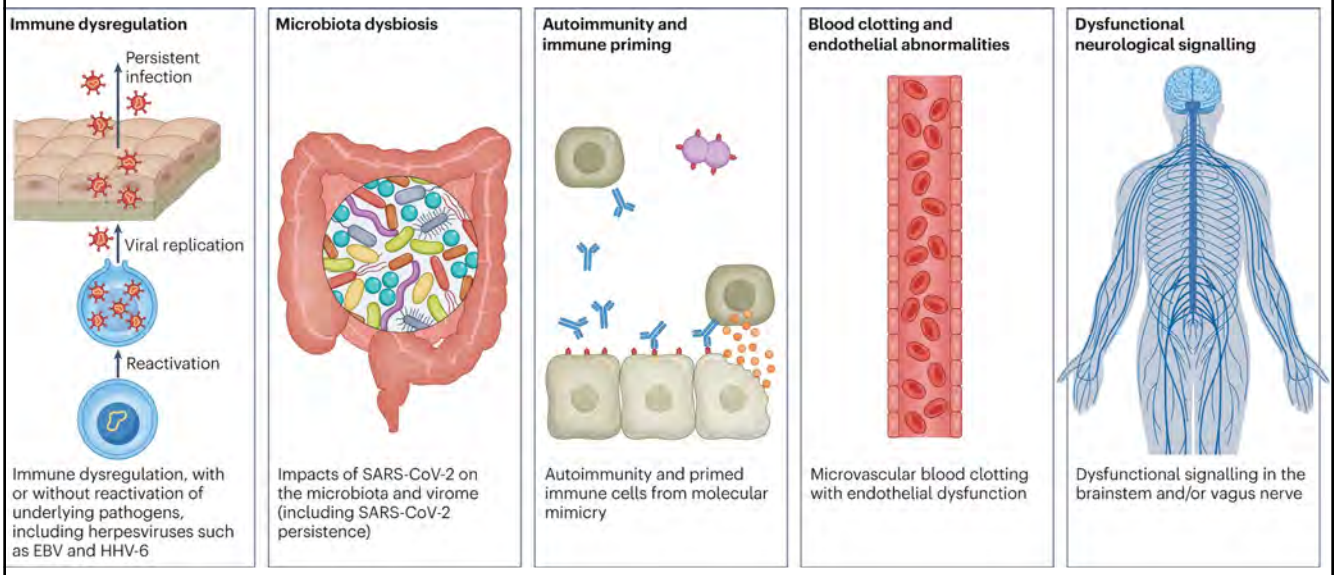
Pathophysiology



Davis et al Nature Microbio 2023

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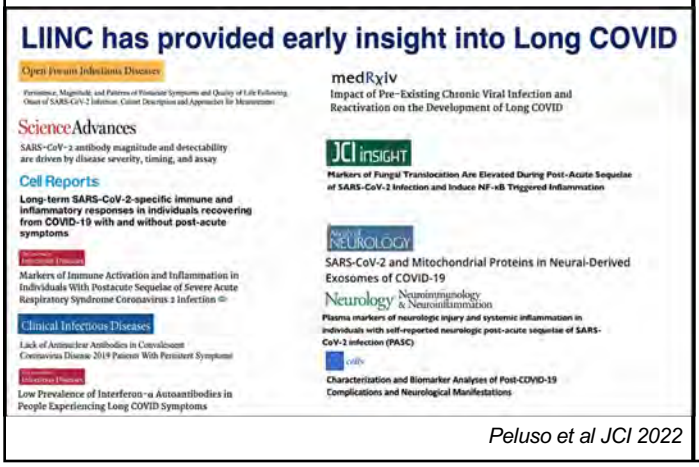
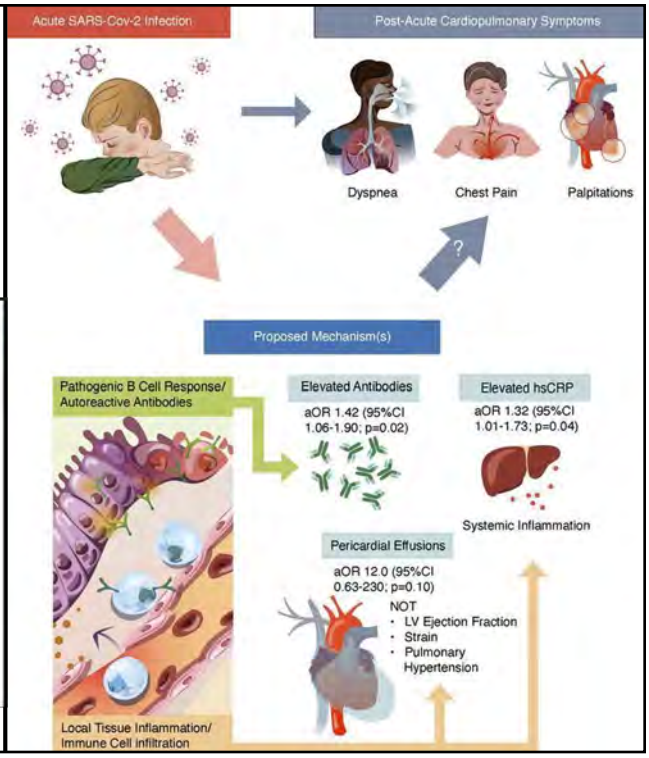
Pathophysiology

Numerous Insights from LIINC Study
https://www.liincstudy.org/en/study-findings



Peluso et al JCI 2022



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WHO Case Definition: Post-COVID-19 Condition

Post COVID-19 condition occurs in individuals with **a history of probable or confirmed SARS-CoV-2** infection, **usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.** Common symptoms include **fatigue, shortness of breath, cognitive dysfunction** but also others (see **Table 3** and **Annex 2**) which generally have an **impact on everyday functioning.** Symptoms may be **new onset,** following initial recovery from an acute COVID-19 episode, or **persist** from the initial illness. Symptoms may also **fluctuate** or **relapse** over time. A separate definition may be applicable for children.

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There is **no one "long COVID."** Each patient is unique & there are some common **symptom clusters**

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RECOVER Initiative -PASC Symptoms

- Observational Cohort Study of 9750 Patients
  - Using PROMIS Questionnaires
- Points Given Based On Specific A Symptoms is for PASC
  - Not most distressing
- 13 Most Common Symptoms
- More to come as imaging, pathology, and labs are collected

Table 2. Model-Selected Symptoms That Define PASC and Their Corresponding Scores[a]

Symptom	Log odds ratio	Score
Smell/taste	0.776	8
Postexertional malaise	0.674	7
Chronic cough	0.438	4
Brain fog[b]	0.325	3
Thirst	0.255	3
Palpitations	0.238	2
Chest pain[b]	0.233	2
Fatigue[b]	0.148	1
Sexual desire or capacity	0.126	1
Dizzines	0.121	1
Gastrointestinal	0.085	1
Abnormal movements	0.072	1
Hair loss	0.049	0

Abbreviation: PASC, postacute sequelae of SARS-CoV-2 infection.

