

NDSU CENTER FOR IMMUNIZATION RESEARCH AND EDUCATION

Long-Haul COVID: The Next National Health Crisis?

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The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Confronting Our Next National Health Disaster — Long-Haul Covid

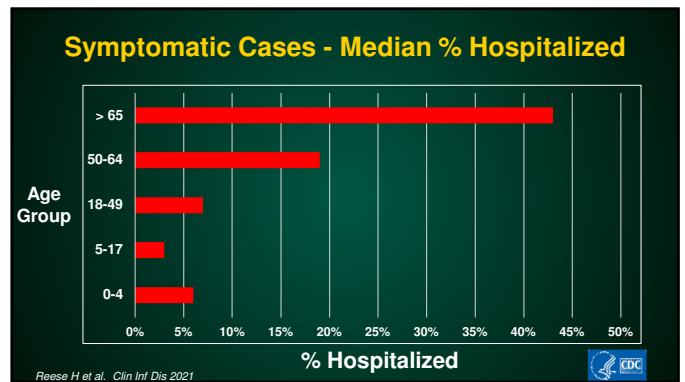
Steven Phillips, M.D., M.P.H., and Michelle A. Williams, Sc.D.

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“99.9% of people with COVID survive... I’m healthy, I’ll take my chances”

Actual Overall Case-Fatality Rate in U.S. | **1.6%**

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After 100 days in Sanford's COVID unit, young Cass County man goes home

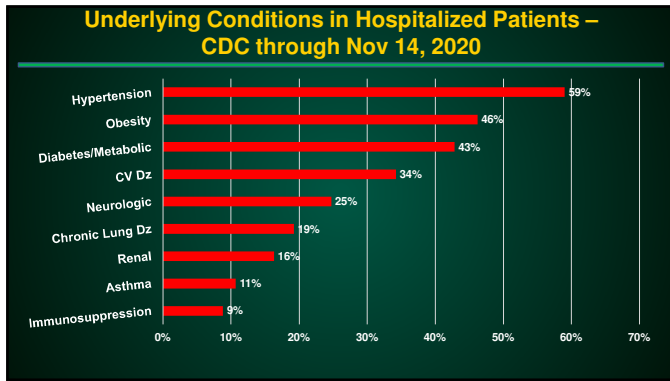
Fundraiser for Brady Munro, battling COVID-19

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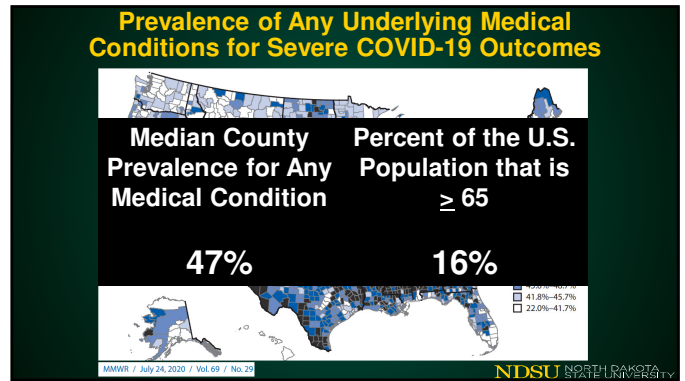
Williston woman gives birth, and then finds herself in a life battle with COVID

Justin and Nicole Roberts

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Risk of Readmission and Mortality After Surviving COVID-19 Hospitalization

- British study of over 47,000 people hospitalized with COVID-19 in 2020
- Mean follow up 140 days post-discharge
- 29.4% readmitted
- 12% died

Ayoubkhani D. BMJ 2021;372:m693

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Definition of Post-Acute Sequelae

WHO (Post COVID-19):

A condition that 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**. Symptoms may be new following initial recovery from an acute COVID-19 episode, or persist from the initial illness. Symptoms may also fluctuate or relapse over time.

Common symptoms include:

- Fatigue
- Shortness of breath
- Cognitive dysfunction
- Others which generally have an impact on everyday functioning

ICD-10 - U09.9, and considered a disability covered under ADA

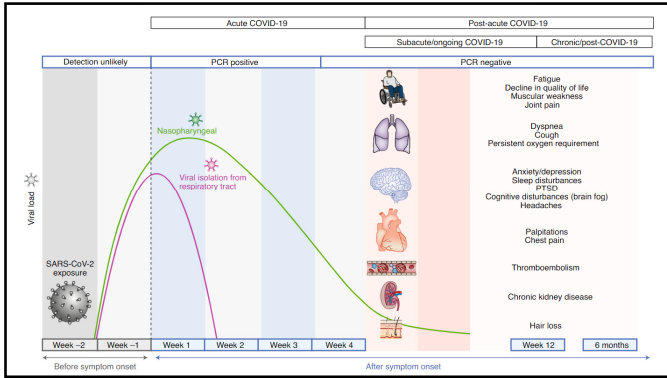
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CDC: Most Commonly Reported Symptoms

