

# COVID-19 Update: What is Our Current Status?

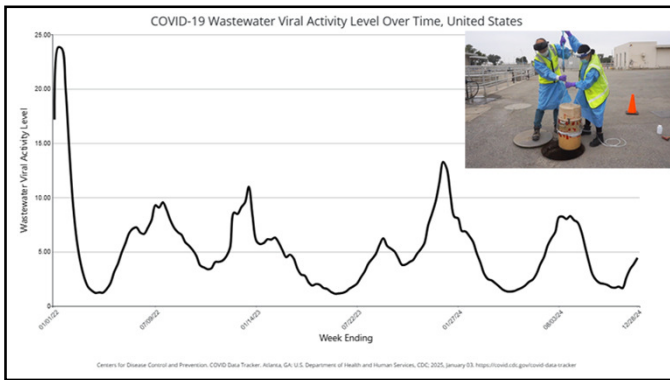
Paul J Carson, MD, FACP

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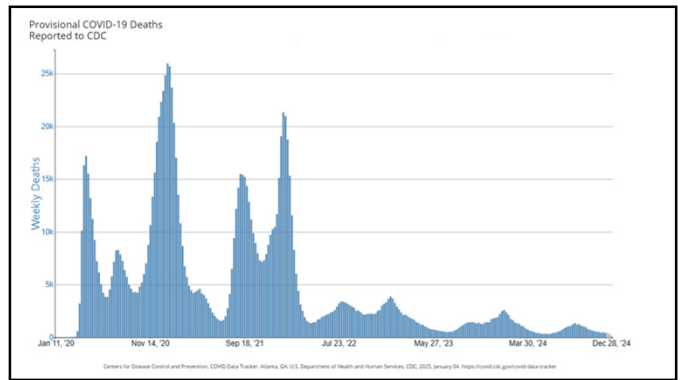
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# Update: EPIDEMIOLOGY

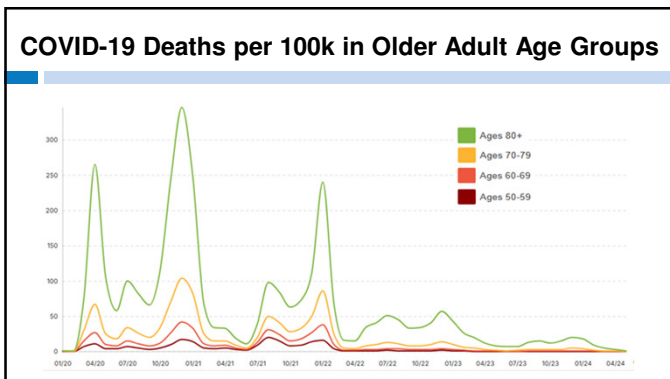
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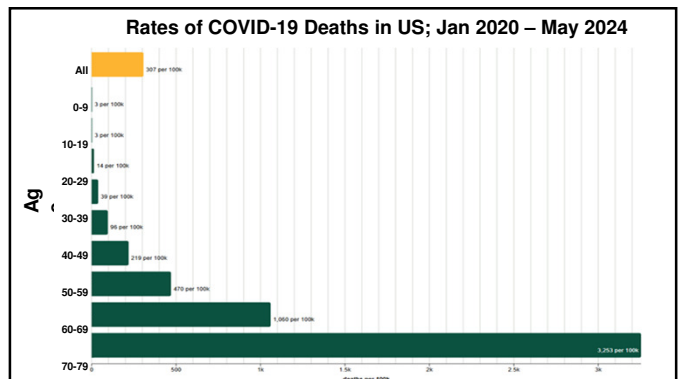
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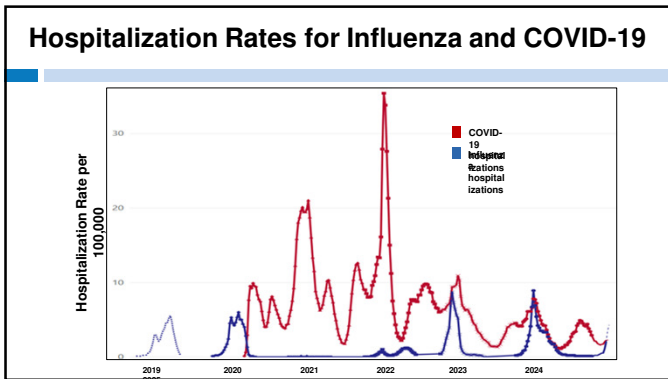
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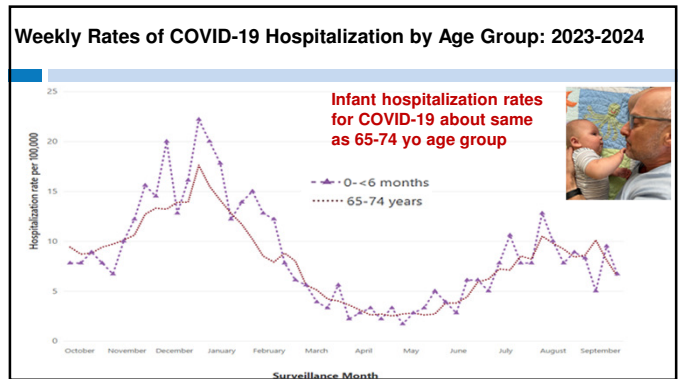
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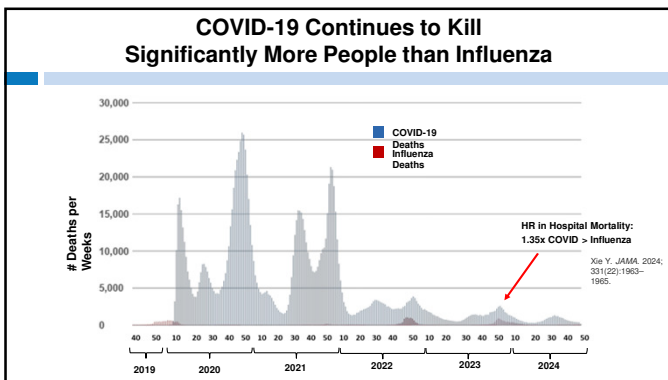
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### CDC recommends the 2024-25 COVID-19 vaccine for everyone 6 months and older

**An updated vaccine protects against:**

- COVID-19 variants spreading now
- Severe illness, hospitalization, and death

**CDC** [bit.ly/mm7337e2](https://bit.ly/mm7337e2) SEPTEMBER 10, 2024 **MMWR**

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### CDC recommends the 2024-25 COVID-19 vaccine for everyone 6 months and older

**2 Doses of 2024-2025 Vaccine Recommended:**

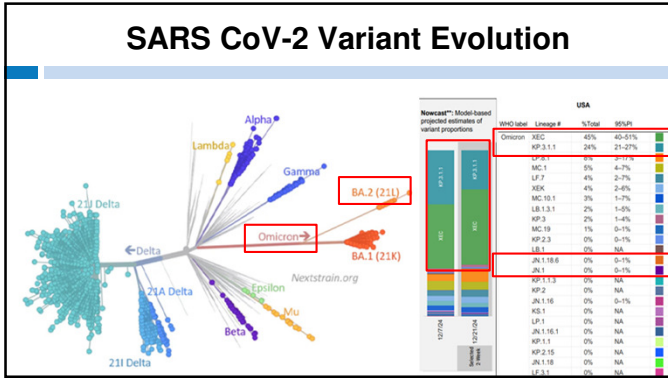
- Adults aged > 65
- 6 mos or older with moderate or severe immunosuppression

