Twitter Thread by CapOrbit

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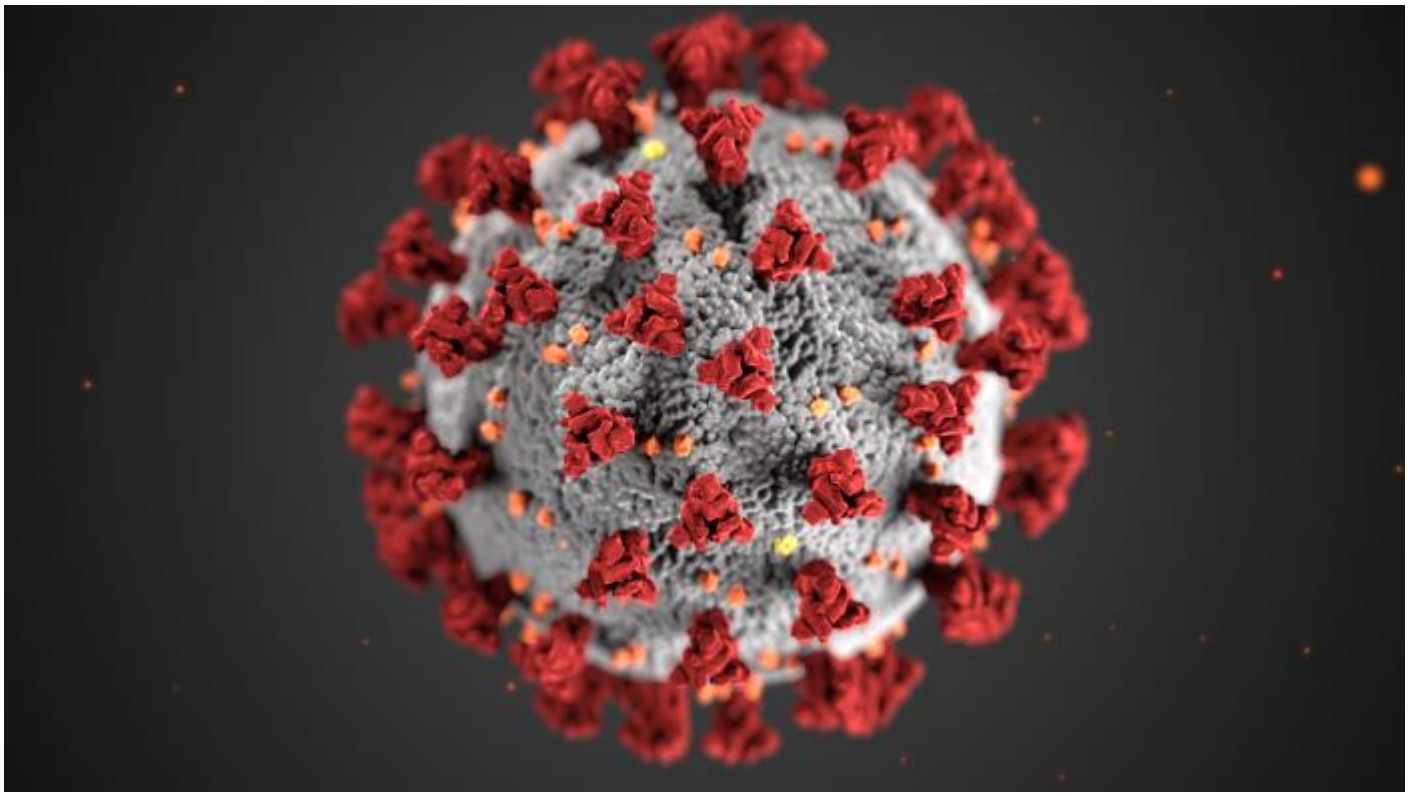
Thread on long Covid and health risks.

Recovery from Covid is understood by most to be when acute phase symptoms, including fever, cough, fatigue, headaches, go away.

Are there hidden risks beyond the acute phase? Are some of them even fatal? Could some be prevented?
1/n



There is ample evidence that the body does not come back to pre-Covid equilibrium for some people, partly due to permanent damage to cells in different organs (as varied as pancreas, brain, lungs) for some and/or heightened inflammatory state in the body.