[a] Least absolute shrinkage and selection operator was used to identify which symptoms defined PASC. A symptom score was assigned by dividing the estimated log odds ratio by 0.10 and rounding to the nearest integer. For each person, the total score was defined as the sum of the scores for each symptom a person reported.

[b] Additional severity criteria required (eTables 1 and 2 in Supplement 3).

Thaweethai JAMA 2023

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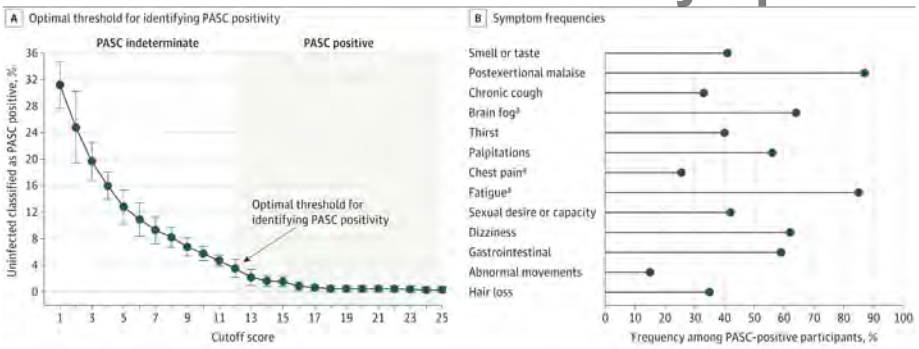
RECOVER Initiative -PASC Symptoms



C Distribution of PROMIS Global 10 responses

PROMIS Global 10 Q2: general quality of life

	0	1-2	3-6	7-11	12-16	≥17
Excellent	29	17	13	12	6	4
Very good	44	46	38	36	22	17
Good	21	30	37	36	41	32
Fair	5	6	10	14	25	33
Poor	1	0	2	2	7	14
No. of participants	3951	1412	1106	1264	998	1033

PASC score (quintile above 0), %

PROMIS Global 10 Q3: general physical health

	0	1-2	3-6	7-11	12-16	≥17
Excellent	15	6	4	4	1	0
Very good	41	31	27	20	11	7
Good	31	43	42	41	34	26
Fair	10	18	24	29	42	41
Poor	1	1	4	6	12	26
No. of participants	3951	1412	1106	1264	998	1033

PASC score (quintile above 0), %

PROMIS Global 10 Q6: ability to carry out everyday physical activities

	0	1-2	3-6	7-11	12-16	≥17
Completely	78	71	59	47	27	15
Mostly	12	17	21	25	27	22
Moderately	6	9	14	20	28	30
A little	3	3	6	8	17	31
Not at all	0	0	0	0	1	1
No. of participants	3951	1412	1106	1264	998	1033

PASC score (quintile above 0), %

Thaweethai JAMA 2023

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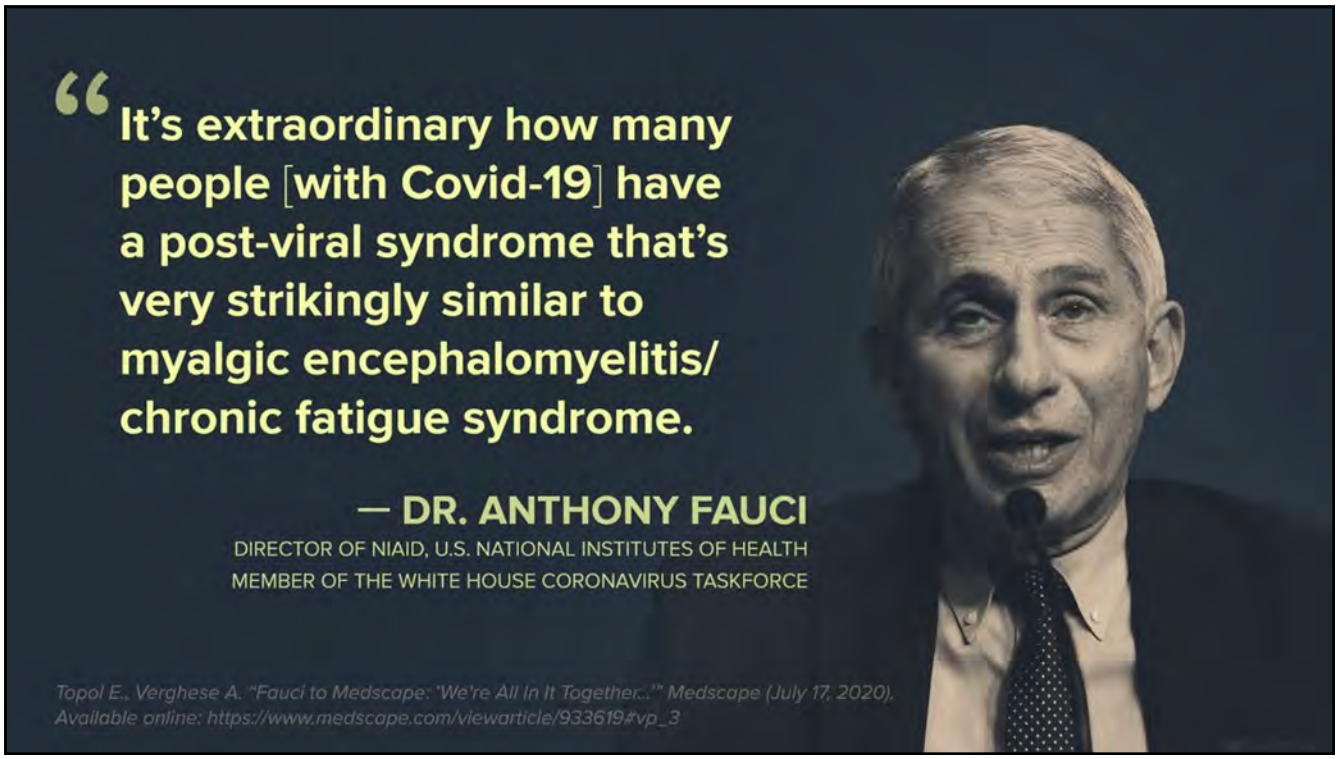

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At LEAST 3-5 Main Symptom Clusters