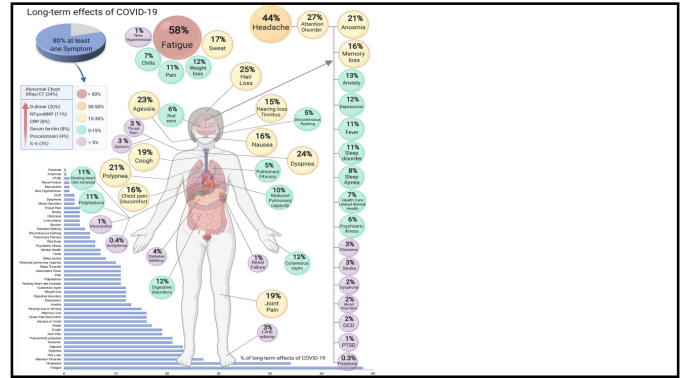
- Dyspnea or increased respiratory effort
- Fatigue
- Post-exertional malaise and/or poor endurance
- “Brain fog,” or cognitive impairment
- Cough
- Chest pain
- Headache
- Palpitations and/or tachycardia
- Arthralgia
- Myalgia
- Paresthesia
- Abdominal pain
- Diarrhea
- Insomnia and other sleep difficulties
- Fever
- Lightheadedness
- Impaired daily function and mobility
- Pain
- Rash (e.g., urticaria)
- Mood changes
- Anosmia or dysgeusia
- Menstrual cycle irregularities

* **Post-exertional malaise (PEM)** is the worsening of symptoms following even minor physical or mental exertion, with symptoms typically worsening 12 to 48 hours after activity and lasting for days or even weeks.

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Systematic Review of "Long-COVID"

- 57 eligible studies out of 2100; 250,351 patients – 79% were inpatient, 1-6 mos follow up.

No major differences by:

- High income vs low-income country
- High vs low hospitalization rates

Groff D. JAMA Network Open, Oct 2021

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Systematic Review of "Long-COVID"

- 57 eligible studies out of 2100; 250,351 patients – majority were inpatient, at least 60 days of follow up.

Symptom	Median % of Population Reporting Symptom (IQR)
Any Symptom	54% (31%-67%)
Chest imaging abnormal	62% (46%-77%)
General functional impairment	44% (23%-63%)
Fatigue	38% (25%-55%)
General anxiety disorder	30% (14%-44%)
Difficulty Concentrating	24% (20%-26%)

Groff D. JAMA Network Open, Oct 2021

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Articles

www.thelancet.com Vol 398 August 28, 2021

1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study

N = 1,276

Symptom or Problem	6 mos	12 mos
Any symptom	68%	49%
Fatigue or weakness	52%	40%
Sleep problems	27%	17%
Smell disorder	11%	12%
Anxiety or depression	23%	26%
Persistent abnormality on CT of the chest	100%	39%
Abnormal gas exchange in lungs	21%	23%
Ongoing shortness of breath	26%	30%

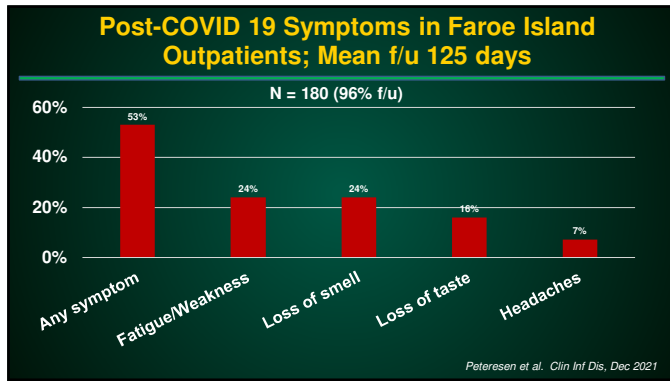
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Disability Persisting after Discharge to Home

