Frontline Workers: A Global Perspective



Frontline Worker Safety in the Age of COVID-19 Health Watch USAsm



Webinar Sept. 14th, 2022 - Registration Now Open <u>https://healthconference.org</u>

Long Covid: a brief overview Ziyad Al-Aly, MD Chief, Research and Development Service VA Saint Louis Health Care System Twitter: @ alaly





Disclosures

- Consulting: Gilead, Tonix
- The opinions expressed in this presentation do not represent the views of the US Department of Veterans Affairs or the US Government
- Funding: US Department of Veterans Affairs and American Society of Nephrology



Outline

- What led us to study long Covid?
- Broad overview of Long Covid
- Long-term:
 - cardiovascular outcomes
 - kidney outcomes
 - diabetes
 - mental health outcomes
- Effect of vaccination on Long Covid
- Implications for health systems and communities
- Summary





How do we do our part in this pandemic?



Non-recovery from Coronavirus infection

The New York Times

OPINION

We Need to Talk About What Coronavirus Recoveries Look Like

They're a lot more complicated than most people realize.

April 13, 2020

By Fiona Lowenstein

Fiona Lowenstein is a writer, producer and yoga teacher.



Pinned Tweet



Fiona Lowenstein @fi_lowenstein · Mar 17

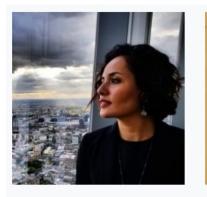
Last year on this day, I was being treated for Covid-19 in the hospital. Today, I'm in touch with thousands of patients who never recovered. My latest for @nytopinion with @ahandvanish looks at why #LongCovid needs to be our focus in year 2.



Report: What Does COVID-19 Recovery Actually Look Like?

An Analysis of the Prolonged COVID-19 Symptoms Survey by Patient-Led Research Team

Originally Released: May 11th, 2020. Generated from survey data organized by decentralized team of COVID-19 patients, exported on May 2, 2020 (640 Responses)

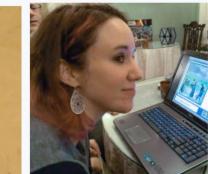




Day 1 on March 17th.



Day 1 on March 14th.







Gina Assaf

Lisa McCorkell

Hannah Davis

Day 1 on March 25th.

Hannah Wei Day 1 on March 11th.

Day 1 on March 20th.

Patient-Led Research Collaborative www.patientresearchcovid19.com





Early reports from patient-led groups

- Weakness
- Fatigue

7

- Brain fog
- Muscle pain
- Other manifestations



- Long Covid
- Long haulers





What is Long Covid?

8



Accelerated Article Preview

High-dimensional characterization of post-acute sequalae of COVID-19

Received: 18 January 2021

Ziyad Al-Aly, Yan Xie & Benjamin Bowe

Accepted: 14 April 2021

9

Accelerated Article Preview Published online 22 April 2021

Cite this article as: Al-Aly, Z. et al. High-dimensional characterization of post-acute sequalae of COVID-19. *Nature* https://doi.org/10.1038/s41586-021-03553-9 (2021). This is a PDF file of a peer-reviewed paper that has been accepted for publication. Although unedited, the content has been subjected to preliminary formatting. Nature is providing this early version of the typeset paper as a service to our authors and readers. The text and figures will undergo copyediting and a proof review before the paper is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers apply.





COVID-19: Lasting impact



Cardiovascular

acute coronary disease, heart failure, palpitations, arrythmias



Respiratory system

cough, shortness of breath, low blood oxygen

Musculoskeletal

joint pain, muscle

weakness



General malaise, fatigue, anemia

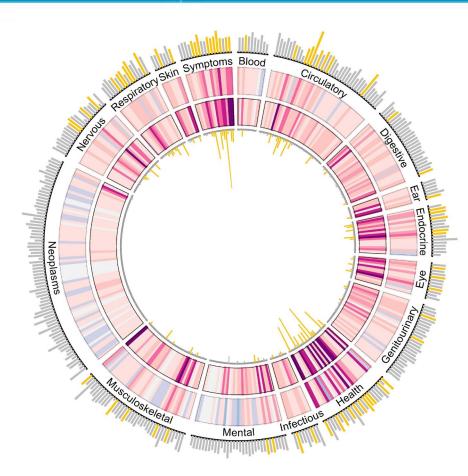
Al-Aly et al. Nature 2021

Mental health anxiety, depression, sleep problems, substance abuse Nervous system stroke, headaches, memory problems, smell problems Metabolic/ endocrine obesity, diabetes, high cholesterol Gastrointestinal constipation, diarrhea, acid reflux Skin disorders hair loss, rash Coagulation disorders blood clots



Covid vs seasonal influenza

- Magnitude of risk is higher
- Breadth of organ involvement
- It is a different kind of post-viral syndrome