Fewer Symptoms

Joint Pain-Myalgias-HA

Chest Pain-DOE-Palps

B Symptom frequencies by PASC status

	1 (n=477)	2 (n=405)	3 (n=587)	4 (n=562)	Positive (n=2031)	Unspecified (n=7733)
Fatigue[a]	56	84	94	94	85	23
Fever, sweats, or chills	27	26	28	56	35	5
Postexertional malaise[c]	55	99	99	94	87	9
Swelling of legs	22	23	18	40	26	6
Chest pain[d]	13	26	14	50	26	2
Palpitations[e]	38	59	44	86	57	9
Hair loss[f]	29	31	21	58	35	13
Skin color changes	10	17	16	38	21	3
Skin pain	5	6	8	18	9	1
Skin rash	12	16	17	32	20	5
Hearing	40	38	40	62	46	14
Vision	19	20	25	51	30	4
Abdominal pain	7	11	12	36	17	2
Dry mouth	29	42	26	55	38	7
Gastrointestinal[g]	42	60	45	88	59	14
Teeth	18	21	17	43	25	8
Thirst[h]	30	48	20	62	40	6
Back pain	26	31	32	58	38	8
Foot pain	15	19	15	36	22	3
Joint pain	32	33	36	64	42	9
Muscle pain	27	33	34	60	39	6
Weakness	24	33	41	67	42	4
Abnormal movements[i]	5	10	8	33	15	1
Brain fog[a]	38	0	100	94	64	7
Dizziness[j]	31	56	62	94	62	10
Headache	23	26	37	64	39	5
Smell or taste[k]	100	3	6	53	41	4
Tremor	14	14	15	34	20	3
Anxiety	18	17	30	40	27	7
Depression	17	17	32	44	29	6
Sexual desire or capacity[l]	29	33	35	66	42	11
Sleep disturbance	18	22	32	49	32	5
Chronic cough[a]	33	43	16	43	33	5
Shortness of breath	22	30	31	58	36	3
Sleep apnea	30	36	32	44	36	12
Throat pain	5	5	7	24	11	1
Bladder	20	25	23	49	30	8

Thaweethai JAMA 2023

Kenny et al OFID 2022

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Pulmonary Comorbities increase Risk?

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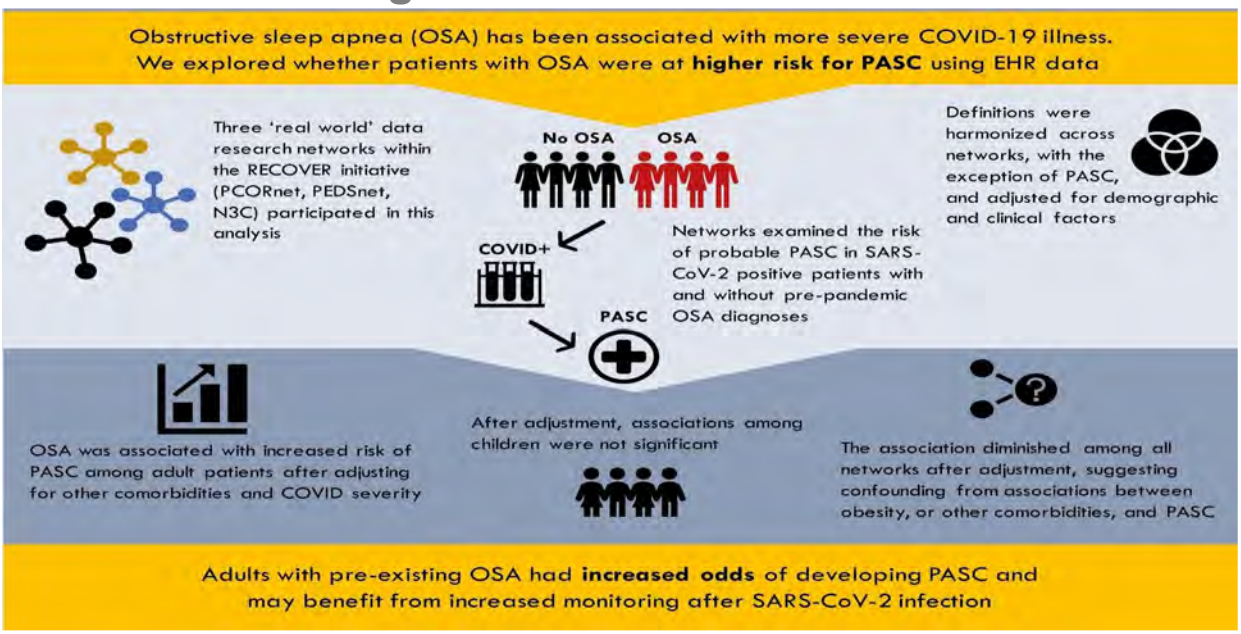
OSA Increase Long COVID RISK In Adults and Not Children



Mandel Sleep 2023

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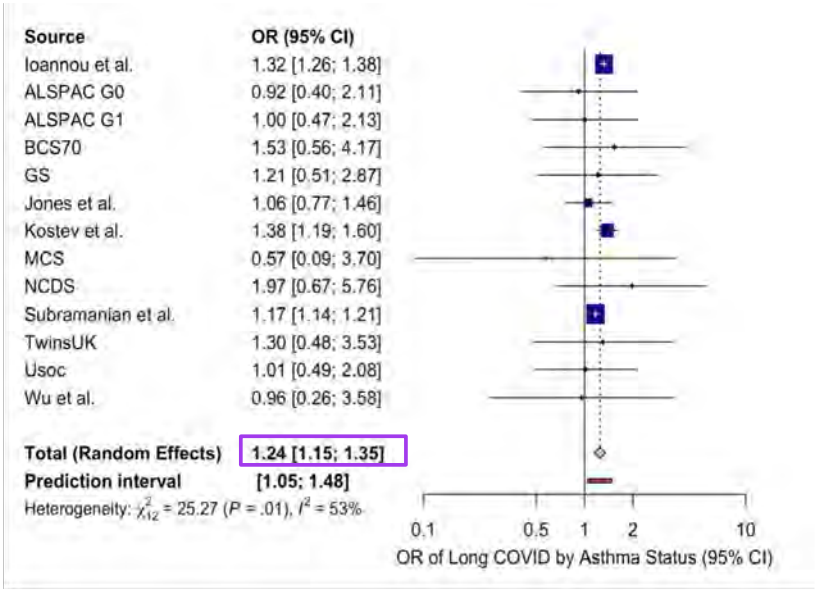
Asthma Associated with Increased Long COVID



- Meta-analysis of 13 studies
- 639 397 patients

- effect size = −0.0001; 95% CI, −0.0003 to −0.0001; *P* < .001),
- No significant publication bias