2/n

In light of this, it is important to recognize that there is need for caution even later. The impact of some of these long-covid conditions can be non-fatal but chronic. More worrying is the potential risk of death even months later.
3/n

I had heard of anecdotes first-hand from multiple friends of people passing away due to heart attacks, strokes, and pulmonary embolism. My interest in researching this in more detail was because it is affecting so many of us in India at the moment.
4/n

After a lot of perusing through medical papers through databases, I came across this study published in Nature.

High-dimensional characterization of post-acute sequalae of COVID-19
https://t.co/9C1EjHBUID
PDF can be downloaded here

5/n

nature

https://doi.org/10.1038/s41586-021-03553-9

Accelerated Article Preview

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

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Ziyad Al-Aly, Yan Xie & Benjamin Bowe

First, what is a sequela?
A typical sequela is a chronic complication of an acute condition - in other words, a long-term effect of a temporary disease or injury - which follow immediately from the condition.
6/n

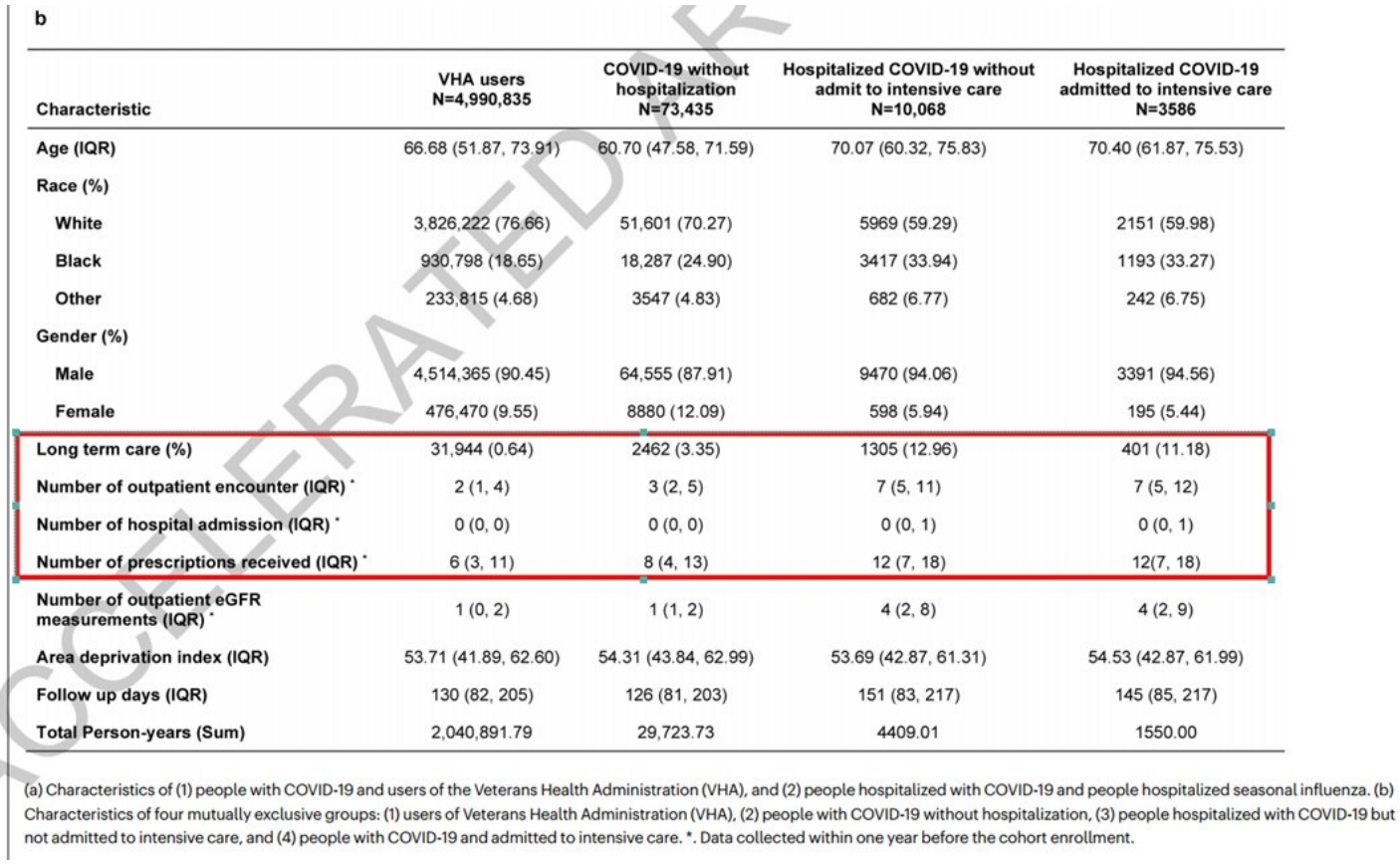
Examples and uses [edit]