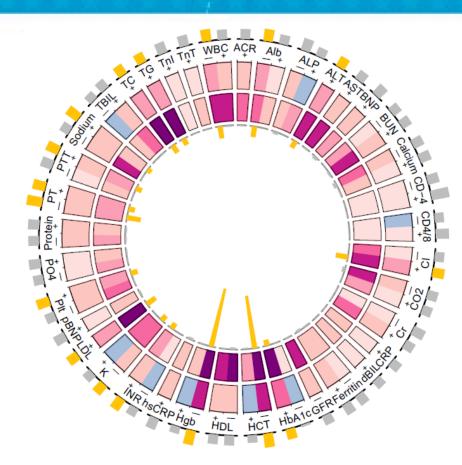


Al-Aly et al. Nature 2021

Post-acute Sequelae

• The risk is evident among non-hospitalized

• The risk increases according to the severity of the acute infection





Al-Aly et al. Nature 2021

	Overall	Age ≤60	Age 60 - 70	Age >70	Black	White	Male	Female	No comorbidities	1 - 3 comorbidities	>3 comorbidities	_S Chronic kidney disease –		-	Acute kidney injury -	H	Muscle weakness -	· •	Fatigue -	
Shortness _ of breath	28.80	23.56	32.41	27.82	30.13	28.39	28.04	33.55	20.27	29.79	37.50	Fatigue -	H		Diabetes mellitus -	H	GERD -		Muscle weakness -	
Sleep	19.51	25.07	19.51	19.38	17.32	20.48	20.31	15.22	16.73	18.39	25.51	Muscle weakness -		H	Chest pain -	⊨ ⊣	Fatigue -	·	Acute kidney injury -	
disorders												Acute coronary disease -	┣━━┣┤	I	Cough -	⊫⊣	Acute coronary disease -	· +	Shortness of breath -	
Hyperlipidemia -	17.09	21.85	21.25	13.32	15.23	17.64	17.78	11.96	19.99	14.29	8.89	Memory problems -	► FI		Substance abuse -	H	Thromboembolism -		Chronic kidney disease -	
Chest _ pain	13.84	16.55	16.13	9.91	16.46	13.07	13.49	18.01	11.16	13.44	12.75	Acute kidney injury -			Thromboembolism -	•	Joint pain -		Acute coronary disease -	
Fatigue -	13.59	5.40	12.87	22.79	13.94	13.29	14.30	7.21	6.96	15.20	33.42	Thromboembolism - Constipation -			Headache - Joint pain -	Ē	Hyperlipidemia - Diabetes mellitus -		GERD - Anxiety -	
GERD -	13.25	8.41	14.46	17.80	11.04	14.11	14.16	6.67	8.96	13.71	22.75	GERD -			Constipation -		Acute kidney injury -	· •	Hypoxemia -	
Thromboembolism -	11.35	5.65	12.55	15.66	13.32	10.64	12.02	5.02	6.96	12.62	18.39	Hypoxemia -	H .		Shortness of breath -	⊫-i	Sleep disorder -	- <u>-</u> .	Thromboembolism -	
Cough -	10.24	9.87	13.37	8.13	12.37	9.37	10.04	13.29	8.57	9.11	9.77	Anxiety -	H		Mood disorder -	н	Memory problems -	· -	Constipation -	
Muscle	9.81	2.54	8.45	19.48	10.89	9.38				12.20	28.12	Diabetes mellitus -	■ ••		Muscle weakness -	H	Chronic kidney disease -	{ <mark>⊨</mark> -1	Joint pain -	
weakness Joint							10.62	2.85	3.62			Joint pain -	⊫⊣		Tachycardia -	H	Hypoxemia -	· - ••	Memory problems -	
pain	8.92	6.52	9.42	11.47	10.25	8.42	9.65	3.30	5.60	9.65	15.75	Heart failure -	H		Anxiety -		Anxiety -	⊨ -1	Sleep disorder -	
Anxiety -	8.75	5.04	11.03	12.33	9.83	8.52	9.20	5.86	4.84	9.14	18.40	Shortness of breath			Fatigue -		Substance abuse =		Heart failure	
Diabetes mellitus -	8.47	4.67	10.46	11.07	11.31	7.29	9.18	3.37	8.11	7.98	10.59	Shortness of breath - Bradycardia -	H		Stroke - Depression -		Heart failure = Stroke =		Depression - Diarrhea -	
Arrythmias -	7.85	8.06	7.00	6.81	7.66	7.83	7.51	10.90	6.76	6.82	8.11	Tachycardia -	H.		Diarrhea -	H	Constipation -	- F.	Tachycardia -	■ H
Depression -	7.61	8.51	8.19	7.81	7.93	7.41	7.83	7.25	4.98	7.98	12.77	Diarrhea -	H		Heart failure -	H.	Bradycardia -	н н –	Stroke -	
Chronic _	7.19	0.87	6.53	19.24	6.63	7.52	7.84	3.34	3.60	10.57	20.17	Skin rash -	Η		Myocarditis -	l l	Depression -	- ++-	Mood disorder -	⊨ ⊣