Tanayott Jama 2023

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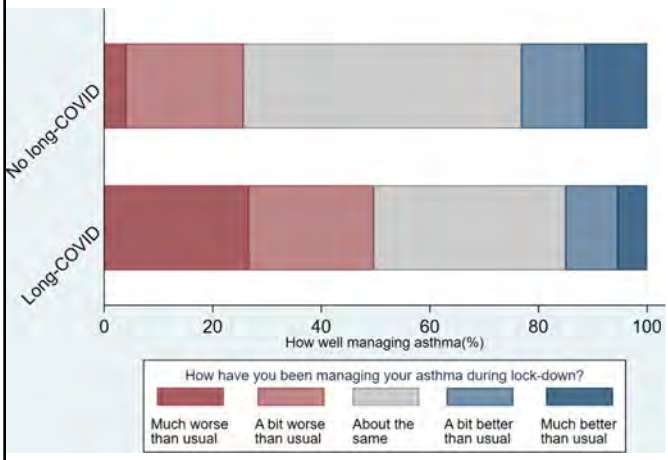
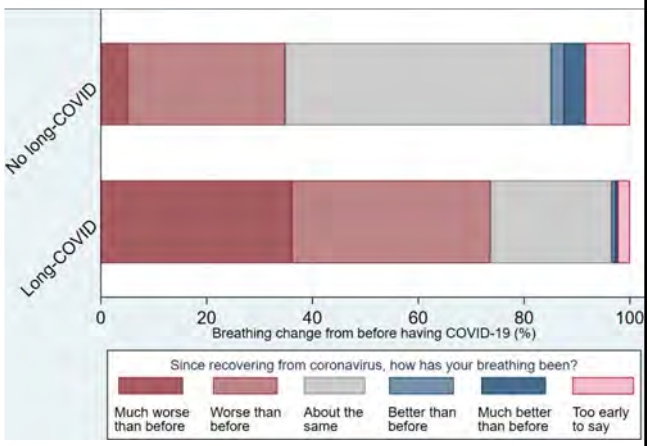
Asthma Control Worse After COVID





Philip Asthma 2021

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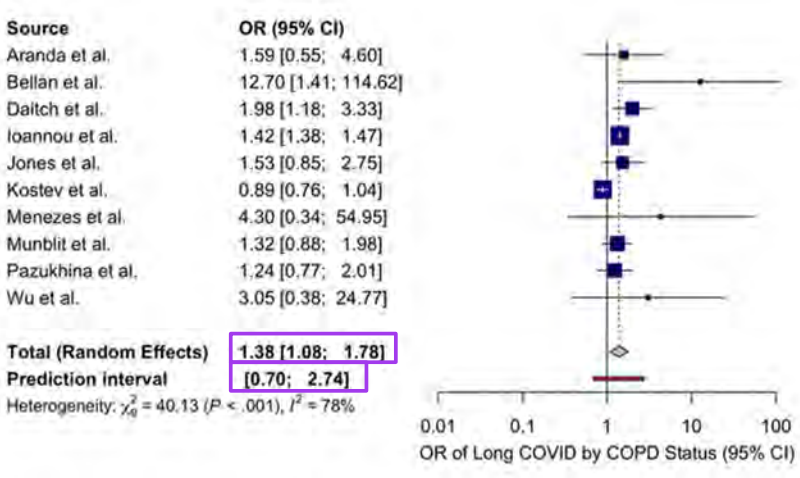
COPD Likely Associated with Long COVID

- Analysis of 10 studies
- 257 340 patients
- COPD was a risk factor associated with persistent symptoms after COVID-19 infection

- Significance may not be seen in all future studies (95% PI, 0.70 to 2.74)
- Concern that the results maybe less at COPD was a RF for death

Meta-regression analysis for study size (effect size = −0.0002; 95% CI, −0.0003 to 0.0001; $P = .66$) and Egger test (ntercept = 0.23; 95% CI, 0.14 to 0.33; $P = .69$,) were both nonsignificant



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CASE

- 45 yo F with PMHX for COVID in late 2020 who then developed PASC/Long COVID symptoms predominately brain fog, shortness of breath, fatigue, exercise intolerance, and chronic cough.

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CASE

- 45 yo F with PMHX for COVID in late 2020 who then developed PASC/Long COVID symptoms predominately brain fog, shortness of breath, fatigue, exercise intolerance, and chronic cough.

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Work Up for Dyspnea, Fatigue, and Chronic Cough

- Dyspnea
  - Cardiac Pulmonary Evaluation Test
- Fatigue
  - Sleep Evaluation (Could need specialized Evaluation)
  - Exercise evaluation (6 min walk v CPET)
- Chronic Cough
  - Pulmonary Evaluation

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TESTING

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Imaging

Pulmonary

- Chest X- Ray
- CT Scan
- PFT

Cardiac

- EKG/Halter (tilt table?)
- Echocardiogram
- 6 Min Walk Test v CPET

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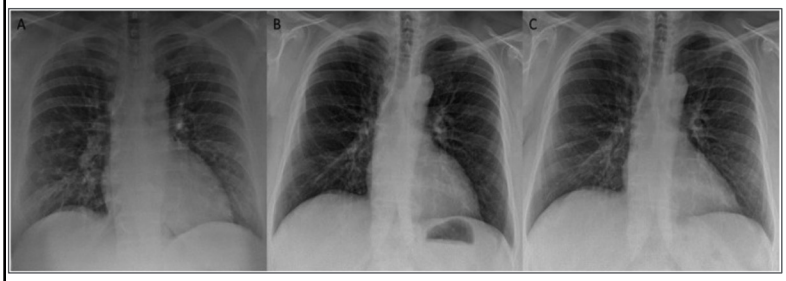
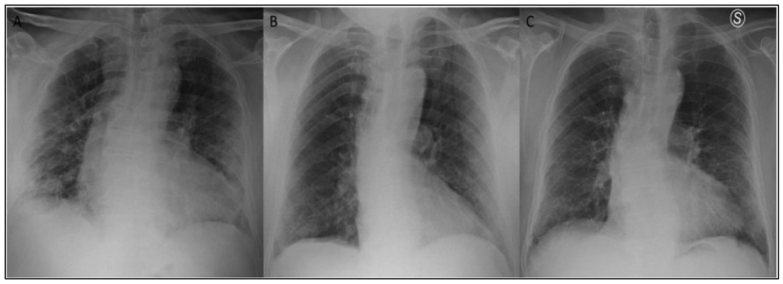
CXR



- Helpful screening tool
- About 50% of patients still had CXR abnormalities at 3 months
- But hard to get a lot of information



Fogante et al Radiology 2022

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CT Scan

- 41 patients
- Gradual recovery after hospital discharge on serial CT scores.
- 47% of the pt with abnormal CT at 1 year
- Predominate Pattern with ground-glass opacity (GGO) with reticular pattern
- Correlated with PFTs
  - decreased total lung capacity and residual volume
- Patients with radiological abnormalities
  - older
  - current smokers
  - hypertensives
  - lower SaO_2
  - secondary bacterial infections during acute phase