**CDC** [bit.ly/mm7337e2](https://bit.ly/mm7337e2) SEPTEMBER 10, 2024 **MMWR**

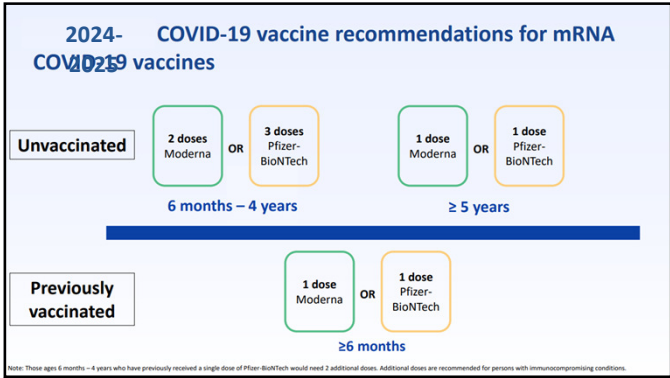
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### Current Status of Vaccine Necessity and Efficacy

- Nearly all the population has some degree of immunity to SARS CoV-2 (> 97% seroprevalence by Fall 2022)
- Morbidity and mortality markedly reduced due to less virulent strains and baseline cross-protective immunity from prior infections +/- vaccines
- mRNA vaccine efficacy is limited due to rapid waning of immune response, changing variants, and overall less morbidity
  - 2023 Monovalent XBB.1.5 vaccine **VE = 60%** against symptomatic SARS Cov-2 infxn and **49%** against JN.1 strain in 2023-2024
  - 50%** protection against hospitalization and **67%** against critical illness for 4-6 mos in elderly and immunosuppressed

Roper L.E. MMWR Morb Mortal Wkly Rep 2024;73:1118-1123  
Link-Gelles R. MMWR Morb Mortal Wkly Rep 2024;73:77-83

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### Who's Getting Vaccinated? Vaccine Uptake with a Current Booster

Demographic ('23-'24)	% Vaccinated
6-23 mos	4.2%
5-17 yo	11.6%
18-49 yo	15%
50-64 yo	25%
65+ yo	39%
Nursing home residents ('24-'25)	37%
Pregnant women ('24-'25)	12.6%

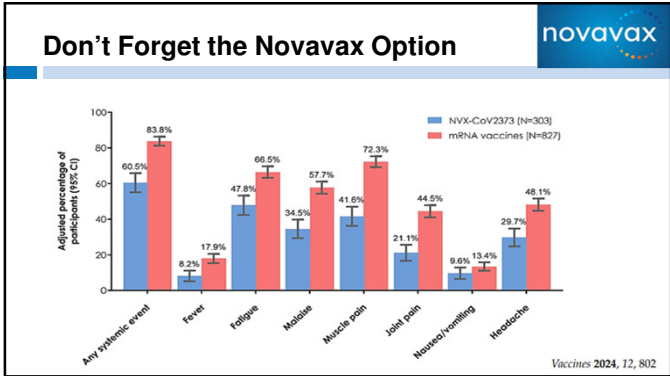
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### PC's Recommendations for COVID-19 Vaccines:

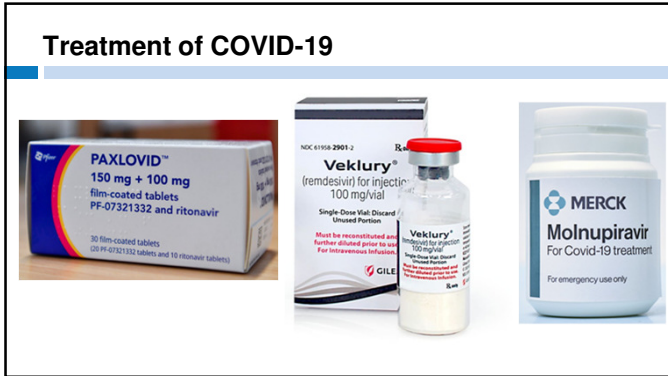
- To industry: Make a better vaccine!
- Until then, following should get annual variant-updated vaccine:
  - Everyone 65+ y.o. (especially 75+ yo) - ? 2 doses
  - LTCF residents
  - Anyone with moderate to severe immunosuppression – 2 doses
  - Newborn infants after 6 mos if no prior SARS CoV-2 infxn
  - Any adult frequently around newborn infant
  - ≥ 6 mos with chronic illness (DM, heart dz, asthma, chronic lung dz, obesity, etc.)
  - Pregnant women

Healthy children, 2-4 and adults, 65 yo 2 - shared decision making

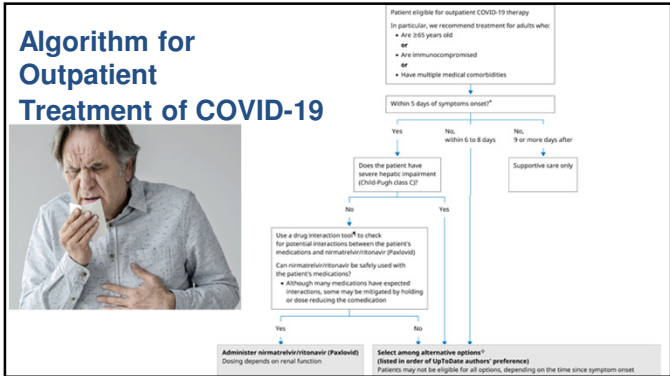
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### Outpatient Management

- Paxlovid:** 300mg/100mg bid x 5 days, symptoms ≤ 5 days
  - Outpatient only – no hypoxia
  - Use drug interaction checker: <https://www.covid19-druginteractions.org/checker>
  - Need renal adjustment for GFR <60
  - Efficacy only in high risk – 89% reduction in hosp'n or death in primary trials (high risk, mainly Delta variant, unvaccinated) N ENGL J MED 386:15 NEJM.ORG APRIL 14, 2022
- Remdesivir:** 200 mg IV day 1, then 100 mg IV days 2&3, symptoms ≤ 7 days
  - Reduced risk of hosp'n by 87% in high risk unvaccinated during Delta wave
  - Good alternative if can't take Paxlovid and access/availability of OP IV Rx