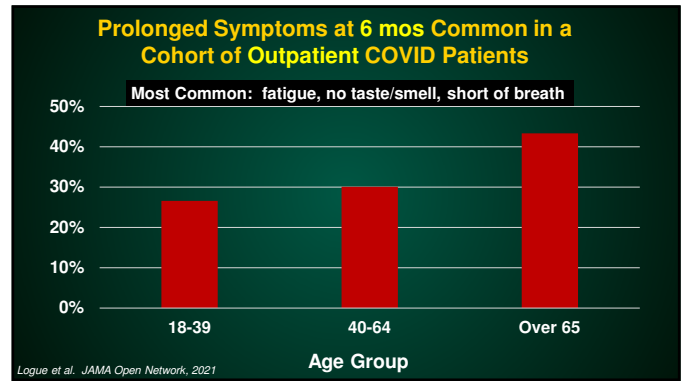
- Retrospective study of 1300 hospitalized patients d/c to home
- Only 40% independent in all ADLs at 30 days¹
- Another study, almost 40% unable to return to normal activity at 60 days²

1. Bowles KH. Ann Intern Med. Nov 2021
2. Chopra V. Ann Intern Med. Nov 2021

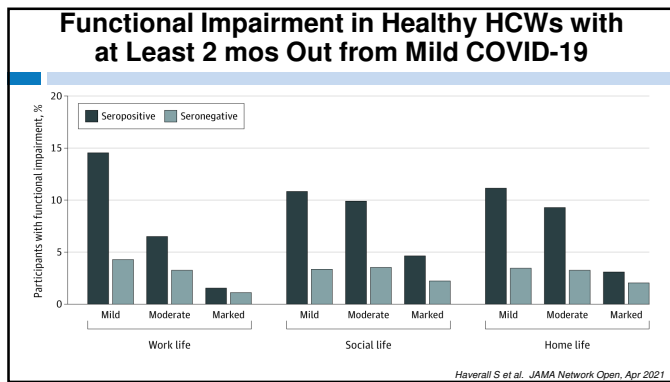
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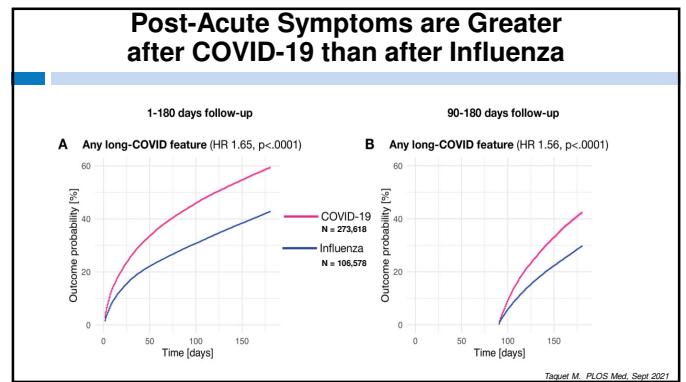
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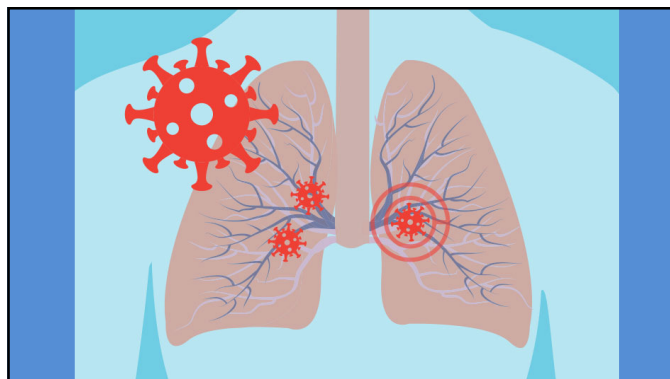
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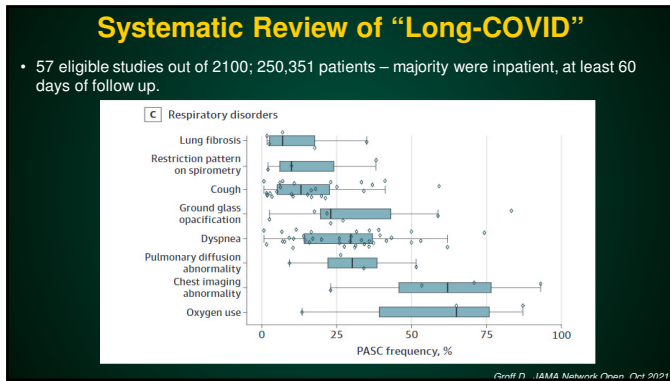
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Persistent Lung Abnormalities