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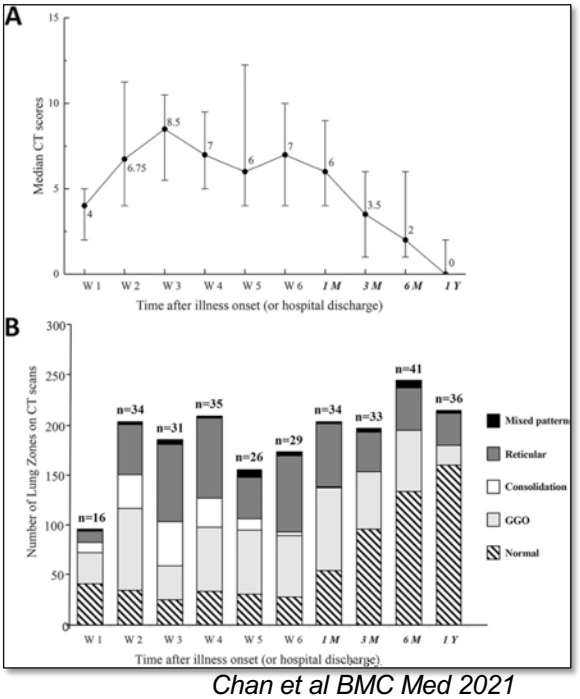

Chan et al BMC Med 2021

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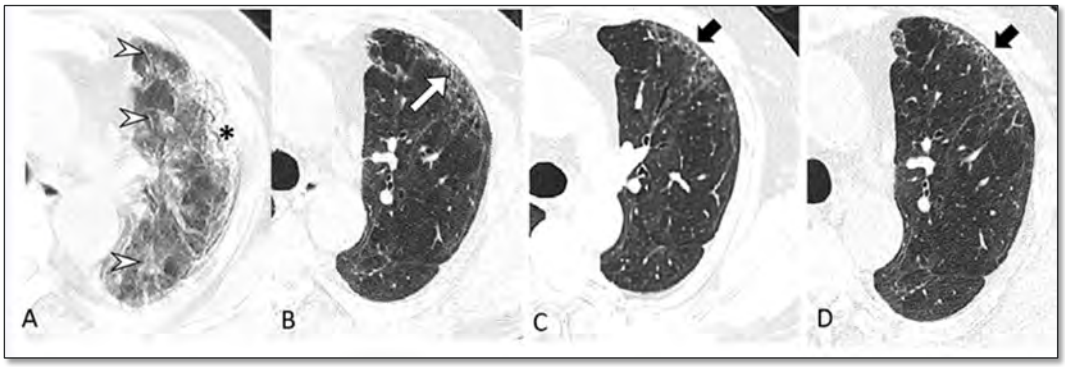
CT Scan



- 144 patients (79 men, median age 60)
- 3 chest CT scans and PFTs at 6, 12 mo and 2 years
- At D/C- fibrosis, thickening, honeycombing, cystic changes and dilation of the bronchi.
- Over two years-> gradually decreased.
- 6m - 54% of patients showed lung abnormalities.
- 2 yr -, 39% (56/144) lung abnormalities,
  - 23% with fibrotic lung
  - 16% with non-fibrotic lung.

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Han et al Radiology 2023

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PFT

Table 4: Comparison of Clinical Characteristics and Pulmonary Function at Three Follow-up Time Points

Characteristic	6 Months	12 Months	2 Years	*P* Value	Adjusted *P* Value
Residual symptoms ($n = 144$)*	43 (30)	36 (25)	32 (22)	.11	.12
Cough	23 (16)	16 (11)	15 (10)	.04	.06
Expectoration	18 (13)	15 (10)	15 (10)	.5	.5
Exertional dyspnea	29 (20)†	27 (19)	20 (14)	.04	.06
Pulmonary function‡					
Ventilation function					
Maximum VC	102 ± 21†§	106 ± 18	109 ± 18	<.001	<.001
FVC	103 ± 22†§	108 ± 19	110 ± 18	<.001	<.001
FEV_1	101 ± 22†§	108 ± 19	108 ± 19	<.001	<.001
FEV_1/FVC	94 ± 10§	96 ± 9.3	95 ± 6.7	.007	.02
Diffusion function					
Dlco	80 ± 17†§	82 ± 14	84 ± 12	.007	.02
Dlco severity*				.08	>.99
Normal	69 (63)†	73 (71)	91 (71)		
Mild	32 (29)	27 (26)	35 (27)		
Moderate	9 (8)	3 (3)	3 (2)		
Severe	0	0	0		
Dlco/VA	97 ± 17	99 ± 18	99 ± 18	.02	.04

Note.—Except where indicated, data are means ± SDs. Residual symptoms are participant-reported. The number of participants for specific residual symptoms does not add up to the total number of participants because some participants had multiple specific symptoms. Pulmonary function results were compared with those in age- and sex-matched control participants and are reported as percentages of predicted values. Dlco severity is indicated as follows: normal, greater than 75%–140%; mild, 60%–75%; moderate, 40%–59%; and severe, less than 40%. *P* values comparing participants among 6-month, 12-month, and 2-year follow-up examinations are from generalized multilevel models, and the adjusted *P* value was computed using the Benjamini-Hochberg method for false discovery rate controlling adjustments. Multiple comparisons between two time points were adjusted using the Bonferroni method. Dlco = diffusing capacity of lung for carbon monoxide, FEV_1 = forced expiratory volume in 1st second of expiration, FVC = forced VC, ILA = interstitial lung abnormality, VA = alveolar volume, VC = vital capacity.

* Data are numbers of participants, with percentages in parentheses.

† Statistically significant compared with 2-year follow-up.

‡ The total number of participants who completed lung function tests at the three time points were 110 at 6 months, 103 at 12 months, and 129 at 2 years.

§ Statistically significant compared with 12-month follow-up.

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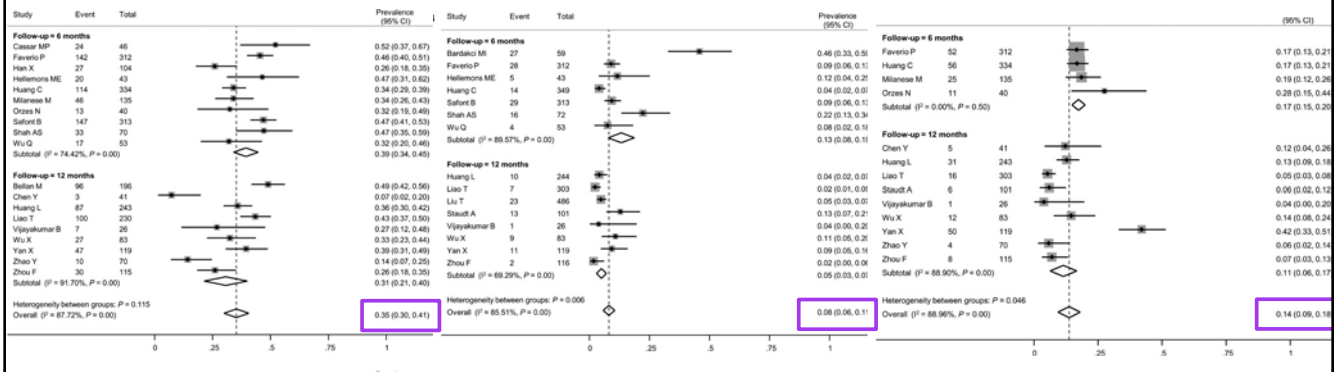
PFT