kidney disease				12.51								Myocarditis -			Arrythmias -	Ψ	Mood disorder -	4 H-1	Diabetes mellitus -	H= -1
Constipation - Memory	7.13	2.77	5.81		8.40	6.67	7.29	6.01	3.31	8.44	14.74	Hair loss -			Hair loss -]	Myocarditis -	¦	Chest pain -	₩ <u></u>
problems	6.46	1.91	4.25	14.63	5.93	6.86	6.99	2.05	4.14	6.44	13.32	Depression -			Smell problems -	1	Diarrhea -		Bradycardia -	
Hypoxemia -	6.43	2.72	6.89	10.25	5.92	6.84	6.89	2.39	3.03	7.69	15.81	Substance abuse - Arrythmias -			Obesity - Acute coronary disease -	ц ц	Smell problems = Obesity =		Arrythmias – Cough –	
Acute coronary _ disease	6.18	1.12	6.84	15.07	5.63	6.45	7.22	0.18	2.69	8.05	17.39	Smell problems	H		Bradycardia -	н	Tachycardia -	, н.	Substance abuse -	iii I
Acute _ kidney injury	6.07	1.33	6.36	12.32	9.15	5.08	6.92	1.30	2.62	8.87	25.07	Cough -	н		Chronic kidney disease -	н	Skin rash =	- + -	Myocarditis -	H
Tachycardia -	4.69	4.04	5.32	4.69	5.75	4.29	4.63	5.31	2.83	5.02	8.18	Mood disorder -	H		Hypoxemia -	н	Cough -	- ⊢ ∎	Headache -	H
Diabetes	4.68	4.62	4.42	4.78	5.15	4.62	4.76	4.62	2.94	4.44	8.41	Obesity -	H		Memory problems -	н	Arrythmias -	┥ ⊢ ┫	Obesity -	Ψ
mellitus Mood	4.57	6.79	4.06	4.78	5.58	4.04	4.71	4.39	3.87	4.14	7.10	Headache -			Skin rash -		Hair loss =		Skin rash -	<u></u> Ч – – – – – – – – – – – – – – – – – –
disorder												Sleep disorder - Chest pain -			Hyperlipidemia - GERD -		Chest pain - Shortness of breath -		Hair loss - Smell problems -	H Langer
Headache -	3.80	7.09	5.60	3.00	5.24	3.32	3.50	11.44	3.74	3.45	4.14	Hyperlipidemia -			Sleep disorder -	i di la constante di la consta	Headache -		Hyperlipidemia	l Legend ■ Significant ■ Non-significant
Obesity -	3.49	5.57	5.11	2.67	3.09	3.78	3.54	4.25	3.54	3.09	3.55	_	-10 0 10	20 30		-10 0 10 20	 30	-10 0 10 20	[-10 0 10 20 30
Skin _ rash	3.30	3.22	3.29	3.30	2.37	3.66	3.05	5.77	2.70	3.39	2.56		Age ≤ 60 Age > 70			– White Black →		← Female Male →		norbidity High comorbidity \rightarrow
Substance _ abuse	3.24	3.43	4.22	2.59	5.28	2.35	3.53	0.92	3.49	2.33	4.64		Burden per 1000 p	persons	В	urden per 1000 persor	IS	Burden per 1000 pers	ons B	urden per 1000 persons
Stroke -	3.11	0.83	3.24	5.44	3.51	2.94	3.31	1.46	1.32	3.69	6.53									
Bradycardia -	2.63	1.43	2.26	4.17	2.03	2.89	2.73	1.67	1.84	2.95	3.27	Xiee	tal Na	atur	e Comr	nunicatio	ons 2021			
Heart	2.02	0.20	1.72	4.88	2.07	1.97	2.27	0.33	0.81	2.80	9.12			atar		lamoati				
failure Smell	1.34	2.09	1.15	0.80	0.88	1.42	1.28	1.70	1.35	1.10	0.89									
problems												_								
Myocarditis - Hair	0.32	0.22	0.30	0.28	0.29	0.30	0.34	0.00	0.11	0.20	0.57	_								
loss	0.22	0.70	0.27	0.06	0.10	0.29	0.13	3.59	0.31	0.20	0.10					Acalu	Care for Heroe	MA I	Defining	
																	A		EVCELL	INCE
Burden																1		HEALTH	EXCELLI	INCE
13 ^{Burden} 0			10			20		30			40					VA St. L	nis Health Care System	CARE	in the 21st Cer	nury