- 55 Chinese pts followed in prospective cohort study¹
 - 4 mild, 51 pneumonia (4 severe)
- At 3 mos
 - 64% had persistent symptoms
 - 71% had interstitial thickening or fibrosis on chest CT
 - 25% had decreased CO diffusion capacity
- Similar study of 57 pts 30d after discharge – 53% with decreased CO diffusion capacity²

1. Zhao Y. EClinMed Aug 2020
2. Huang Y. Resp Research, 21, Jun 2020

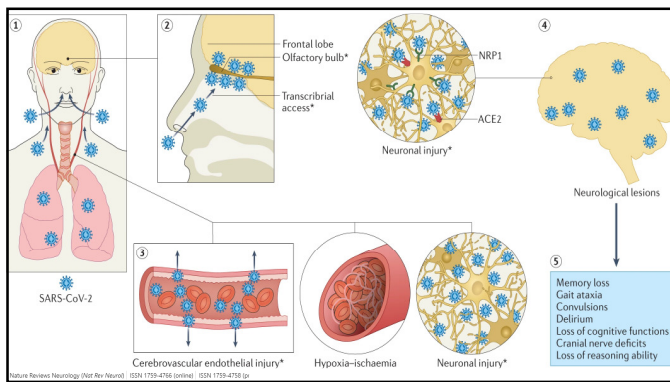
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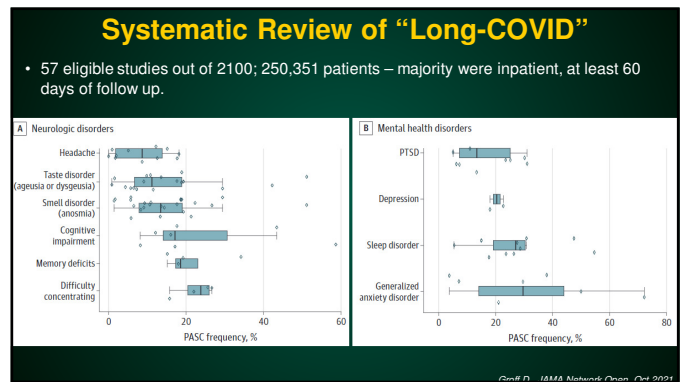
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U.K Biobank Study

- Ongoing study of brain structure over time with serial functional / quantitative MRI scans of the brain
- Compared 394 COVID patients (over 95% were outpatients) with 388 matched controls

Douaud G. medRxiv Jun 2021

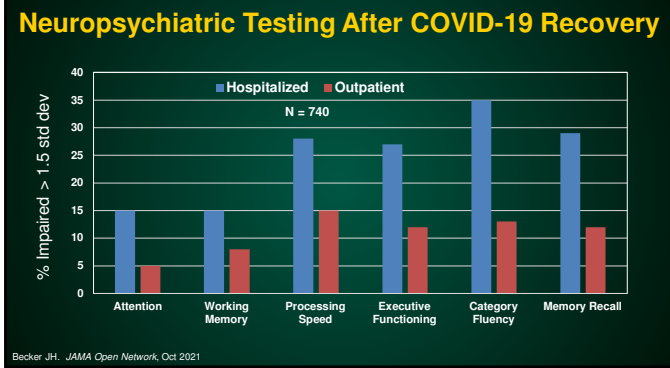
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U.K Biobank Study Findings:

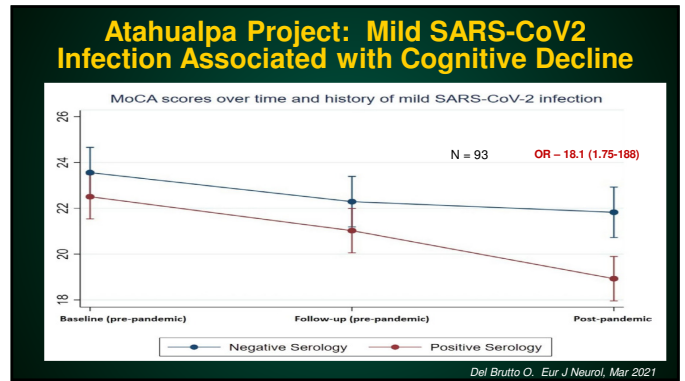
- Grey matter shrinkage in:
 - L parahippocampal gyrus
 - L lateral orbitofrontal cortex
 - L insula
 - Anterior cingulate cortex
 - Supramarginal gyrus
 - Temporal pole