DLCO FVC TLC

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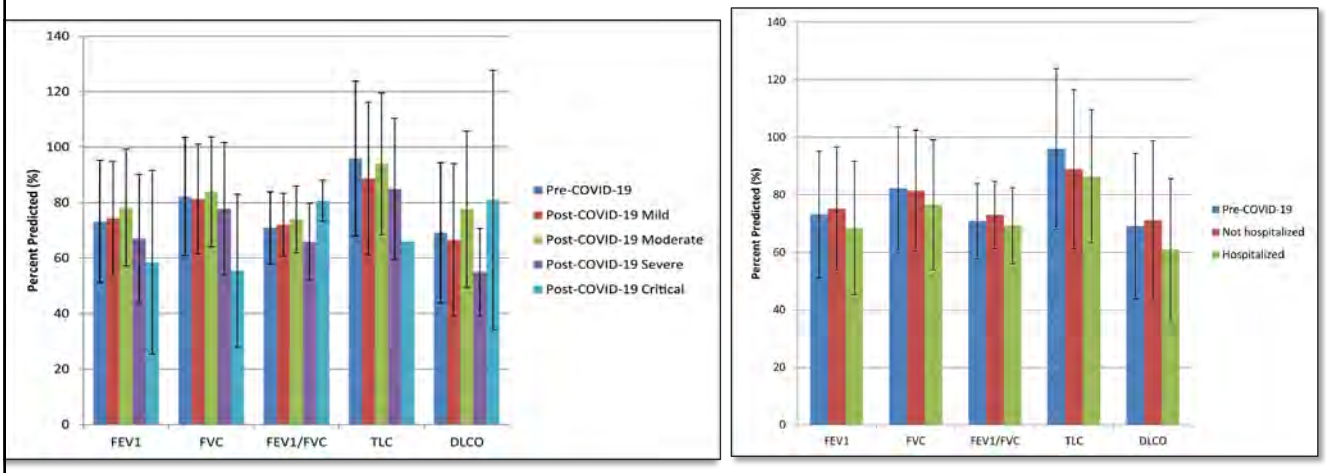
PFT



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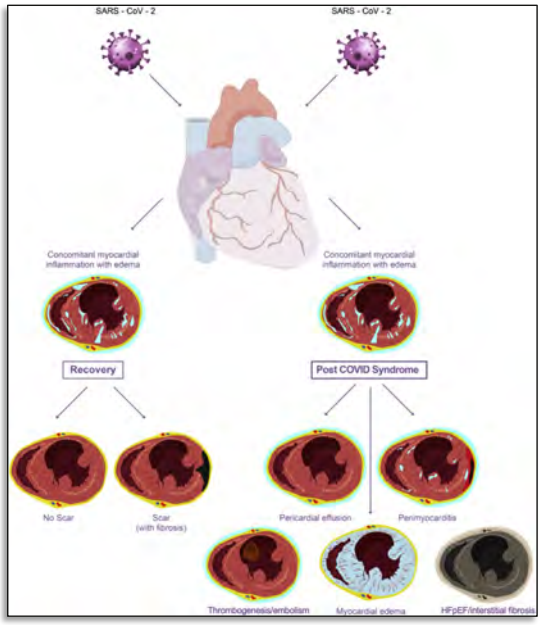
Long COVID and Heart



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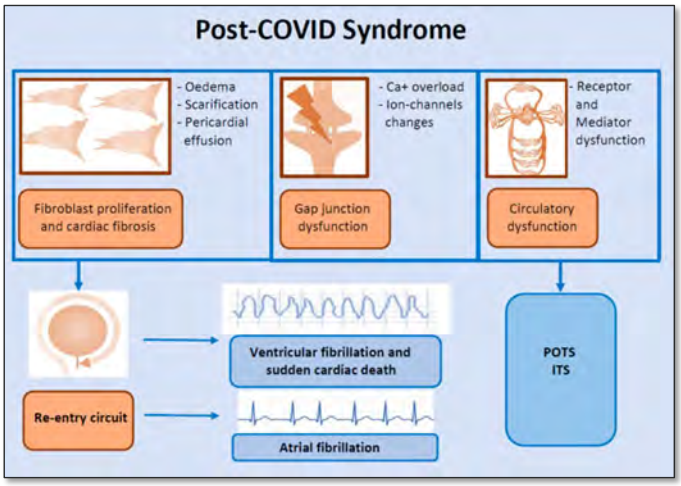
EKG/Halter

- Around 10 % of long COVID patients report palpitations.
- Up to 60 % who reported tachycardia, with increase in heart rate from standing vs. sitting position in 1/3 of those (may be postural orthostatic tachycardia syndrome (POTS)
- Up to 20% had evidence of QTc prolongation



Alsallamin Cureus 2022, Huseynov Viruses 2023

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Cardiac Conditions - Echocardiogram

Table 4 Cardiac complications and their prevalence in patients with long COVID

Cardiac complications	Patients with cardiac complications (%)	Patients included in study (*n*)
Chronic myocarditis	0.4–28.9%	48–543
Chronic pericarditis	1.9–27%	26–105
Myocardial oedema	15.4%	26
Myocardial fibrosis or scar	4%	26
Systolic or diastolic LV dysfunction	0.06–35%	51–8983
RV systolic dysfunction	7–22.6%	50–1414
LV thrombus	2%	51
Coronary artery disease	8%	51
Acute myocardial infarction	1.5–8%	51–47 780
Persistent systemic endothelial dysfunction	2.5–6.1%	72–133
Coronary microvascular disease	18%	22
Heart failure	0.1–2%	543–8983
Pulmonary hypertension	10–50%	102–145

Studies with highly selected patient groups (e.g. only hospitalized and/or intensive care unit treatments, older age, or significant comorbidities, as inclusion criteria) were excluded. LV, left ventricular; RV, right ventricular.