Sequelae of concern

- Cardiovascular disorders
- Diabetes
- Kidney disease
- Neurologic and mental health disorders



medicine

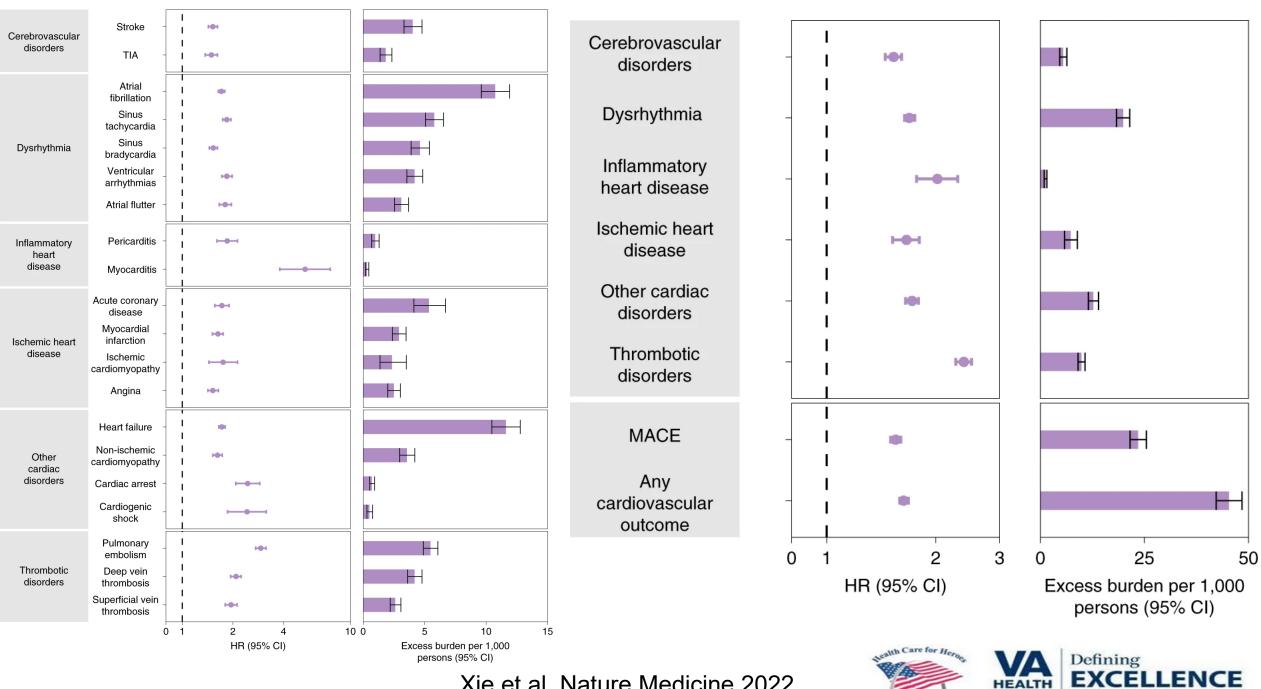
ARTICLES https://doi.org/10.1038/s41591-022-01689-3

OPEN Long-term cardiovascular outcomes of COVID-19

Yan Xie^{1,2,3}, Evan Xu^{1,4}, Benjamin Bowe^{1,2} and Ziyad Al-Aly^{1,2,5,6,7}

The cardiovascular complications of acute coronavirus disease 2019 (COVID-19) are well described, but the post-acute cardiovascular manifestations of COVID-19 have not yet been comprehensively characterized. Here we used national healthcare databases from the US Department of Veterans Affairs to build a cohort of 153,760 individuals with COVID-19, as well as two sets of control cohorts with 5,637,647 (contemporary controls) and 5,859,411 (historical controls) individuals, to estimate risks and 1-year burdens of a set of pre-specified incident cardiovascular outcomes. We show that, beyond the first 30 d after infection, individuals with COVID-19 are at increased risk of incident cardiovascular disease spanning several categories, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure and thromboembolic disease. These risks and burdens were evident even among individuals who were not hospitalized during the acute phase of the infection and increased in a graded fashion according to the care setting during the acute phase (non-hospitalized, hospitalized and admitted to intensive care). Our results provide evidence that the risk and 1-year burden of cardiovascular disease in survivors of acute COVID-19 are substantial. Care pathways of those surviving the acute episode of COVID-19 should include attention to cardiovascular health and disease.