Douaud G. medRxiv Jun 2021

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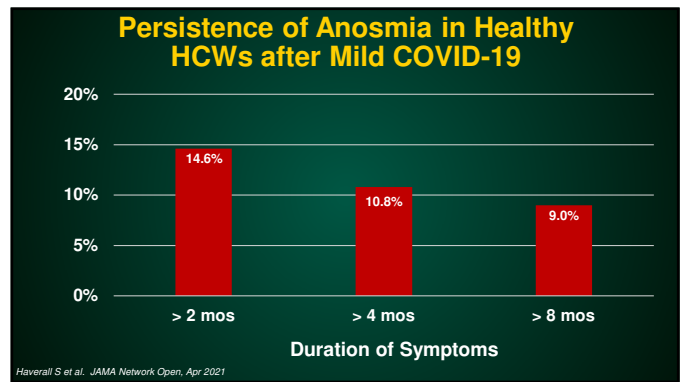
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Loss of Taste and Smell - A Common COVID-19 Finding

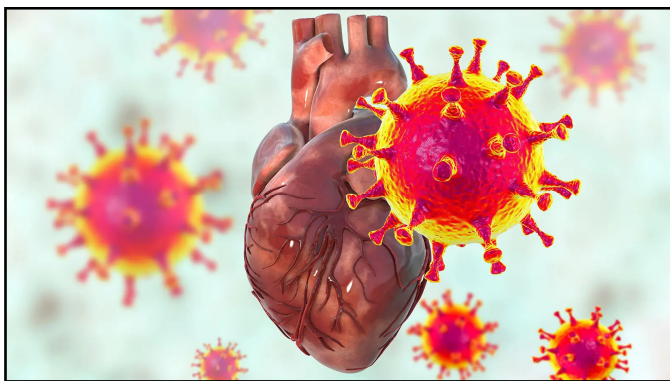
- Prospective study 5-6 days after 283 patients tested positive in Italy
- Did you experience sudden onset of altered smell or taste in 2 weeks prior to positive test? SNOT-22 symptom score
- 64% overall had some alteration in taste or smell
 - 50% - moderate to severe, additional
 - 14% - mild or light
- 5% persist beyond 3 mos

Spinato et al. JAMA, Apr 22, 2020

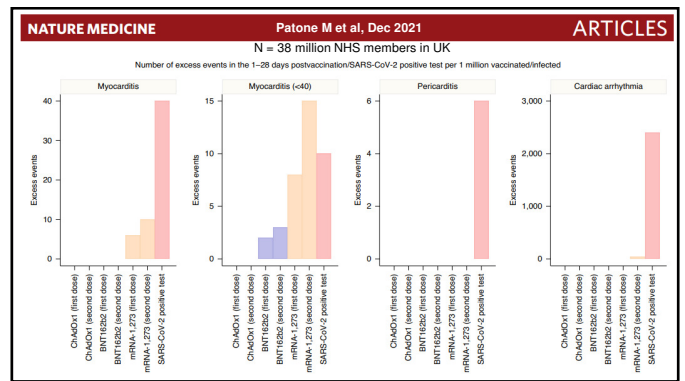
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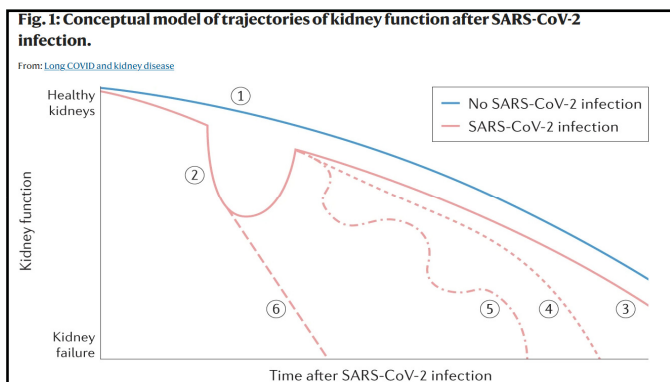
COVID-19 and the Heart

- Evidence of myocardial injury (troponin elevation) in 25-35% of hospitalized patients
 - Predicts worse outcome (OR-10.6)
- Atrial fibrillation in 11% of hospitalized patients
- Other arrhythmias in 7-17%
- Studies from France and Italy – 52% - 60% increase in out-of-hospital cardiac arrest during initial COVID wave