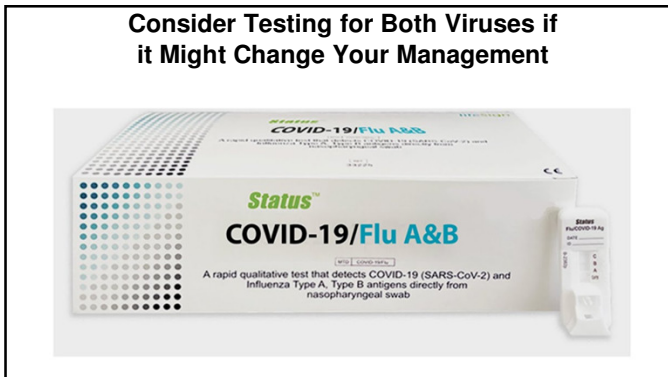
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### Paxlovid of No Benefit in Low-Risk Patients; Uncertain in High-Risk/Vaccinated

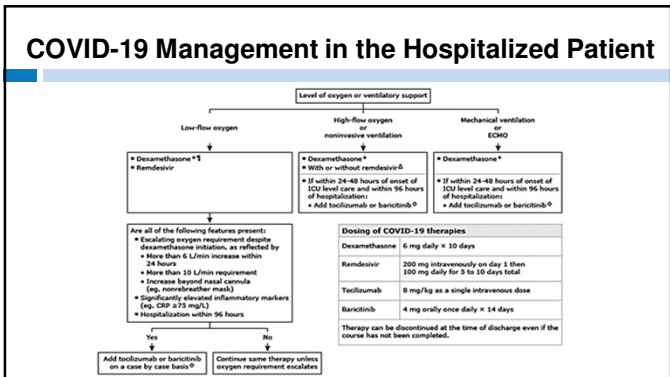
- Follow up study by Pfizer in lower risk patients during Delta
  - Vaccinated with ≥ 1 high-risk factor
  - Standard risk but unvaccinated or no vaccine in prior year
- Results:
  - No difference in symptom duration (~ 12 days), the primary endpoint
  - Trend towards less hospitalization and medical attendance in the high-risk group, but not statistically significant

N Engl J Med 2024;390:1186-1195 | DOI: 10.1056/NEJMoa2309003 | VOL 390, NO 13

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### Got COVID? Here are the new 2024 isolation guidelines



Manage like other resp illnesses, resume normal activities when:

- Symptoms are overall getting better
- No fever > 24 h

**As of March 2024, CDC no longer recommends 5 day isolation for COVID-19**

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## WHAT IS POST COVID SYNDROME?

**-No universal definition**

**-World Health Organization – 10/6/2021**

- A history of probable or confirmed SARS COV-2 infection
- Sx ≥ 3 months from onset of infection
- Sx ≥ 2 months
- Can't be explained by an alternative diagnosis

**-CDC Definition**

- Call it "Post-COVID Conditions"
- ≥ 4 weeks from acute infection start (symptoms or test)
- **ICD-10 - U09.9, and considered a disability covered under ADA**

1. Organization WH. A clinical case definition of post COVID-19 condition by a Delphi consensus. Accessed 10/6, 2021. [https://www.who.int/publications/item/U09-2019-nCoV-Post-COVID-19\\_condition-Clinical\\_case\\_definition-2021.1](https://www.who.int/publications/item/U09-2019-nCoV-Post-COVID-19_condition-Clinical_case_definition-2021.1)
2. @CDCgov. Post-COVID Conditions: Information for Healthcare Providers. @CDCgov. Updated 2021-09-10T04:38:34Z. <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-care/post-covid-conditions.html>

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THE NEW ENGLAND JOURNAL OF MEDICINE

SOUNDING BOARD

FROM THE NATIONAL ACADEMY OF MEDICINE

**Long Covid Defined**

J. Whiteley, M.D., M.P.H., Lisa M. Brown, M.P.H., and Thomas V. Frerking, M.D., Ph.D., for the National Academies of Sciences, Engineering, and Medicine Committee on Learning the Meaning of Definitions for Long Covid\*

N ENGL J MED 393:118 NEJM.ORG NOVEMBER 7, 2024

Acute SARS-CoV-2 Infection	Diagnosable Conditions	Important Features
<ul style="list-style-type: none"> <li>Infection (presymptomatic or asymptomatic) may be asymptomatic, mild, or severe.</li> </ul>	<ul style="list-style-type: none"> <li>Cognitive impairment</li> <li>Migraine</li> <li>Stroke</li> <li>Mood disorders</li> <li>Cardiovascular disease</li> <li>Arrhythmias</li> <li>Blood clots</li> <li>Interstitial lung disease</li> <li>Hypoxemia</li> <li>Chronic kidney disease</li> <li>Myalgic encephalomyelitis/chronic fatigue syndrome</li> <li>Lupus, Sjögren's, rheumatoid arthritis, and other connective tissue diseases or autoimmune disorders</li> </ul>	<ul style="list-style-type: none"> <li>Long Covid can affect children and adults, regardless of health, disability, socioeconomic status, age, sex, gender, sexual orientation, race, ethnicity, or geographical location.</li> <li>Long Covid can resolve over a period of months or can persist for months or years.</li> <li>Long Covid can be diagnosed on clinical grounds. No biomarker currently available demonstrates conclusively the presence of Long Covid.</li> <li>Long Covid can impair affected patients' ability to work, attend school, and care for themselves and can have a profound emotional and physical effect on patients, families, and caregivers.</li> <li>Long Covid is not a diagnosis of exclusion.</li> </ul>
<ul style="list-style-type: none"> <li>Common Symptoms Can be mild to severe</li> <li>Postinfectional malaise</li> <li>Persistent fatigue</li> <li>Memory changes</li> <li>Recurring headaches</li> <li>Lightheadedness or fast heart rate</li> <li>Sleep disturbance</li> <li>Shortness of breath and cough</li> <li>Problems with smell</li> <li>Blurring, constipation, or diarrhea</li> </ul>	<p><b>Pathology of Long Covid</b></p>	

Diagnosable when symptoms or conditions are **intermittently or continuously present for at least 3 months**  
Can be (continued) from acute infection or longer on

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### Dogs can sniff out COVID-19 with up to 94% accuracy, study finds

Published June 1, 2021 | Updated 11/27/21 | Fox 5

### Dogs Can Sniff Out Long Covid-19, French Study Suggests

Lisa Kim Forbes Staff | Forbes




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## Hypothesized Mechanisms of Long COVID Pathogenesis

<p><b>Immune dysregulation</b></p> <p>Persistent infection</p> <p>Viral replication</p> <p>↑ Reactivation</p> <p>Immune dysregulation, with or without reactivation of underlying pathogens, including herpesviruses such as EBV and HHV-6</p>	<p><b>Microbiota dysbiosis</b></p> <p>Impacts of SARS-CoV-2 on the microbiota and virome (including SARS-CoV-2 persistence)</p>	<p><b>Autoimmunity and immune priming</b></p> <p>Autoimmunity and primed immune cells from molecular mimicry</p>	<p><b>Blood clotting and endothelial abnormalities</b></p> <p>Microvascular blood clotting with endothelial dysfunction</p>	<p><b>Dysfunctional neurological signalling</b></p> <p>Dysfunctional signalling in the brainstem and/or vagus nerve</p>
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Approximately **1 in 5 adults** ages 18+ have a health condition that might be related to their previous COVID-19 illness, such as:

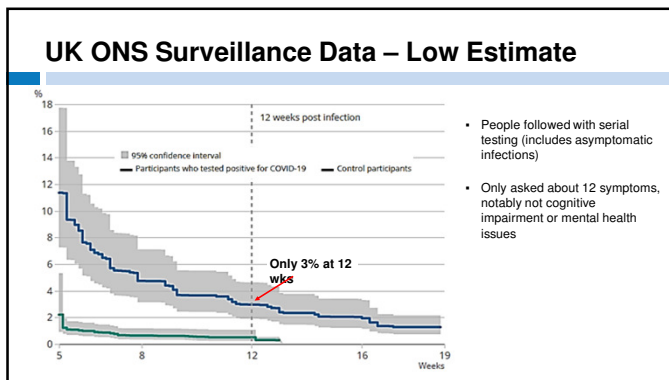
- Neurologic and mental health conditions\*
- Cardiovascular conditions
- Kidney failure
- Respiratory conditions
- Musculoskeletal conditions
- Blood clots and vascular issues

Talk to your health care provider if you have symptoms after COVID-19

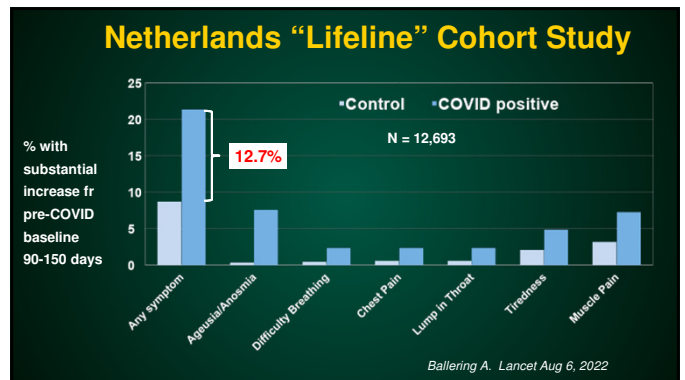
bit.ly/MMWR7121

\* Adults aged 65 and older at increased risk

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- ### Risk Factors for Long-COVID
- Middle age and higher body mass index
  - Females  $\geq$  20 years
  - Pre-existing conditions (eg, depression, anxiety, allergies, obstructive lung disease, untreated obstructive sleep apnea, type 2 diabetes, connective tissue disorders)
  - Infection pre-Omicron (2022)

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www.thelancet.com Vol 398 August 28, 2021

Articles

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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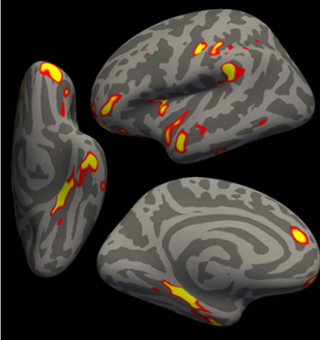
## U.K Biobank Study

*Douaud G. Nature, Mar 2022*



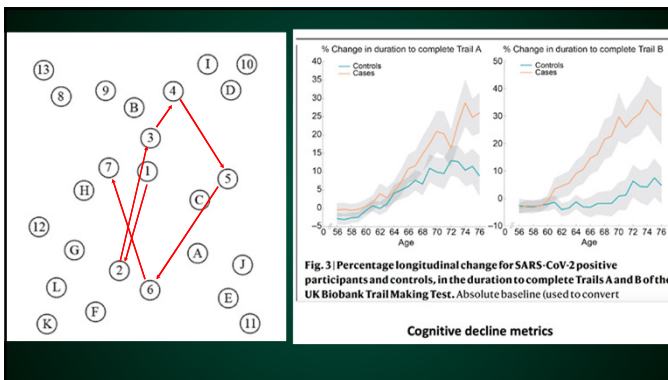
- Ongoing study of brain structure over time with serial functional / quantitative MRI scans of the brain
- Average time between scans, 141 days
- Compared 401 COVID patients (over 96% were outpatients) with 384 matched controls

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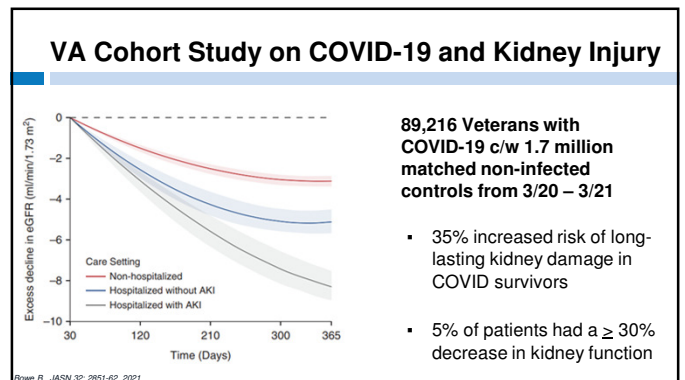


- Normal gray matter loss is ~ 0.2 – 0.3% / yr
- COVID patients lost additional 0.2 – 2.0% more than controls
- Lost overall more brain volume
- Showed evidence of tissue damage
- Main affected areas: orbitofrontal cortex, parahippocampal gyrus, olfactory cortex, temporal pyriform cortex

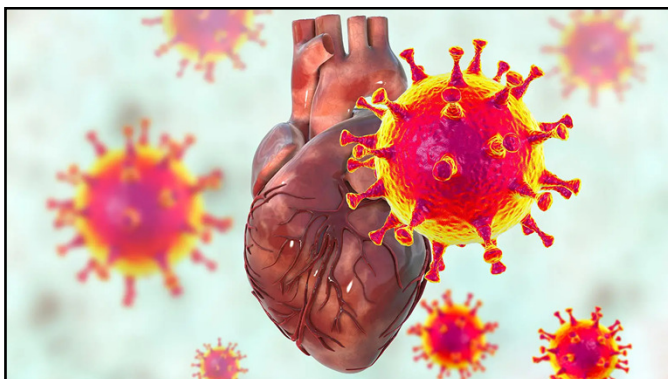
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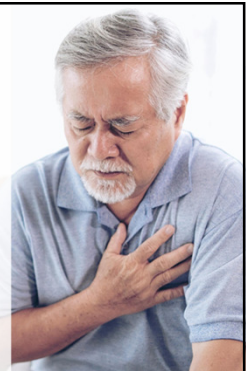
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**People with COVID exhibited increased risk AND 12-month burdens of cardiovascular disease. Including:**

- **Cerebrovascular disorders**
- **Dysrhythmias**
- **Inflammatory heart disease**
- **Ischemic heart disease**
- **Heart failure**
- **Thromboembolic disease**
- **Other cardiac disorders**