Xie et al. Nature Medicine 2022

HEALTH CARE

in the 21st Century



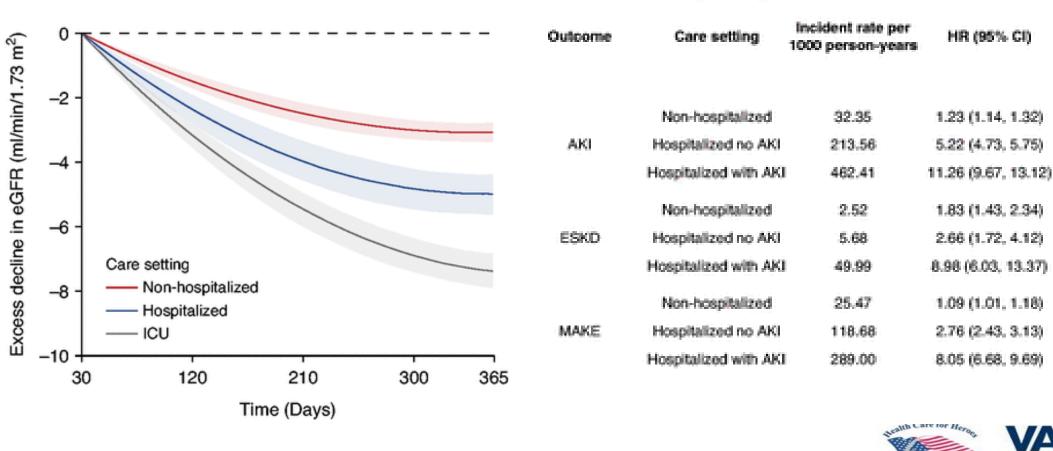
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

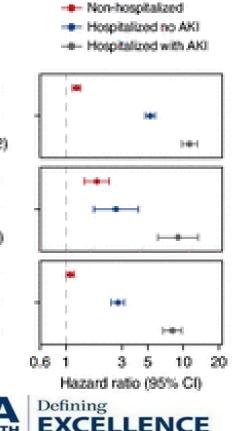
www.jasn.org

Kidney Outcomes in Long COVID

Benjamin Bowe,^{1,2,3} Yan Xie,^{1,2,3} Evan Xu (b,^{1,4} and Ziyad Al-Aly (b^{1,3,5,6,7}

Due to the number of contributing authors, the affiliations are listed at the end of this article.