Chronic kidney disease, for example, is sometimes a sequela of diabetes, "chronic constipation" or more accurately "obstipation" (that is, inability to pass stool or gas) is a sequela to an intestinal obstruction, and neck pain is a common sequela of whiplash or other trauma to the cervical vertebrae. Post-traumatic stress disorder may be a psychological sequela of rape. Sequelae of traumatic brain injury include headache and dizziness, anxiety, apathy, depression, aggression, cognitive impairments, personality changes, mania, psychosis.

Unlike other studies which had much lower number of patients (observations) this was the largest that I have seen to date - around 73,000 patients in the US Veterans database who got Covid.
7/n

A few parameters at the outset was a mean age of ~61, 88% males. They were tracked over a 6 month period and they checked on whether they developed any post-covid conditions, what drugs they needed to take, and what their pathology lab test results came like for key tests.

8/n



b

Characteristic	VHA users N=4,990,835	COVID-19 without hospitalization N=73,435	Hospitalized COVID-19 without admit to intensive care N=10,068	Hospitalized COVID-19 admitted to intensive care N=3586
Age (IQR)	66.68 (51.87, 73.91)	60.70 (47.58, 71.59)	70.07 (60.32, 75.83)	70.40 (61.87, 75.53)
Race (%)				
White	3,826,222 (76.66)	51,601 (70.27)	5969 (59.29)	2151 (59.98)
Black	930,798 (18.65)	18,287 (24.90)	3417 (33.94)	1193 (33.27)
Other	233,815 (4.68)	3547 (4.83)	682 (6.77)	242 (6.75)
Gender (%)				
Male	4,514,365 (90.45)	64,555 (87.91)	9470 (94.06)	3391 (94.56)
Female	476,470 (9.55)	8880 (12.09)	598 (5.94)	195 (5.44)
Long term care (%)	31,944 (0.64)	2462 (3.35)	1305 (12.96)	401 (11.18)
Number of outpatient encounter (IQR) *	2 (1, 4)	3 (2, 5)	7 (5, 11)	7 (5, 12)
Number of hospital admission (IQR) *	0 (0, 0)	0 (0, 0)	0 (0, 1)	0 (0, 1)
Number of prescriptions received (IQR) *	6 (3, 11)	8 (4, 13)	12 (7, 18)	12(7, 18)
Number of outpatient eGFR measurements (IQR) *	1 (0, 2)	1 (1, 2)	4 (2, 8)	4 (2, 9)
Area deprivation index (IQR)	53.71 (41.89, 62.60)	54.31 (43.84, 62.99)	53.69 (42.87, 61.31)	54.53 (42.87, 61.99)
Follow up days (IQR)	130 (82, 205)	126 (81, 203)	151 (83, 217)	145 (85, 217)
Total Person-years (Sum)	2,040,891.79	29,723.73	4409.01	1550.00

(a) Characteristics of (1) people with COVID-19 and users of the Veterans Health Administration (VHA), and (2) people hospitalized with COVID-19 and people hospitalized seasonal influenza. (b) Characteristics of four mutually exclusive groups: (1) users of Veterans Health Administration (VHA), (2) people with COVID-19 without hospitalization, (3) people hospitalized with COVID-19 but not admitted to intensive care, and (4) people with COVID-19 and admitted to intensive care. *. Data collected within one year before the cohort enrollment.

Do pre-existing health conditions affect severity seen in acute Covid? We anecdotally know that to be true and there is research on this too, that suggests so.
9/n

See the red box in the second-last tweet. The patients who had severe Covid (with ICU and without it) already had higher interaction with the Veteran healthcare system in the preceding year - being in long-term care already or more visits as outpatients.