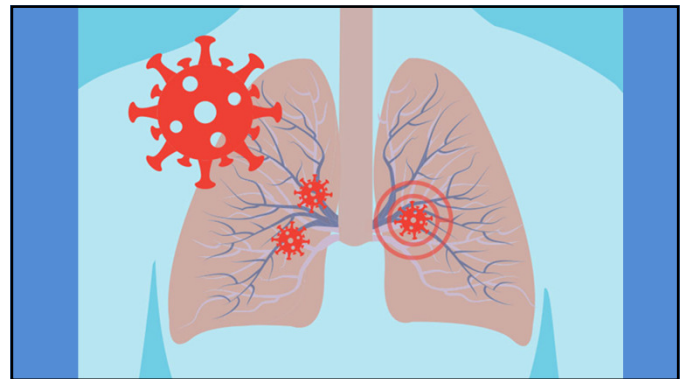
Xie et al. Nature Medicine, 2022

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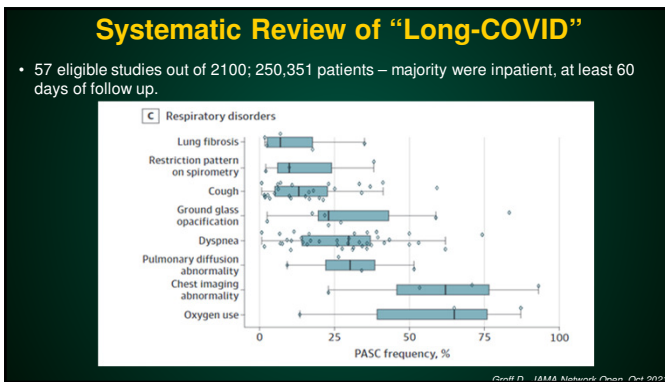
Study	Characteristics	CV outcomes at follow-up	Citation
Veterans Administration	90% males, mean age 61	1.7-fold risk of heart attack; 1.6-fold risk of stroke	Xie et al, Nature Medicine 2022
TriNetX Network	Unvaccinated, mean age 44	2-fold risk of heart attack; 1.6-fold risk of stroke	Wang et al, E Clinical Medicine, 2022
US Insurance Claims Database	Unvaccinated, mean age 50	2-fold risk of stroke, PE, DVT, all-cause death	Devries et al, JAMA Health Forum, 2023
US pandemic through March 2022	US population across 5 Covid waves	4.9% more cardiovascular deaths than expected (2 years)	Han, Nature Cardiovascular Research, 2023
Korea National Database	>62,000 unvaccinated >168,000 vaccinated Mean age ~50	>2-fold risk of heart attack and stroke for unvaccinated vs vaccinated	Kim Y-E, JAMA, 2022
NCATS (US Consortium, NIH)	Mean age 45 >1.9 million patients	2-fold risk of heart attack and stroke for unvaccinated vs vaccinated	Jiang, JACC, 2023

Korea and NCATS studies compare vaccinated vs unvaccinated @erictopol

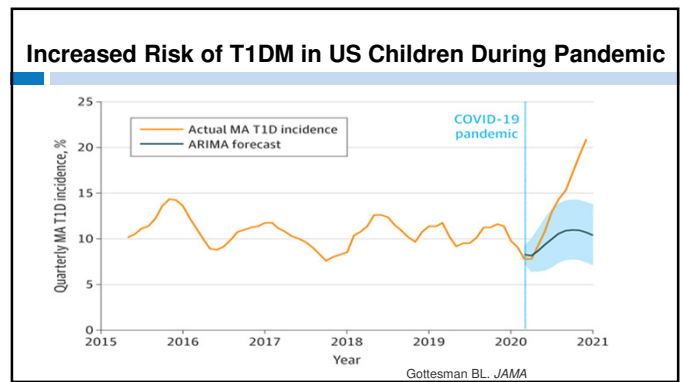
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### Now 12 Studies Showing Increased Risk of Diabetes Post-Acute COVID19

Study Cohort	N People w/ Covid	Increased Risk vs Controls	Age Mean	Male %	Citation
British Columbia	125,987	17%	32	49%	Naveed, JAMA Network Open 18 April 2023
Veteran Affairs	181,280	40%	61	88%	Xie, Lancet Diabetes Endo 2022:311-21
US, United Health	266,586	39%	42	52%	Daugherty, BMJ 2021:373:n1098
US TriNetX, 63 health systems	600,055	54%*	NA	NA	Birabakaran, Diabetes Obes Metab 2022: 1176-9
Germany	35,865	28%			949-954
US HealthVerity*	80,893	31%			
Veteran Affairs	126,710	95%—men 4%—women (NS)	59	86%	Wander, Diabetes Care 2022:872-788
UK (hospitalized)	47,780	50%	64	55%	Ayoubkhani, BMJ 2021: 372:n693
US, Medicare	133,366	97%	76	44%	Cohen, BMJ 2022: 376:e068414
UK (hospitalized)	77,347	65%	77	47%	Tazare, Wellcome Open Research 2022 7:142
US, Cedars-Sinai	23,709	58%	47	56%	Kwan, JAMA Network Open 14 February 2023
UK	428,650	27%	35	44%	Rezel-Potts, PLOS Medicine 2022 19: e1004052

\*Type 1 and 2 diabetes not partitioned in this age < 18 population; NA not available; NS not significant @erictopol

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JAMA Network Open

Research Letter | Infectious Diseases

### Association of COVID-19 Vaccination With Risk for Incident Diabetes After COVID-19 Infection

Alan C. Kwan, MD, MSc; Joseph E. Ehinger, MD; Patrick Botting, MSPH; Jesse Navarrete, MPA; Brian Claggett, PhD; Susan Cheng, MD, MPH, MMSc

- Cohort study of 23,709 adult patients in Cedars-Sinai Health System
- Risk of diabetes in 90 day interval after COVID-19 infection vs 90 days before infection

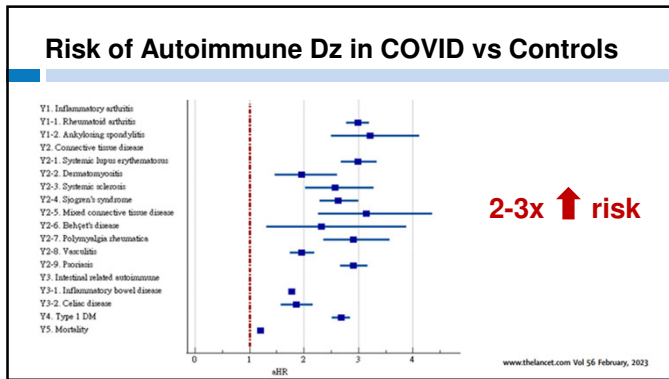
Results:

- 78% increased risk of diabetes following COVID-19 infection in unvaccinated after adjusting for multiple risk factors in cohort
- No increased risk in vaccinated cohort

JAMA Network Open 2023;6(2):e2255965. doi:10.1001/jamanetworkopen.2022.55965 February 14, 2023

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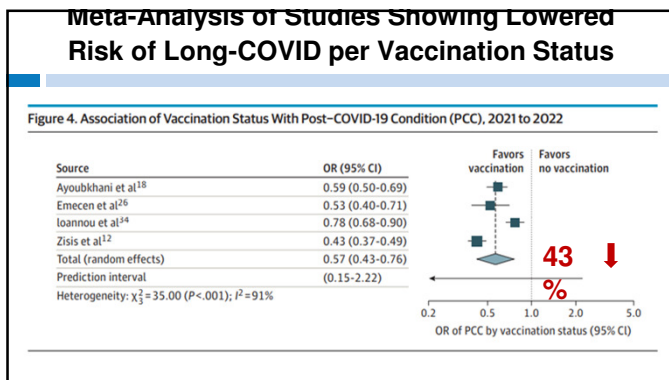