in the 21st Century

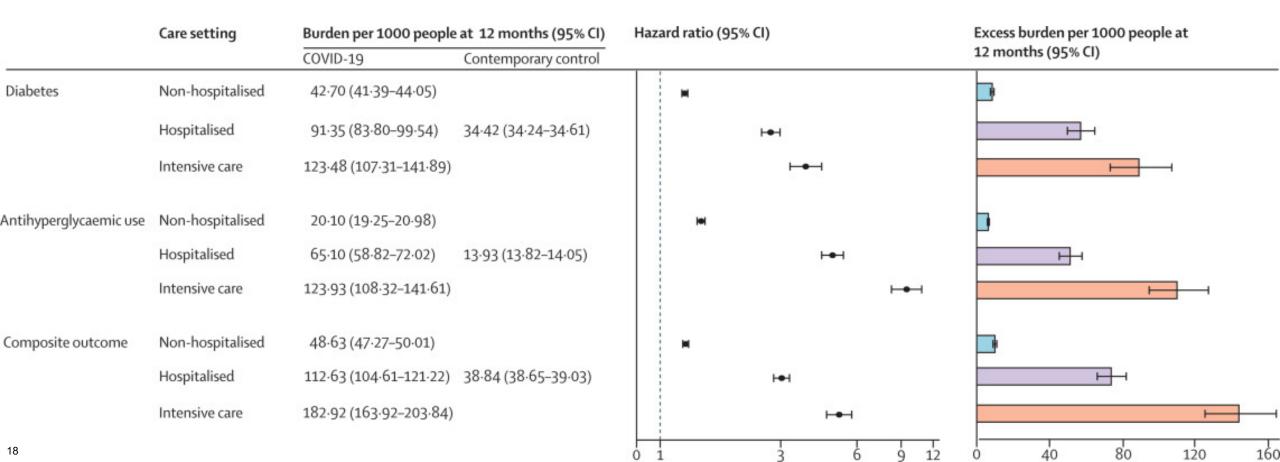
CARE

Care Setting

THE LANCET Diabetes & Endocrinology

Risks and burdens of incident diabetes in long COVID: a cohort study

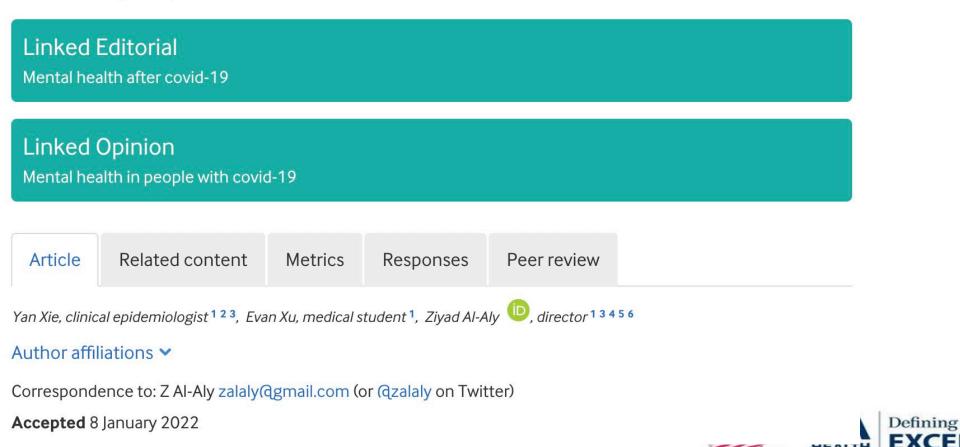
Yan Xie, MPH 🛛 Ziyad Al-Aly, MD 🛛 🖄 🖂



Research

Risks of mental health outcomes in people with covid-19: cohort study

BMJ 2022 ; 376 doi: https://doi.org/10.1136/bmj-2021-068993 (Published 16 February 2022) Cite this as: *BMJ* 2022;376:e068993



in the 21st Century

CARE

Outcome	Hazard ratio (95% Cl)	Hazard ratio (95% CI)	Risk difference per 1000 people at one year (95% CI)	Risk difference per 1000 people at one year (95% CI)
Anxiety disorders	1.35 (1.30 to 1.39)	•	11.06 (9.64 to 12.53)	-
Generalized anxiety disorder	1.34 (1.30 to 1.39)	· •	10.56 (9.18 to 11.99)	-
Mixed anxiety disorder	1.41 (1.30 to 1.54)	-+	1.66 (1.21 to 2.15)	+
Panic disorder	1.28 (1.17 to 1.41)	-+-	0.84 (0.49 to 1.22)	÷
Depressive disorders	1.39 (1.34 to 1.43)	-	15.12 (13.38 to 16.91)	-
MDD - single episode	1.42 (1.37 to 1.47)	· •	12.53 (11.15 to 13.95)	-
MDD - recurrent	1.29 (1.24 to 1.34)		7.86 (6.58 to 9.18)	-
Suicidal ideation	1.46 (1.35 to 1.57)	-+-	2.25 (1.73 to 2.81)	-
Stress and adjustment disorders	1.38 (1.34 to 1.43)		13.29 (11.71 to 14.92)	-
Acute stress and adjustment disorder	1.48 (1.42 to 1.54)		8.05 (7.08 to 9.07)	-
PTSD	1.30 (1.24 to 1.36)		6.60 (5.39 to 7.85)	-
Antidepressants	1.55 (1.50 to 1.60)	-	21.59 (19.63 to 23.60)	
SSRI	1.54 (1.49 to 1.60)	-+-	17.13 (15.47 to 18.84)	-
SNRI	1.22 (1.17 to 1.28)		3.23 (2.45 to 4.06)	-
Other antidepressants	1.56 (1.48 to 1.64)	-+-	5.98 (5.14 to 6.86)	-
Benzodiazepines	1.65 (1.58 to 1.72)		10.46 (9.37 to 11.61)	-
Opioids				
Opioid prescription	1.76 (1.71 to 1.81)	· .	35.90 (33.61 to 38.25)	
Opioid use disorder	1.34 (1.21 to 1.48)	-+-	0.96 (0.59 to 1.37)	÷
Naloxone or naltrexone	1.23 (1.18 to 1.29)	-+-	3.08 (2.32 to 3.86)	-
Methadone	1.94 (1.47 to 2.56)	•	0.27 (0.14 to 0.46)	+
Buprenorphine	1.34 (1.12 to 1.62)		0.45 (0.15 to 0.80)	+
Substance use disorders				
Any substance use disorder	1.20 (1.15 to 1.26)		4.34 (3.22 to 5.51)	-
Illicit drug disorder	1.24 (1.16 to 1.32)	-+-	2.12 (1.42 to 2.87)	-
Alcohol use disorder	1.29 (1.22 to 1.35)	-+-	4.60 (3.61 to 5.65)	-
Sedative or hypnotics use disorder	1.40 (1.14 to 1.72)		0.28 (0.10 to 0.51)	-
Neurocognitive decline	1.80 (1.72 to 1.89)	-+-	10.75 (9.65 to 11.91)	-
Sleep				
Sleep disorders	1.41 (1.38 to 1.45)	•	23.80 (21.65 to 26.00)	
Sleep medications	1.63 (1.58 to 1.67)	•	25.87 (24.01 to 27.78)	
20		0 1 2 3	3	0 10 20 30 40