10/n

This study is about post-Covid issues. Hence, the results should be seen in this light that if you already have a health issue you will most probably have more severe Covid and in turn, those with more severe Covid have higher risk of complications later on post-covid
11/n

There will still be cases of people who were relatively healthy to begin with but got Covid / had to go to hospital / ICU. I could not see separate data in this paper for this.
12/n

A fair question would be whether they have different risk as compared to already unhealthy people. Although, it is probably better to take greater care in any case because some of the outcomes as listed out are possibly fatal even.
13/n

Going on to the main study results.
Hazard ratio definition from wiki -> For example, in a drug study, the treated population may die at twice the rate per unit time of the control population. The hazard ratio would be 2, indicating higher hazard of death from the treatment.
14/n

In the figure below you will see hazard ratio comparison of covid +ve cases, hospital without ICU, and ICU cases.
15/n

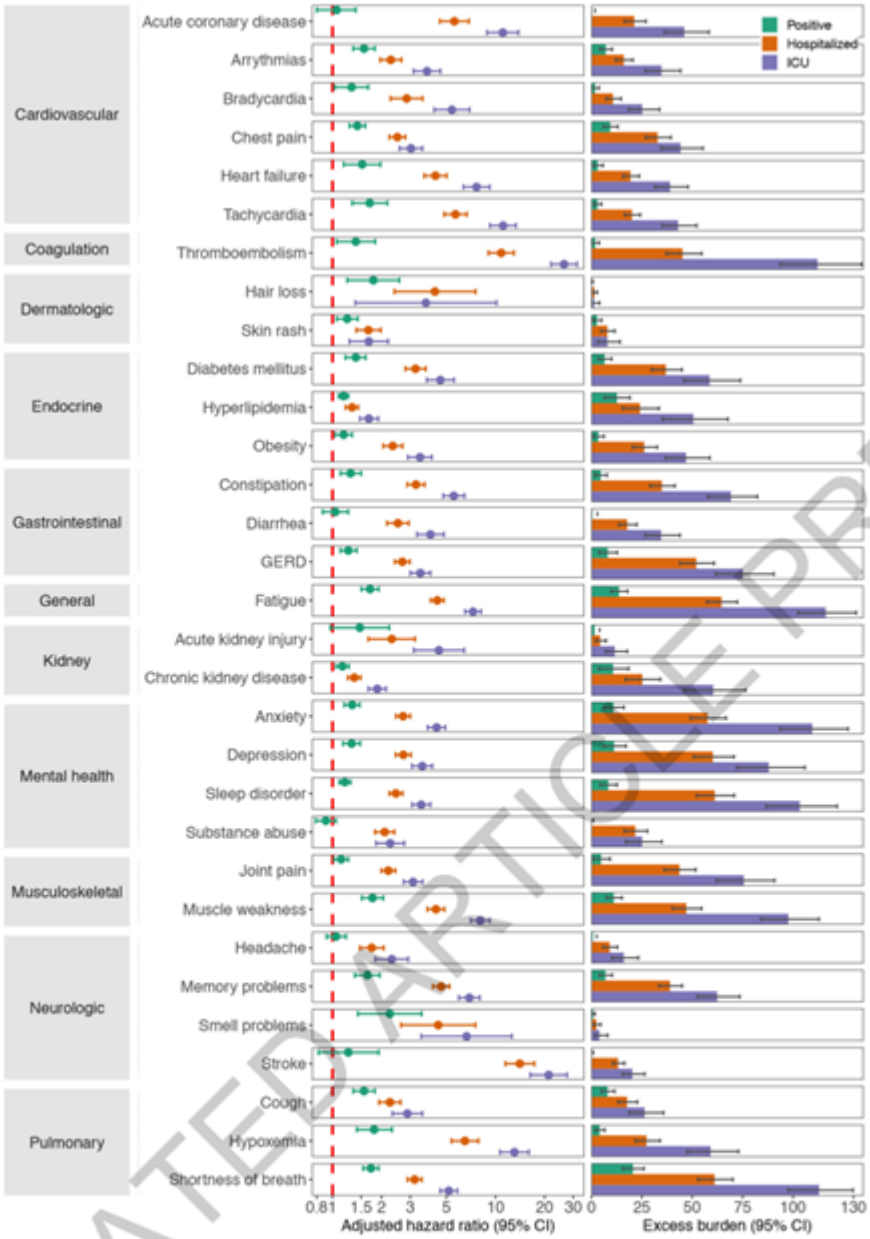


Fig. 3 | Risks and burdens of incident pre-specified high resolution post-acute COVID-19 outcomes at 6 months in mutually exclusive cohorts of people with non-hospitalized COVID-19 (green), people hospitalized for COVID-19 (orange), and people admitted to intensive care for COVID-19 (blue) during the acute phase (first 30 days) of the infection. ; all users of the Veteran Health Administration healthcare system served as the referent category. Outcomes were ascertained from day 30 after COVID-19 diagnosis until end of follow-up. Hazard ratios and 95% confidence intervals and excess burdens per 1000 patients and 95% confidence intervals at 6-months are presented.