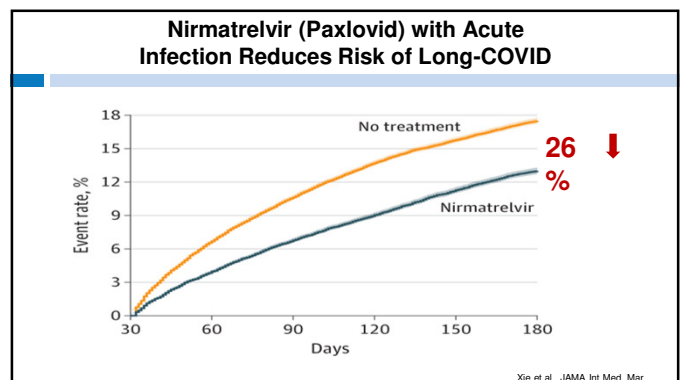
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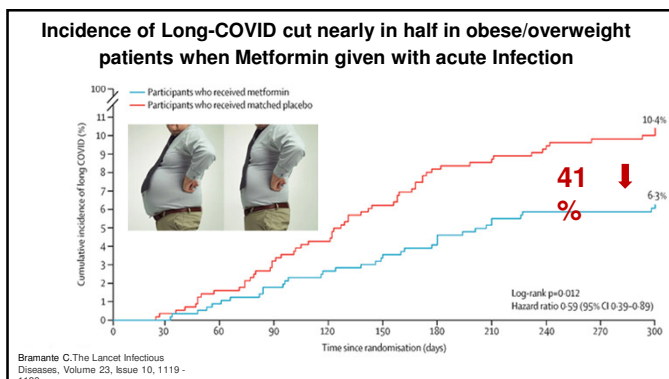
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- ### COVID-19 Summary:
- Transmission is still widely prevalent without typical resp virus seasonality
  - Widespread population immunity and trend towards less virulent strains has markedly reduced the morbidity and mortality
  - SARS CoV-2 still causes more morbidity, mortality and chronic sequelae than influenza, particularly at the extremes of age
  - Continued vaccine updates target evolving strains
  - Vaccine uptake and treatment is poor, even among high-risk groups
  - Serious illness and Long-COVID may be prevented by vaccination and early treatment of

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# Clinical management of COVID-19

LIVING GUIDELINE  
13 JANUARY 2023



World Health Organization

<https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.2>

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# LONG COVID PHYSIO

Our website is for everybody living with Long COVID and anyone wanting to learn more

<https://longcovid.physio/>

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## EXTRA SLIDES for Ref and Q&A

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Biological Sciences - Article

### SARS-CoV-2 infection and persistence throughout the human body and brain

nature portfolio

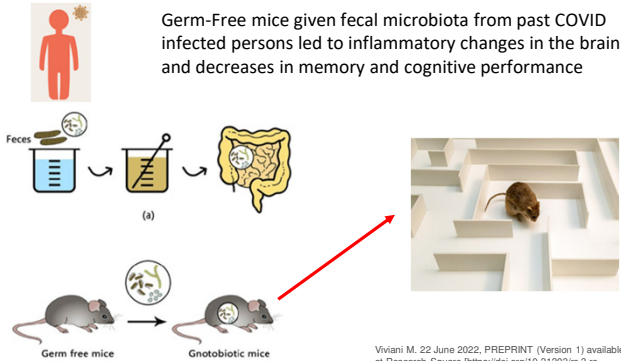
Daniel Chertow, Sydney Stein, Sabrina Ramelli, Alison Grazioli, and 29 more



- NIH study of 44 autopsies after COVID-19
- Asx to severe dz; acute infxn - 7 mos
- Findings:
  - SARS CoV2 RNA widely distributed throughout body, including brain
  - RNA persists up to 230 days fr onset
  - Paucity of inflammation or cytopathology outside of lungs
  - Viral replication outside lung suggested as late as day 99 from onset

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Germ-Free mice given fecal microbiota from past COVID infected persons led to inflammatory changes in the brain and decreases in memory and cognitive performance



Feces → (a) → Germ free mice → Gnotobiotic mice

Viviani M. 22 June 2022, PREPRINT (Version 1) available at Research Square ([https://doi.org/10.21203/rs.3.rs-](https://doi.org/10.21203/rs.3.rs-3)

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### National Center for Health Statistics Household Pulse Survey

Ever experienced long COVID, as a percentage of all adults

Phase Time Period Group	Phase 3.8 Mar 29 - Apr 10, 2023		
	Percent	95% CI	
<b>National Estimate</b>			
United States	15.5	14.9 - 16.1	
<b>By Age</b>			<b>By Race/Hispanic ethnicity</b>
18 - 29 years	17.8	16.0 - 19.7	Hispanic or Latino
30 - 39 years	18.3	16.9 - 19.7	Non-Hispanic Asian, single race
40 - 49 years	17.4	16.0 - 18.8	Non-Hispanic Black, single race
50 - 59 years	16.6	15.7 - 17.6	Non-Hispanic White, single race
60 - 69 years	12.5	11.6 - 13.4	Non-Hispanic, other races and multiple races
70 - 79 years	9.3	8.1 - 10.5	
80 years and above	8.8	6.1 - 12.1	<b>By Disability status</b>
<b>By Sex</b>			With disability
Female	19.0	18.2 - 19.9	Without disability
Male	11.9	11.1 - 12.7	

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eCDC  
EUROPEAN CENTRE FOR  
DISEASE PREVENTION  
AND CONTROL

## TECHNICAL REPORT

### Prevalence of post COVID-19 condition symptoms: a systematic review and meta-analysis of cohort study data, stratified by recruitment setting

27 October 2022

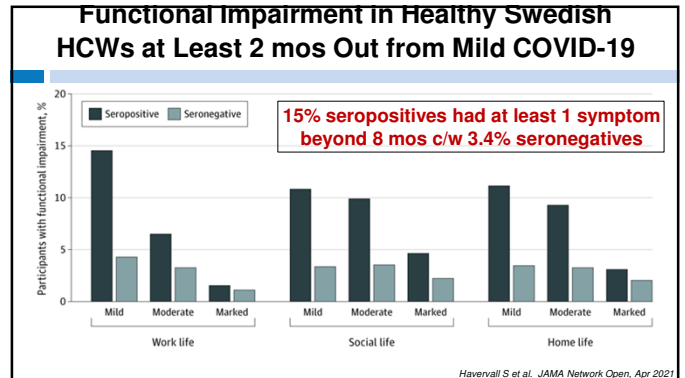
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**Table 1. Estimated prevalence of post COVID-19 condition symptoms reported among patients recruited in both the community and hospital setting**