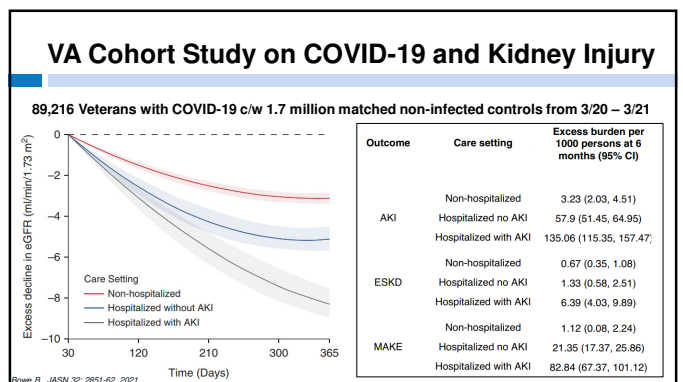
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It's frightening': Alyssa Milano details hair loss, 'brain fog' due to COVID-19
Jenna Ryan | USA TODAY | December 10, 2020, 11:00 a.m. ET | Updated 1:49 p.m. ET Oct. 9, 2020

Category	Sub-category	PASC Frequency (%)
Skin disorders	Skin rash	~5
	Hair loss	~20
Digestive disorders	Abdominal pain	~5
	Diarrhea and vomiting	~10
	Decreased appetite	~15
	Digestive disorders (any)	~20

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Received: 25 January 2021 | Revised: 8 March 2021 | Accepted: 16 March 2021
DOI: 10.1111/andr.13003

ORIGINAL ARTICLE **ANDROLOGY** WILEY

“Mask up to keep it up”: Preliminary evidence of the association between erectile dysfunction and COVID-19

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Abstract
Background: Erectile dysfunction (ED), as the hallmark of endothelial dysfunction, could be a short- or long-term complication of COVID-19. Additionally, being ED a clinical marker and predictor of non-communicable chronic diseases, particularly cardiovascular, subjects with ED could potentially have a higher risk of contracting COVID-19.
Objectives: To investigate the prevalence of ED among subjects with a reported diagnosis of COVID-19 and to measure the association of COVID-19 and ED.

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TABLE 1 Characteristics of the study population

	COVID+ (n = 25)	COVID- (n = 75)	p-value
Age (years)	39.00 [29.00, 45.00]	42.00 [32.50, 49.00]	0.142 ^a
BMI (kg/m ²)	22.65 [20.83, 23.74]	22.74 [20.98, 24.53]	0.266 ^a
GAD-7 score	4.00 [2.00, 6.00]	4.00 [2.00, 5.00]	0.741 ^a
PHQ-9 score	5.00 [3.00, 6.00]	4.00 [2.00, 5.00]	0.873 ^a
Erectile dysfunction	7 (28%)	7 (9.33%)	0.027^b


After adjusting for age, BMI, and mental health issues, risk of ED from COVID-19 → **5.7x**

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COVID-19 Morbidity as of 12/28/21

U.S.

- 52,809,291 cases
- Seroprevalence through 10/31/21:
 - 7% in VT, 50% in TX, US avg – 30.8%
- 2.8 - 3.8 million hospitalized (estimated)
- Long-COVID?



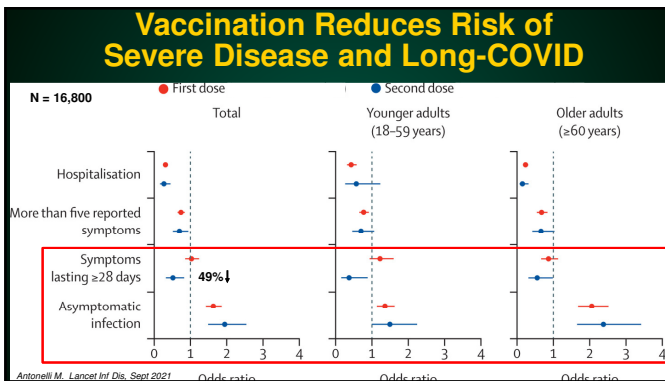
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Management of Long-COVID-19

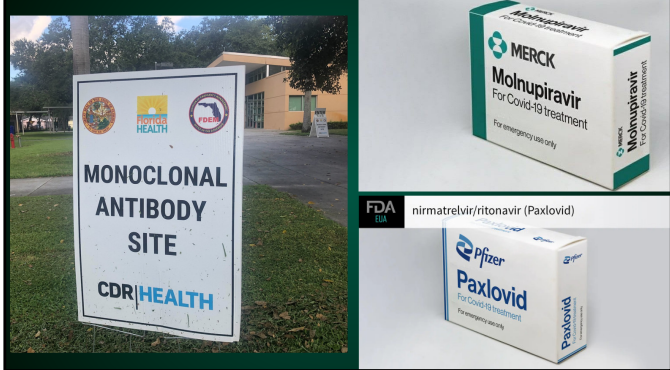
- Don't get it in the first place!
- Vaccinated with breakthrough infection at lower risk
- Early diagnosis and treatment