Please see thromboembolism (blood clots leading to blockage as an example). Someone who went to hospital due to Covid (in that cohort with mean age 60 years) had a 10x risk compared to the general population. Someone who had an ICU stay had a 30x chance of an event.

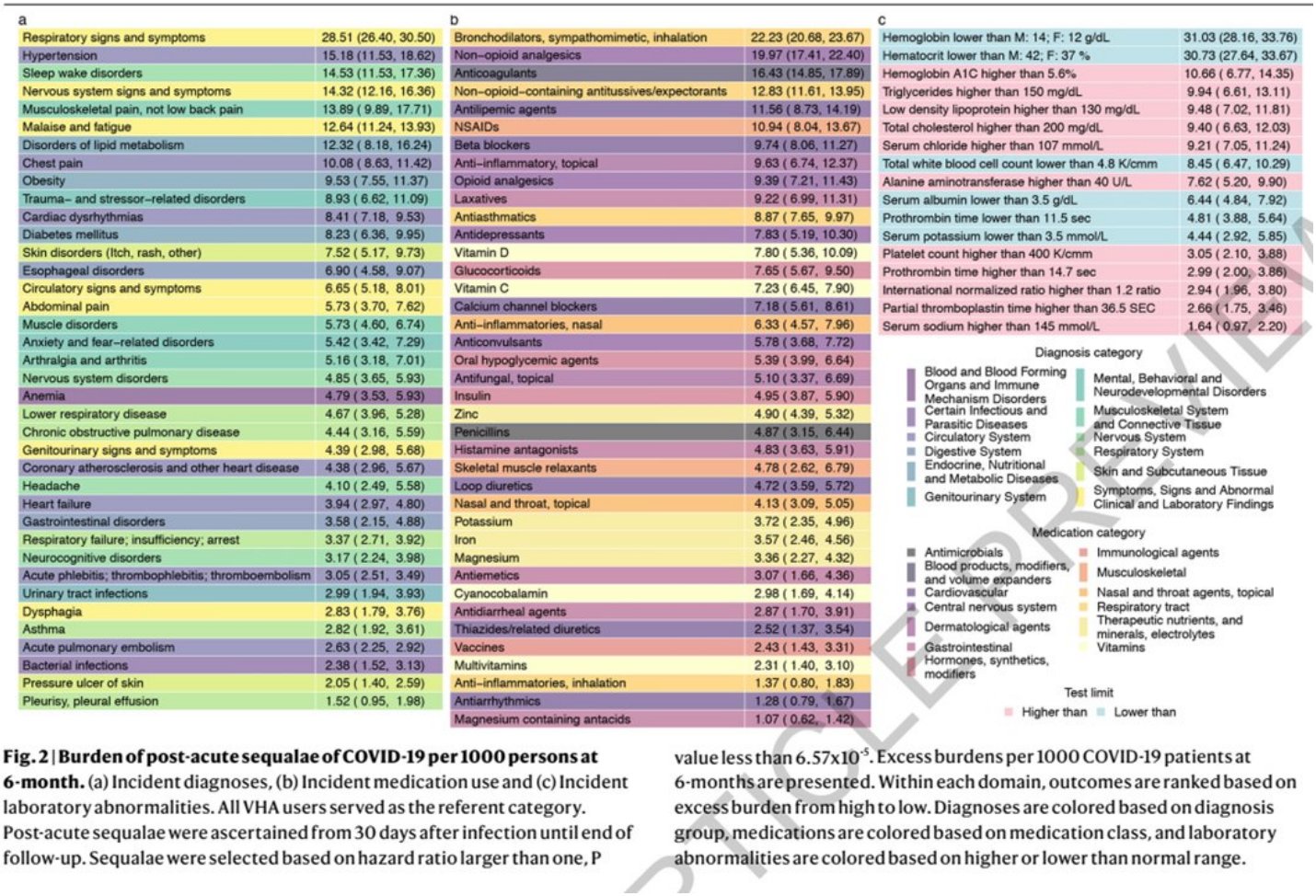
16/n

Or see heart failure. Someone who went to hospital due to Covid (in that cohort with mean age 60 years) had a ~4x risk compared to the general population. Someone who had an ICU stay had a ~7x chance of a heart failure event.