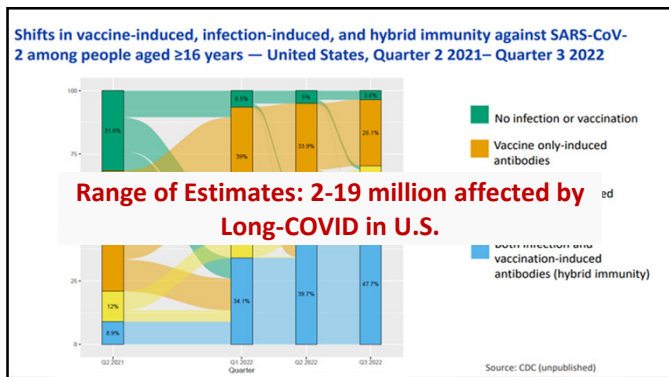
Post COVID-19 condition symptom	Community setting prevalence	Hospital setting prevalence
Fatigue	30.8% 95% CI: 21.0–41.6	46.1% 95% CI: 37.5–54.9
Shortness of breath	20.9% 95% CI: 12.1–31.3	45.4% 95% CI: 31.9–59.2
Depression	17.3% 95% CI: 9.0–27.5	23.3% 95% CI: 15.0–32.8
Headache	14.4% 95% CI: 7.9–22.4	16.5% 95% CI: 9.2–25.3
Dizziness	10.2% 95% CI: 4.7–17.4	18.3% 95% CI: 6.1–35.0

*Considering only prevalence estimates supported by evidence scored as moderate or high certainty (See Figures 2 and 3).*

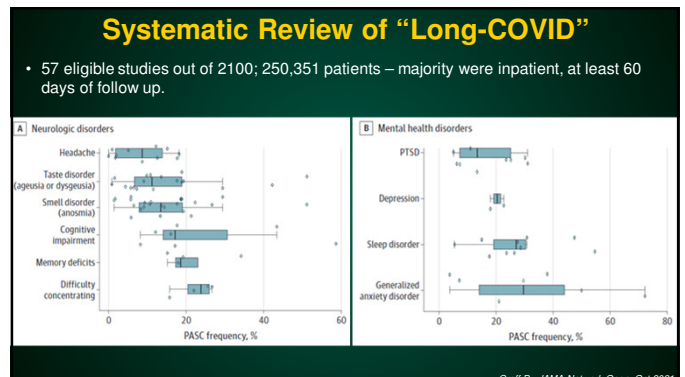
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### Disability Persisting after Discharge to Home

- Retrospective study of 1300 hospitalized patients d/c to home
- Only 40% independent in all ADLs at 30 days<sup>1</sup>
- Another study, almost 40% unable to return to normal activity at 60 days<sup>2</sup>



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

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**Mayo CARP Pop'n**

**"COVID Activity Rehab Program"**

- Fatigue 80%
- Respiratory 59%
- Neurologic 59%
- Cognitive impairment 45%
- Sleep disturbance 30%
- Mental health sx 26%

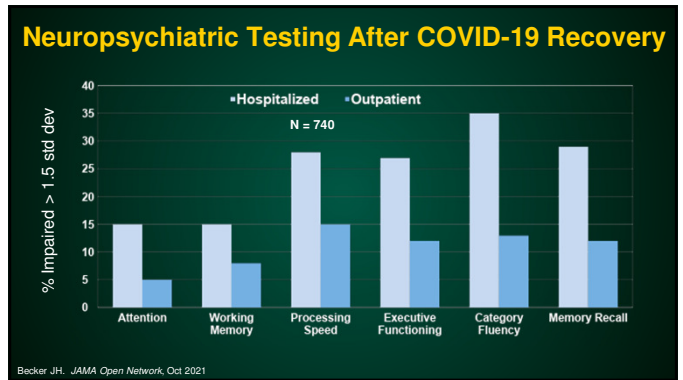
Vasilevichrom G, Vasilevichrom.gmg@mayo.edu, Newcomb R, et al. Post COVID-19 Syndrome (Long Haul Syndrome): Description of a Multidisciplinary Clinic at the Mayo Clinic and Characteristics of the Initial Patient Cohort. Mayo Clinic Proceedings. 2021;96(10):1016-1021. doi:10.1016/j.mayop.2021.04.02

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**CARP POPULATION UNIQUE SX**

- Tinnitus
- Prolonged loss of taste and smell
- Hair shedding (telogen effluvium)
- Syncope
- Sinus discomfort
- Eye changes

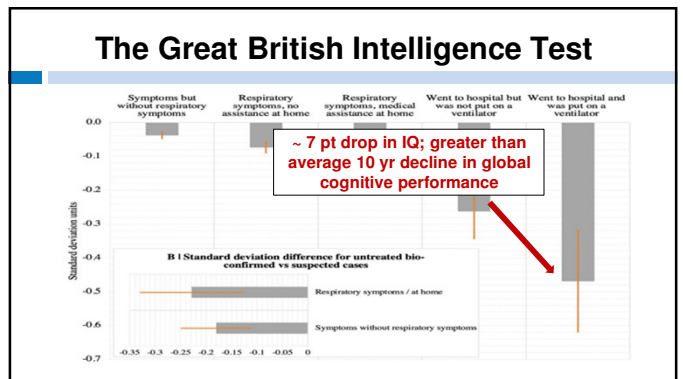
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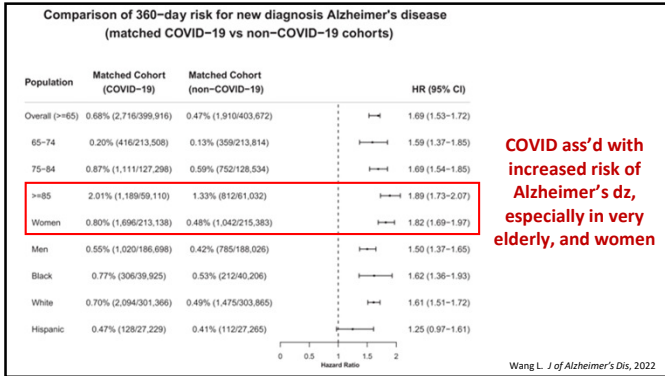
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**Persistent Cardiac Inflammation After COVID-19 Recovery**

- German study of 100 patients 64-92 days after dx with cardiac MRI and hsTroponin
- 2/3 recovered at home with 18 asymptomatic, and 49 mild to moderate
- 78% had cardiac involvement, 60% had ongoing inflammation**
- Independent of pre-existing conditions or severity of illness
- Abnormalities persisted beyond 3 mos

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**Myocarditis in Big 10 Athletes After Recent SARS CoV2**

Cardiac MRI scans on 1597 athletes after recovering from recent SARS CoV-2 infection

**2.3% of athletes diagnosed with COVID-19 myocarditis**

JAMA Cardiology Published online May 27, 2021

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**Persistent Lung Abnormalities**

- 55 Chinese pts followed in prospective cohort study!
  - 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 capacity<sup>2</sup>