- Comprehensive medical assessment
- Multi-disciplinary approach

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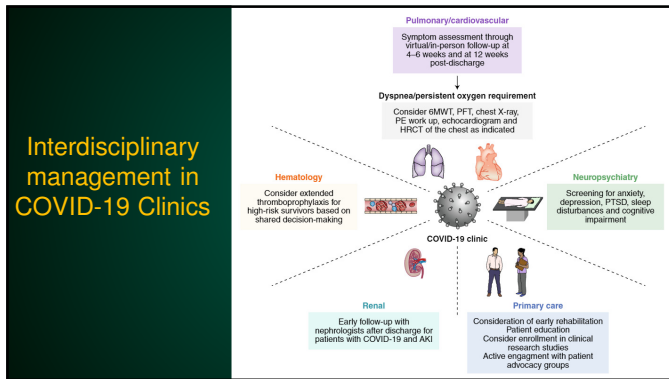
MONOCLONAL ANTIBODY SITE
CDR HEALTH

MERCK Molnupiravir For Covid-19 treatment

FDA EUA nirmatrelvir/ritonavir (Paxlovid)

Pfizer Paxlovid For Covid-19 treatment

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Received: 7 June 2021 | Revised: 26 July 2021 | Accepted: 28 July 2021
DOI: 10.1002/pmj.12684

CLINICAL GUIDANCE
The American Academy of Physical Medicine and Rehabilitation

Multidisciplinary collaborative consensus guidance statement on the assessment and treatment of fatigue in postacute sequelae of SARS-CoV-2 infection (PASC) patients

Joseph E. Herrera DO¹ | William N. Niehaus MD² | Jonathan Whiteson MD³ | Alba Azola MD⁴ | John M. Baratta MD, MBA⁵ | Talya K. Fleming MD⁶ | Soo Yeon Kim MD⁴ | Huma Naqvi MD⁷ | Sarah Sampsel MPH⁸ | Julie K. Silver MD⁹ | Monica Verduzco Gutierrez MD¹⁰ | Jason Maley MD¹¹ | Eric Herman MD¹² | Benjamin Abramoff MD, MS¹³

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A Multidisciplinary NHS COVID-19 Service to Manage Post-COVID-19 Syndrome in the Community

Journal of Primary Care & Community Health
Volume 12: 1-9
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DOI: 10.1177/21501327211010994
journals.sagepub.com/home/jpc
SAGE

Amy Parkin¹, Jennifer Davison², Rachel Tarrant², Denise Ross¹, Stephen Halpin^{1,2,3}, Alex Simms¹, Rashad Salman¹, and Manoj Sivan^{1,2,3}

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Table 1. Composition of Level 1 COVID-19 MDT (Banding Levels as per NHS Agenda for Change).

Rehabilitation therapists	Medical
Band 8a pathway co-ordinator (1.0 whole time equivalent, WTE)	Consultant in rehabilitation medicine (0.1 WTE)
Band 7 physiotherapist (2.0 WTE)	Consultant in respiratory medicine (0.1 WTE)
Band 7 occupational therapist (2.0 WTE)	Consultant cardiologist (0.1 WTE)
Specialist Allied Health Professionals	Research
Band 6 respiratory nurse (1.0 WTE)	Consultant in rehabilitation medicine (research) (0.1 WTE)
Band 6 respiratory physiotherapist (1.0 WTE)	Band 6 AHP researcher (1.0 WTE)
Band 7 dietitian (0.2 WTE)	Others
Band 6 dietitian (0.5 WTE)	Project manager (0.1 WTE)
Band 7 neuro occupational therapist (0.5 WTE)	Admin support (0.1 WTE)
Band 6 neuro occupational therapist (0.2WTE)	Post doctoral clinical psychologist trainee (0.5WTE)

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Table 3. Core set of Outcome Measures.

Symptom	Outcome measure
Fatigue	<ul style="list-style-type: none"> COVID-19 Yorkshire Rehabilitation Scale (C19-YRS) Modified Impact Fatigue Scale (MIFS) Euro-QoL-5D-SL (EQ5D-SL)
Breathlessness	<ul style="list-style-type: none"> C19-YRS Medical Research Council Breathlessness Scale (MRC) 30second sit-stand test The Borg Rating of Perceived Exertion (Borg RPE)
Deconditioning	<ul style="list-style-type: none"> C19-YRS 30second sit-stand test EQ5D-SL
Cognition	<ul style="list-style-type: none"> C19-YRS Addenbrooke's Cognitive Examination (ACE-3)
Anxiety and depression	<ul style="list-style-type: none"> C19-YRS EQ5D-SL Generalized Anxiety Disorder Assessment (GAD7) Depression Severity (PHQ9)
Pain	<ul style="list-style-type: none"> C19-YRS

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Table 4. Symptom and Interventions.