17/n

There was additional data on excess burden. Basically, for every 1k people who got Covid, as compared to the general population, how many more people satisfied a condition as given in the tables (got a medical condition, had to take a medicine, had test levels as mentioned)

18/n



a

Respiratory signs and symptoms	28.51 (26.40, 30.50)
Hypertension	15.18 (11.53, 18.62)
Sleep wake disorders	14.53 (11.53, 17.36)
Nervous system signs and symptoms	14.32 (12.16, 16.36)
Musculoskeletal pain, not low back pain	13.89 (9.89, 17.71)
Malaise and fatigue	12.64 (11.24, 13.93)
Disorders of lipid metabolism	12.32 (8.18, 16.24)
Chest pain	10.08 (8.63, 11.42)
Obesity	9.53 (7.55, 11.37)
Trauma– and stressor–related disorders	8.93 (6.62, 11.09)
Cardiac dysrhythmias	8.41 (7.18, 9.53)
Diabetes mellitus	8.23 (6.36, 9.95)
Skin disorders (Itch, rash, other)	7.52 (5.17, 9.73)
Esophageal disorders	6.90 (4.58, 9.07)
Circulatory signs and symptoms	6.65 (5.18, 8.01)
Abdominal pain	5.73 (3.70, 7.62)
Muscle disorders	5.73 (4.60, 6.74)
Anxiety and fear–related disorders	5.42 (3.42, 7.29)
Arthralgia and arthritis	5.16 (3.18, 7.01)
Nervous system disorders	4.85 (3.65, 5.93)
Anemia	4.79 (3.53, 5.93)
Lower respiratory disease	4.67 (3.96, 5.28)
Chronic obstructive pulmonary disease	4.44 (3.16, 5.59)
Genitourinary signs and symptoms	4.39 (2.98, 5.68)
Coronary atherosclerosis and other heart disease	4.38 (2.96, 5.67)
Headache	4.10 (2.49, 5.58)
Heart failure	3.94 (2.97, 4.80)
Gastrointestinal disorders	3.58 (2.15, 4.88)
Respiratory failure; insufficiency; arrest	3.37 (2.71, 3.92)
Neurocognitive disorders	3.17 (2.24, 3.98)
Acute phlebitis; thrombophlebitis; thromboembolism	3.05 (2.51, 3.49)
Urinary tract infections	2.99 (1.94, 3.93)
Dysphagia	2.83 (1.79, 3.76)
Asthma	2.82 (1.92, 3.61)
Acute pulmonary embolism	2.63 (2.25, 2.92)
Bacterial infections	2.38 (1.52, 3.13)
Pressure ulcer of skin	2.05 (1.40, 2.59)
Pleurisy, pleural effusion	1.52 (0.95, 1.98)

b

Bronchodilators, sympathomimetic, inhalation	22.23 (20.68, 23.67)
Non–opioid analgesics	19.97 (17.41, 22.40)
Anticoagulants	16.43 (14.85, 17.89)
Non–opioid–containing antitussives/expectorants	12.83 (11.61, 13.95)
Antilipemic agents	11.56 (8.73, 14.19)
NSAIDs	10.94 (8.04, 13.67)
Beta blockers	9.74 (8.06, 11.27)
Anti–inflammatory, topical	9.63 (6.74, 12.37)
Opioid analgesics	9.39 (7.21, 11.43)
Laxatives	9.22 (6.99, 11.31)
Antiasthmatics	8.87 (7.65, 9.97)
Antidepressants	7.83 (5.19, 10.30)
Vitamin D	7.80 (5.36, 10.09)
Glucocorticoids	7.65 (5.67, 9.50)
Vitamin C	7.23 (6.45, 7.90)
Calcium channel blockers	7.18 (5.61, 8.61)
Anti–inflammatories, nasal	6.33 (4.57, 7.96)
Anticonvulsants	5.78 (3.68, 7.72)
Oral hypoglycemic agents	5.39 (3.99, 6.64)
Antifungal, topical	5.10 (3.37, 6.69)
Insulin	4.95 (3.87, 5.90)
Zinc	4.90 (4.39, 5.32)
Penicillins	4.87 (3.15, 6.44)
Histamine antagonists	4.83 (3.63, 5.91)
Skeletal muscle relaxants	4.78 (2.62, 6.79)
Loop diuretics	4.72 (3.59, 5.72)
Nasal and throat, topical	4.13 (3.09, 5.05)
Potassium	3.72 (2.35, 4.96)
Iron	3.57 (2.46, 4.56)
Magnesium	3.36 (2.27, 4.32)
Antiemetics	3.07 (1.66, 4.36)
Cyanocobalamin	2.98 (1.69, 4.14)
Antidiarrheal agents	2.87 (1.70, 3.91)
Thiazides/related diuretics	2.52 (1.37, 3.54)
Vaccines	2.43 (1.43, 3.31)
Multivitamins	2.31 (1.40, 3.10)
Anti–inflammatories, inhalation	1.37 (0.80, 1.83)
Antiarrhythmics	1.28 (0.79, 1.67)
Magnesium containing antacids	1.07 (0.62, 1.42)