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

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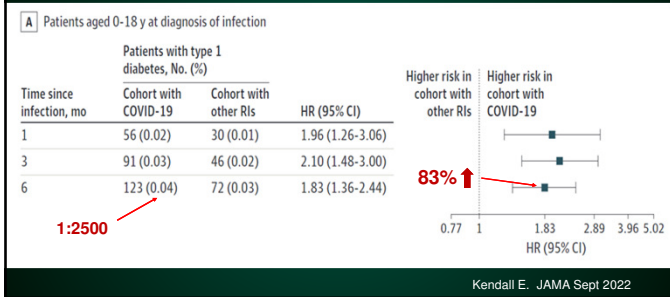
**Does Asymptomatic Mean Harmless?**

- 76 asymptomatic cases – CT scan of chest
- 41 (54%) had ground glass infiltrates

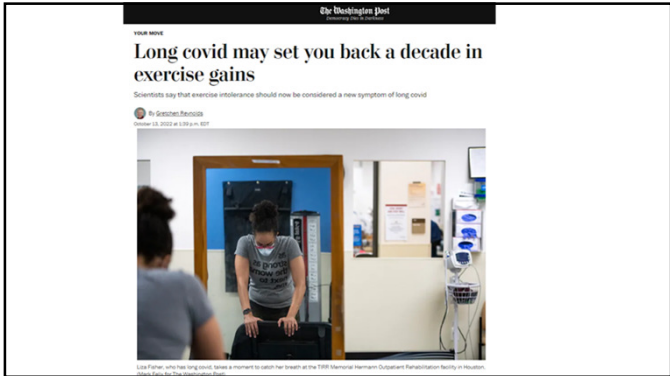
Inui S et al. *Radiology*, Mar 2020

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## Increased Risk of T1DM in Children under 18



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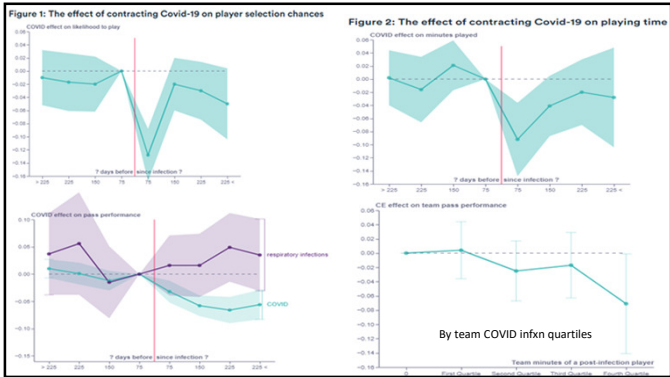
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### Could mild COVID-19 Affect Athletic Performance?

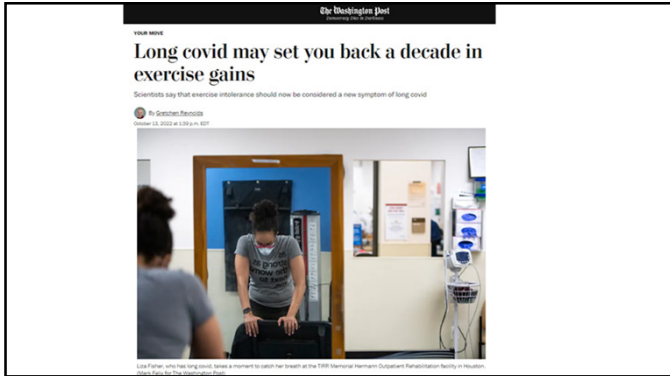
#### Study in elite soccer players

Fischer, DICE Discussion Paper, No. 368, ISBN 978-3-86304-367-4

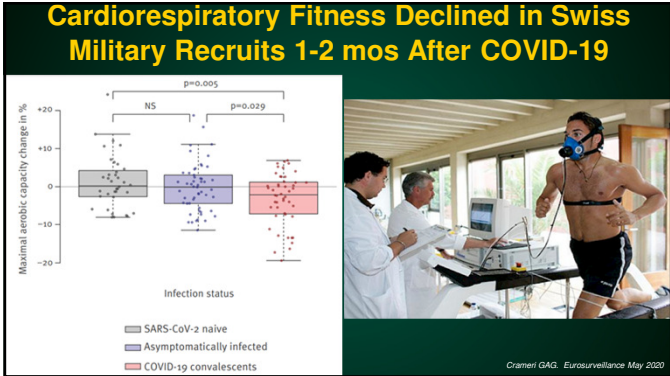
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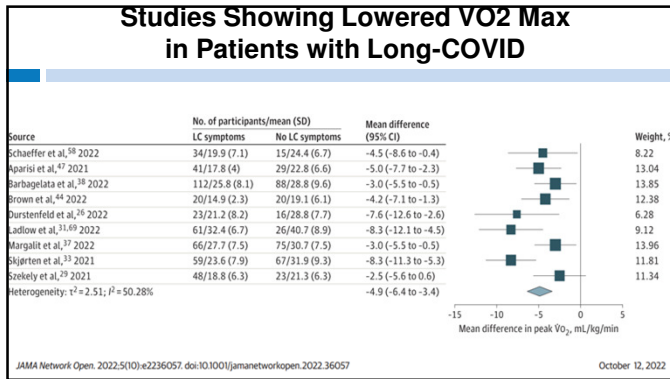
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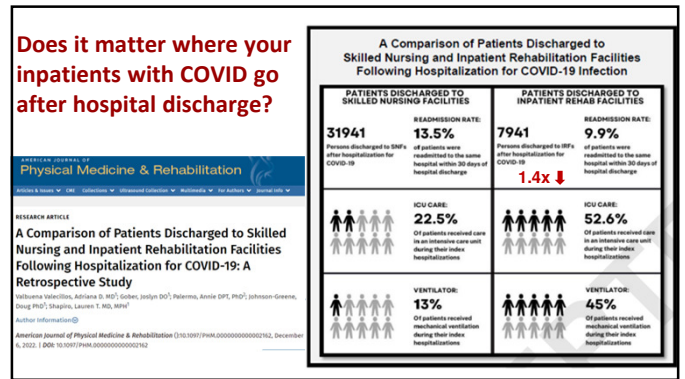
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### Elements of Rehab Program

- Thorough medical evaluation
  - Cardiac, Pulmonary, Psych, Neuro, Dysautonomia
- Autonomic reconditioning
  - Breathing exercises: increase vagal tone
  - Salt intake, mineralocorticoids, beta-blockers
- Avoid post-exertional fatigue
  - Slow and graded exercise program, PT, OT
- Sleep hygiene, sleep referral

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### Treatment of Post-Viral Olfactory Dysfunction

- 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

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### Clinical management of COVID-19

LIVING GUIDELINE  
13 JANUARY 2023

<https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2>

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Our website is for everybody living with Long COVID and anyone wanting to learn more

<https://longcovid.physio/>

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## Summary

- PASC (i.e. "Long-COVID") appears to be common, even among outpatients and young adults
  - True incidence needs better defining with more controlled studies
  - Long-term effects on CNS/Kidney/Heart/Lung/Brain are yet to be realized
- Given the enormous attack rate from COVID-19, we should expect major impacts on clinical practice
- Patients will benefit most from multi-disciplinary approach with a graded rehabilitation program

~~Antiviral treatment, immune modulation, post-acute COVID vaccination warrant~~