Symptom	Example interventions considered:
Chest and pleuritic pain	<ul style="list-style-type: none"> Education of self-management strategies (avoiding over exertion) Medical management occasionally required such as electrocardiogram (ECG) screening to rule out potentially life threatening diagnoses
Repeated chest infections	<ul style="list-style-type: none"> Secretion clearance strategies Swallowing screen for aspiration then medical management if required
Muscular and joint pain	<ul style="list-style-type: none"> Medical management to optimize underlying respiratory conditions may be required Hot/cold therapy Exercise prescription for pain related deconditioning
Shortness of breath at rest	<ul style="list-style-type: none"> Multi-disciplinary team discussion if potentially neuropathic pain Assessment of breathing pattern to rule out Breathing Pattern Disorder Use of Borg Rating of Perceived Exertion Scale (RPE) and oximetry Breathing retraining (Diaphragmatic and nasal) Assessment of N-terminal pro-brain natriuretic peptide (NT-proBNP) if indicated Diffusing capacity for carbon monoxide (DLCO) and overnight pulse oximetry warranted in a minority of complicated cases
Shortness of breath on exertion	<ul style="list-style-type: none"> Breathing techniques whilst moving Purse lip breathing strategies if nasal breathing effortful Positioning Use of fan Using Borg-RPE scale and oximetry with activity to guide and educate patient to safe level exercise
Desaturation on exertion	<ul style="list-style-type: none"> Assessment of NT-proBNP if indicated Use of pulse oximetry to relate to breathlessness score on Borg-RPE scale, and recovery time Review how patient manages desaturation Grade up activity gradually starting with non-de-saturation tasks Education of self-management and breathing control for recovery/managing desaturation Positioning Assessment of NT-proBNP if indicated Assessments of need for further respiratory investigation

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Table 4. Symptom and Interventions.

Symptom	Example interventions considered:
Palpitations and tachycardia	<ul style="list-style-type: none"> Medical assessments such as ECG, ambulatory ECG, and thyroid function, biomarkers and exercise testing Advice around exercise Medical management including salt loading and hydration volume, medications
Dizziness	<ul style="list-style-type: none"> Vestibular retraining if indicated Investigate whether related to postural drop or Postural Tachycardia Syndrome (PoTS) Education/advice around postural drop and positional changes
Post viral fatigue or post-exertional malaise	<ul style="list-style-type: none"> Medication review Diaries (fatigue/sleep/thinking) Education around pacing and prioritization Identification of own unique occupational balance Education on relaxation strategies and "quality" rest Lifestyle management (diet, sleep and stress management) Enrolment onto virtual fatigue course
Anxiety and depression	<ul style="list-style-type: none"> Vocational support Enrolment onto virtual fatigue course Education on relaxation and mindfulness Use of restorative activity Referral to psychological services/Leeds Wellbeing service
Poor memory and concentration	<ul style="list-style-type: none"> Cognitive assessment if indicated Education around cognitive processes and post viral syndrome Brain Training exercises (eg. Luminosity) Diaries- fatigue/sleep/thinking Vocational support

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Table 4. (continued)

Symptom	Example interventions considered:
Voice Disorders	<ul style="list-style-type: none"> Memory aids Education on relaxation and mindfulness Use of restorative activity Voice care advice and therapy
Upper airways Disorders	<ul style="list-style-type: none"> Inducible laryngeal obstruction (ILO) management
Reflex related laryngeal symptoms	<ul style="list-style-type: none"> Cough suppression techniques Education and support of post viral laryngeal recovery Specific relaxation techniques and CBT strategies
Word finding difficulties (anomia)	<ul style="list-style-type: none"> Linguistic approach to improve semantics Cognitive approach to improve verbal short-term memory and speed of naming Compensatory approach, for example, circumlocution Interventions may be provided in person and/or via computer therapy to support dosage/independent practice

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Treatment of PVOD

- Trial of nasal steroids
- PT for the nose
 - Smell familiar essential oils or herbs for 20 sec while focusing on memories of that scent. 2x daily for 4-6 mos.
 - Commonly used: rose, lemon, clove, eucalyptus
 - Review showed improvement in a standardized scoring tool



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