Xie et al. BMJ 2022



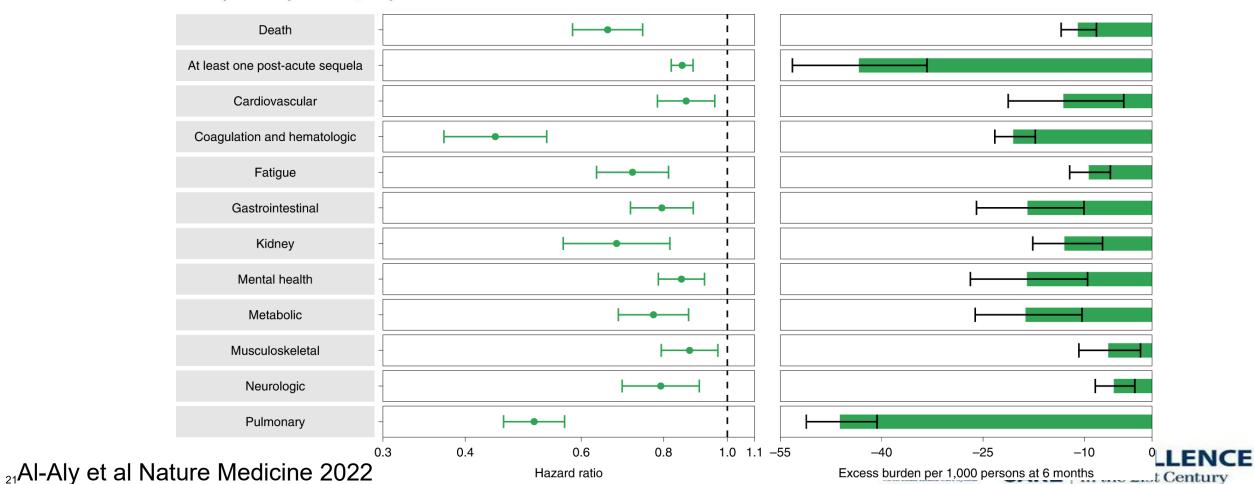


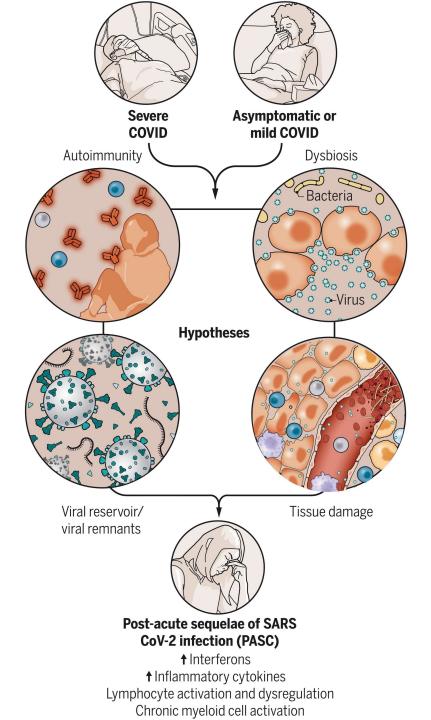


ARTICLES

OPEN Long COVID after breakthrough SARS-CoV-2 infection

Ziyad Al-Aly^{01,2,3,4,5}, Benjamin Bowe^{1,2} and Yan Xie^{1,2,6}





Putative Mechanisms of Long Covid

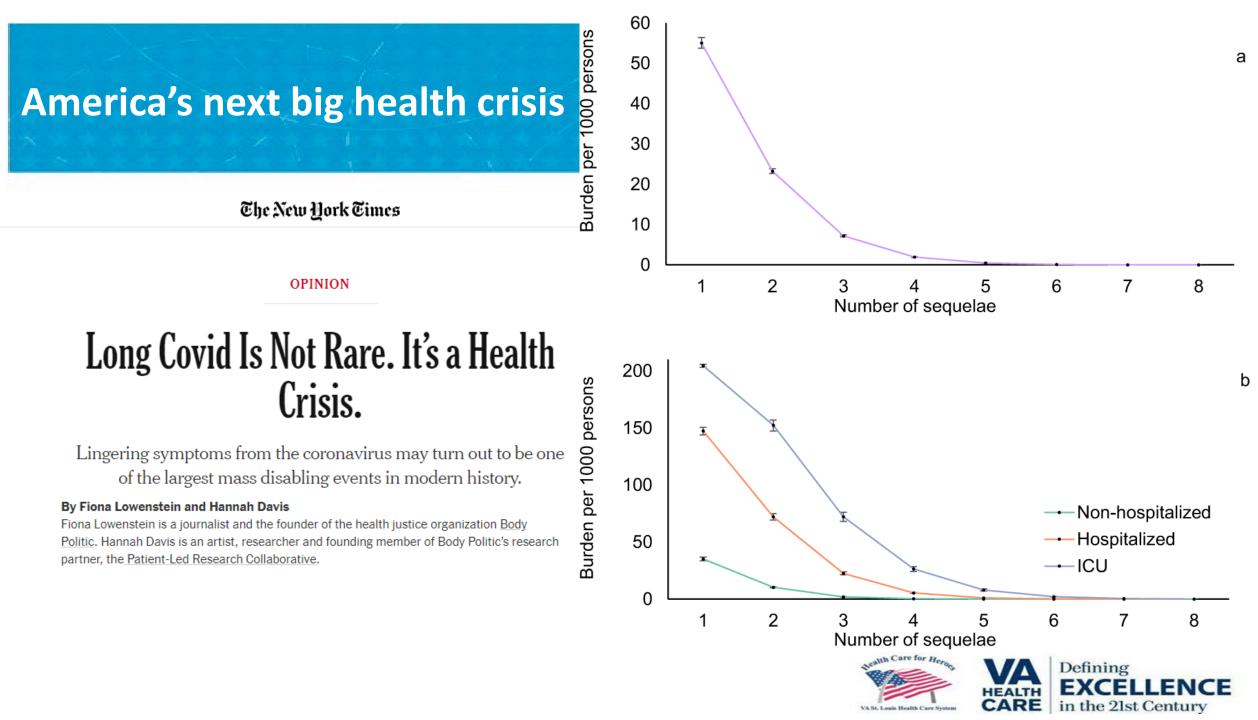
Merad et al. Science 2022



Long Covid – an umbrella term

- Overlap with
 - Post hospitalization
 - Post ICU
- Similarities and differences with:
 - Other post-viral illnesses
 - Post-flu (encephalitis lethargica (EL) or 'sleepy sickness', post-encephalitic parkinsonism)
 - Measles (subacute sclerosing panencephalitis)
 - EBV (multiple sclerosis)
 - Post-Ebola syndrome
 - Post-Polio syndrome
 - Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)





Implications for health systems I

- Burden of long Covid is likely substantial (4-7% of people with COVID-19)
- Long Covid is a multifaceted disease that can affect nearly every organ system
 - Rise in burden of chronic diseases (cardiovascular disease, diabetes, kidney diseases, etc..)
 - Based on our work, the Institute of Health Metrics and Evaluation (IHME) estimates 200,000 and 40,000 additional cases of ischemic heart disease and stroke in the US



Implications for health systems II

- It is imperative that governments and health systems prepare for people in need of post covid care
 - UK National Health Service
 - Several other health systems in the US