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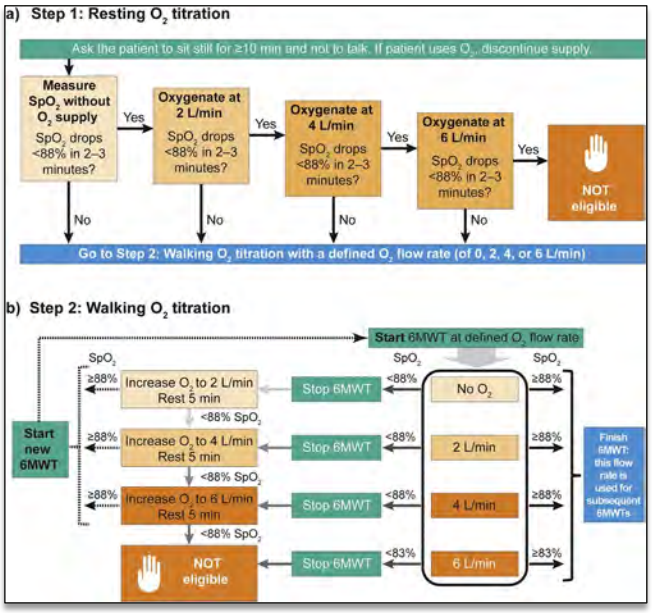
6 min walk test (6MWT)



49 Lancaster Clincial trials 2021

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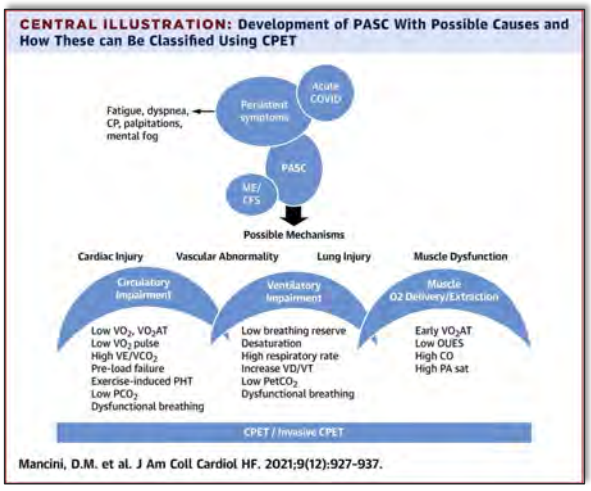
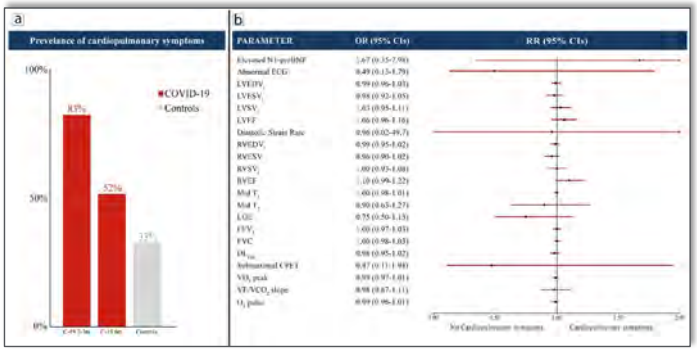
Cardiopulm Exercise Test





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TREATMENT

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Pulmonary Trajectory

- Patients have seen improvement for around 1 year
  - This is in most not all patients
  - This improvement was most pronounced between 6-9 months
- Fibrosis is the least likely to improve
  - We have seen some improvement – something we did not think possible before
  - Traction bronchiectasis stayed and in some cases evolved
- Ground Glass persisted for longer
  - in most cases did regress

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Pulmonary Treatments

- Persistent Ground Glass Opacities – Steroids or Immunosuppression (NCT04657484)
- Anti-fibrotic agents (pirfenidone and nintedanib) (NCT04541680, NCT04607928)
- Pulmonary Rehab - *post exertional malaise needs to be accounted for*
- Persistent Viral Infection– Paxlovid (NCT05576662).
- Inflammation? – Metformin
- Microthrombi (Decreased DLCO) – Anticoagulation/ASA – small clinical trials

Clinical trials.gov

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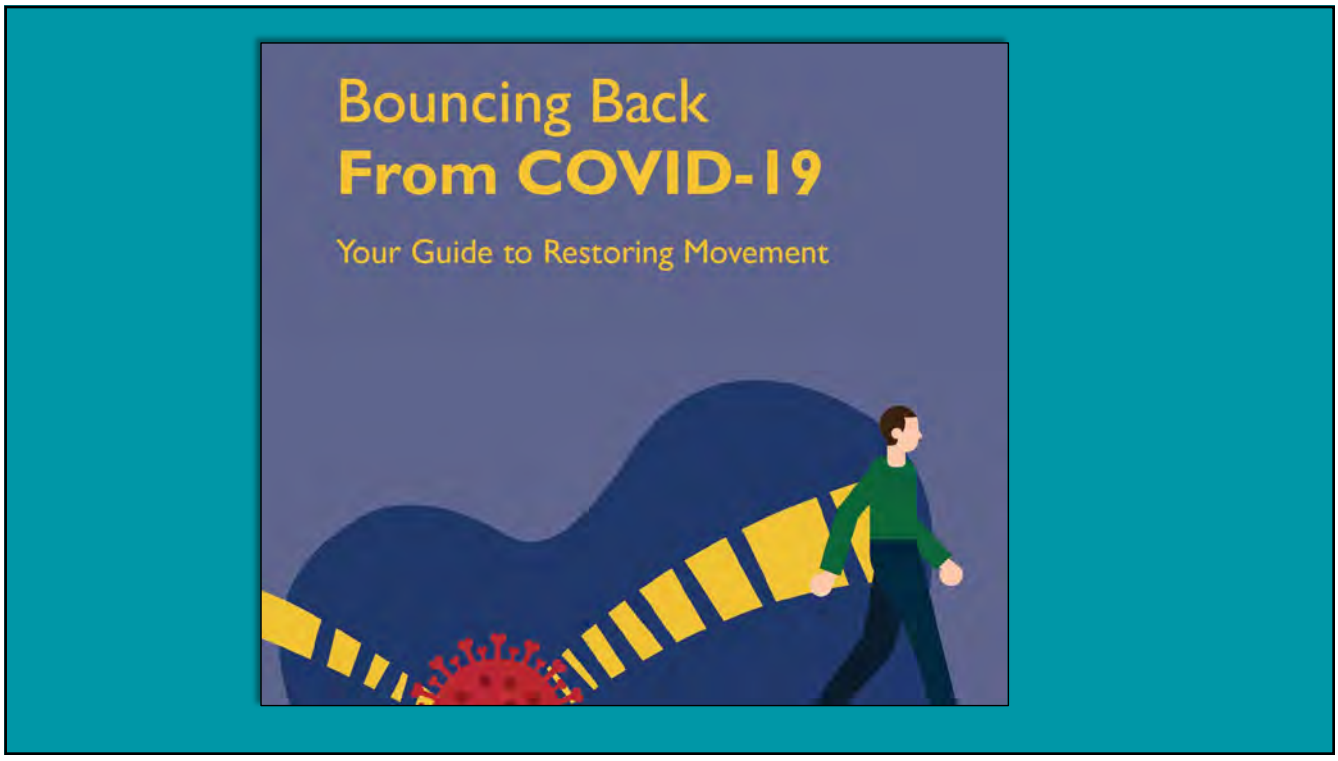