c

Hemoglobin lower than M: 14; F: 12 g/dL	31.03 (28.16, 33.76)
Hematocrit lower than M: 42; F: 37 %	30.73 (27.64, 33.67)
Hemoglobin A1C higher than 5.6%	10.66 (6.77, 14.35)
Triglycerides higher than 150 mg/dL	9.94 (6.61, 13.11)
Low density lipoprotein higher than 130 mg/dL	9.48 (7.02, 11.81)
Total cholesterol higher than 200 mg/dL	9.40 (6.63, 12.03)
Serum chloride higher than 107 mmol/L	9.21 (7.05, 11.24)
Total white blood cell count lower than 4.8 K/cmm	8.45 (6.47, 10.29)
Alanine aminotransferase higher than 40 U/L	7.62 (5.20, 9.90)
Serum albumin lower than 3.5 g/dL	6.44 (4.84, 7.92)
Prothrombin time lower than 11.5 sec	4.81 (3.88, 5.64)
Serum potassium lower than 3.5 mmol/L	4.44 (2.92, 5.85)
Platelet count higher than 400 K/cmm	3.05 (2.10, 3.88)
Prothrombin time higher than 14.7 sec	2.99 (2.00, 3.86)
International normalized ratio higher than 1.2 ratio	2.94 (1.96, 3.80)
Partial thromboplastin time higher than 36.5 SEC	2.66 (1.75, 3.46)
Serum sodium higher than 145 mmol/L	1.64 (0.97, 2.20)

Fig. 2 | Burden of post-acute sequalae of COVID-19 per 1000 persons at 6-month. (a) Incident diagnoses, (b) Incident medication use and (c) Incident laboratory abnormalities. All VHA users served as the referent category. Post-acute sequalae were ascertained from 30 days after infection until end of follow-up. Sequalae were selected based on hazard ratio larger than one, P value less than 6.57×10^{-5}. Excess burdens per 1000 COVID-19 patients at 6-months are presented. Within each domain, outcomes are ranked based on excess burden from high to low. Diagnoses are colored based on diagnosis group, medications are colored based on medication class, and laboratory abnormalities are colored based on higher or lower than normal range.

Key takeaway - There are continuing risks for aggravations / chronic conditions in anybody who has had Covid and even more so for anyone who has been to a hospital without ICU and high risks for those who went to an ICU, in older age groups.

19/n

Key takeaway - Data for younger people is not there in this study. Risks will be lesser for younger people in a non-linear way per my reading but some risks surely will be there nevertheless.

20/n

My purpose for sharing this data, like an earlier thread I shared was that doctors that you go to may or may not have read this. Covid is new for the world as much as the medical community.

21/n

It is in YOUR interest to share data like this with your doctor and ask for the best advice based for yourself or people you know to prevent whatever can be prevented.

22/n

For example, per this earlier thread I shared that a good question to ask your doc would be whether it is useful to do a D-dimer test after a month or even 2 months and what does the doc have to say about thinners if the level is high? https://t.co/puY0RaUDi5
23/n

> A thread on possible clotting risks, elevated D-Dimer and Long Covid.
> Disclaimer - this is not medical advice. In health matters speak to a doc. You do have a right to ask your doc though on things you read about, it is your health after all
> 1/n
>
> — CapOrbit (@CapOrbit) April 3, 2021

If you find this useful, do a good deed and share it with others. I have heard of enough preventable cases related to blood clotting for example.

Watch out for yourself and take care. Prevention is better than cure was never so apt.

24/n