 - US VA Healthcare System



Implications for communities

- Best way to prevent long covid is to prevent covid through vaccination
- Misinformation, disinformation and gaslighting
- The power of patient advocacy



The long shadow of Covid

- The toll of hospitalization and death from acute covid is only the tip of the iceberg
- Long Covid
 - Disease and disability
 - Life expectancy
 - Development and educational attainment
 - Economic implications
 - Social implications

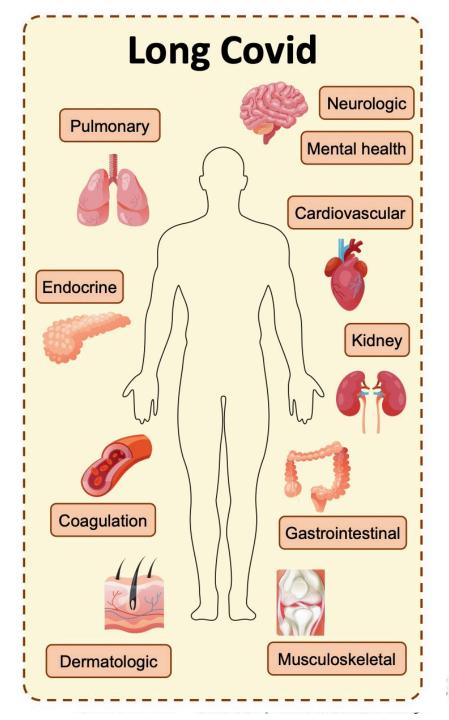




Summary

• Long Covid is a multifaceted disease; it can affect nearly every organ system

- The burden of Long Covid around 4-7%
 - Some Long Covid manifestations are chronic conditions that last a lifetime
- Governments and health systems must adapt quickly and establish post-covid care strategies



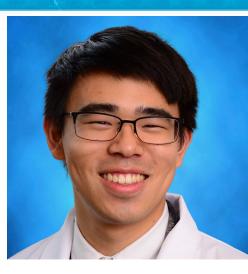
Grateful!



Yan Xie Data Scientist



Benjamin Bowe Data Scientist



- Other Team Members:
 - Miao Cai
 - Andrew K. Gibson
 - Taeyoung Choi
 - John Ciconte
 - Uly Labilles

Evan Xu

Funding:

- US Department of Veterans Affairs
- American Society of Nephrology

Administrative Support:

- Research and Development Service at VA Saint Louis Health Care System
- Public Affairs at Washington University
 in Saint Louis

Long haulers who inspired and continue to inspire us!



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Thank you Twitter @azalaly