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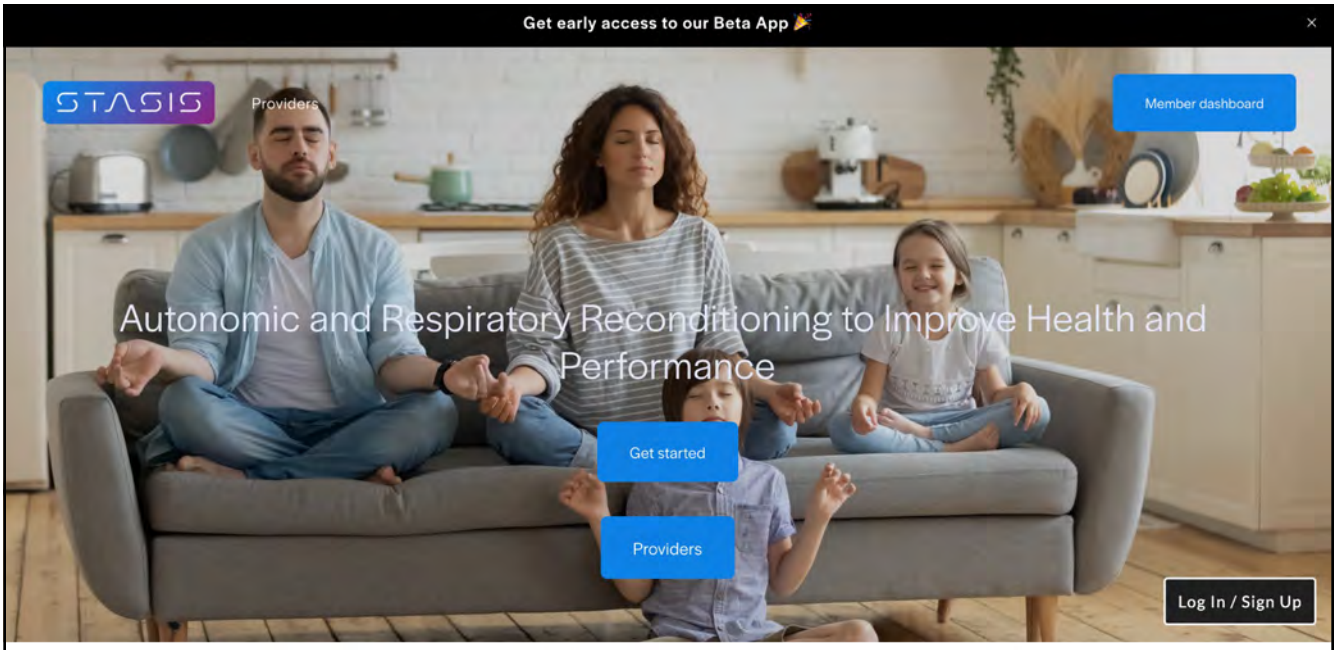

Figure 3: Progressive or graded increase in activity to increase functional capacity

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All that "Long-Hauls" is not COVID.

Avoid anchoring & keep ddx broad throughout.

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Table 1 Summary of candidate treatments and supporting evidence

From: Long COVID: major findings, mechanisms and recommendations

Davis et al Nature Microbio 2023

Symptoms and/or biological mechanism	Treatments	Supporting evidence	Comments
Postexertional malaise	Pacing	ME/CFS literature	Exercise, cognitive behavioural therapy and graded exercise therapy are contraindicated
POTS	Pharmacological: β-blockers, pyridostigmine, fludrocortisone, midodrine	POTS and ME/CFS literature	Options can be prioritized on the basis of a specific constellation of symptoms
	Non-pharmacological: increase salt and fluid intake, intravenously administered salt, compression stockings	POTS and ME/CFS literature	–
Immune dysfunction	Intravenous immunoglobulin	ME/CFS literature	Consider consulting an immunologist on implementation
Cognitive dysfunction	Cognitive pacing	ME/CFS literature	Consider implementation alongside pacing physical exertion
Cognitive dysfunction	Postconcussion syndrome protocols	ME/CFS and postconcussion syndrome literature	–

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Possible Treatments Continued

Pain, fatigue, neurological symptoms	Low-dose naltrexone	ME/CFS and other literature	Substantial anecdotal reports of success within the patient community
Fatigue, unrefreshing sleep, brain fog	Low-dose aripiprazole	ME/CFS literature	–
Autoimmunity	BC007	Long COVID case report	Neutralizes G protein-coupled receptor autoantibodies
Abnormal clotting	Anticoagulants	Long COVID pilot study	Additional trials in progress
Abnormal clotting	Apheresis	ME/CFS literature, long COVID pilot study	–
Viral persistence and antivirals (COVID-19)	Paxlovid	Long COVID case reports	No active trials, despite strong evidence for viral persistence
Viral persistence and antivirals (reactivations such as of EBV, HCMV and VZV)	Valaciclovir, famciclovir, valganciclovir and other antivirals	ME/CFS literature	–

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Possible Treatments Continued

Endothelial dysfunction	Sulodexide	Long COVID pilot study	–
Gastrointestinal symptoms	Probiotics	Long COVID pilot study	Resolved gastrointestinal and other symptoms
Dysautonomia	Stellate ganglion block	Long COVID case report	Effects may wane over time and require repeated procedures
Endothelial function, microcirculation, inflammatory markers and oxidative stress	Pycnogenol	COVID-19 pilot study	–
MCAS	H_1 and H_2 antihistamines, particularly famotidine	Long COVID case reports, MCAS literature	Expected to treat symptoms; not underlying mechanism
Autonomic dysfunction	Transcutaneous vagal stimulation	Long COVID pilot study	–

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Take Home Points

- Disentangling the PASC- E Unibus Pluram (From Many, One) & remember **all that Long Hauls isn't COVID**
- **Pulmonary or Cardiac Imaging** can be helpful but does not tell the whole story
- If there are abnormalities seen inline other conditions then we can treat with medications for those conditions **(fibrosis, obstruction, arrhythmia,** etc)
- PASC treatments – will not be right for everyone – need to **direct treatment both clinically and as research trials** progress
- Listen to everyone in the room. **Believe patients.**

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Thank You!

Questions?

Shari.Brosnahan@nyulangone.org
@ShariBrosnahan

Lekshmi.Santhosh@ucsf.edu
@LekshmiMD

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QUESTIONS

Put your questions in the question box
We'll get to as many as we can!

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Have ideas for webinars? Want to provide feedback?
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Thank you!

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