Post- COVID – Herausforderungen für die Versicherungswirtschaft -

Fachtagung Personenschaden 2022

Achim Regenauer

August 31, 2022

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PartnerRe

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1. Folien in Englisch

2. Kein Fachchinesisch

3. Keine "Folienschlacht"

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OP-ED

Second Opinion :: BIG IDEAS ON GLOBAL CHALLENGES

Inside

Thresho

Karen Rawder

Many 'lon
fully work

**Respondents to gl
systems after infec

● **Coronavirus - la
● **See all our coron

Natalie Grover
and **Ian Sample**

Tue 5 Jan 2021
06.00 GMT

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We're starting to understand long COVID. Next we can fight it

What is the root cause of these lingering symptoms?

By Eric J. Topol

AMI KORN, 14, has suffered from brain fog and memory trouble because of long COVID. Equine therapy has helped the Tarzana teen to raise his spirits and structure his time.

W e've been chasing the coronavirus since the pandemic began with vaccines and drugs, never getting ahead of it. In fact, well into its third year, COVID-19 is still causing often disabling symptoms among many people who were infected in early 2020.

The condition of long COVID, also known as post-acute sequelae of SARS CoV-2 infection, is rife with mysteries. While its incidence among adults who have been infected has been estimated at 5% to 40%, a recent study that tracked symptoms before infections and compared participants to controls has given us one of the best snapshots to date. It indicated that 1 in 8 people who have had COVID experience prolonged symptoms over many months.

With vaccinations and different variants, the incidence may be lower, but even if it were half as many (6% of adults who have been infected), and we assume two-thirds of adults have had COVID, that would equate to more than 10 million Americans who have endured persistent symptoms that interfere with their daily life activities, frequently impairing their ability to return to work.

One of the mysteries: As opposed to those most likely to get severe COVID, the vast majority of people affected by long COVID are younger (30 to 50 years old) and previously healthy. The typical symptoms include marked fatigue, exercise intolerance, difficulty breathing, brain fog, muscle pain and weakness, chest pain, headaches and fast heart rate. While the list of troubling symptoms is long, the number of proven therapies is very short — zero.

The first step for identifying candidate therapies is to demystify the biology of long COVID. A better understanding of its basis has come from recent studies that zoom in on an immune response that has gone haywire. That can include antibodies attacking the body's own proteins; persistent antibodies to the virus' spike protein, indicating a reservoir of infection triggering a response; exhausted T-cells; and markers of reactivation of prior virus infections in the herpes virus family (Epstein-Barr and varicella-zoster).

A combined team from Yale and Mount Sinai used artificial intelligence to determine what, of so many factors, may be of central importance in determining whether a COVID patient develops lingering symptoms. There was a singular driver — low cortisol in the blood —

a particularly intriguing finding.

This hormone, produced by the adrenal gland in response to stress, has diverse functions. When it is below healthy levels, as has also been found in chronic fatigue syndrome, it could be tied to some of the symptoms of long COVID. Normally a dip in cortisol would trigger the brain to tell the pituitary gland to increase its output of adrenocorticotropic hormone. However, in the new report, ACTH levels were quite low, indicating that the problem is not at the adrenal gland, but localized to the brain. Perhaps that helps explain why preliminary studies of giving steroids to people with long COVID have not shown any benefit. The steroids have

aimed to address symptoms in the body instead of root causes in the brain.

Some people with long COVID have a marked increase in heart rate and lightheadedness (and near fainting) when standing from a reclining position. This is thought to stem from dysfunction of the autonomic nervous system and raises the possibility that inflammation of the nervous system, in or outside the brain, might be a unifying underpinning of long COVID.

While these studies have helped illuminate potential biomarkers, we still do not have one that has been validated in large numbers of people with long COVID, which is

essential to provide an objective measure. Large studies will also be needed to determine effectiveness of treatments inspired by these findings.

We are very late in the process of doing randomized clinical trials to find a treatment that relieves symptoms or provides full resolution. There are more than 25 trials that have been launched with many different types of drugs or supplements, but all of them are quite small. The trials have generally not been partitioned by the cluster of patient symptoms, such as those with lightheadedness or people who are predominantly suffering from difficulty breathing and brain fog. With so many mil-

lions of people impaired, the need for accelerating clinical trials with promising immune-system modulating or virus-inactivating agents is beyond urgent.

The "long" in long COVID has not been emphasized enough. A new report from more than 125 million people with COVID showed an increased risk of developing brain fog, dementia, seizures and psychosis over two years. Similarly, follow-up at one year or longer has shown an increased risk of heart and blood vessel diseases, diabetes, clotting disorders, and lung and kidney damage, even among people who had only mild to moderate COVID and were not hospitalized. Such risk appears to be cumulatively increased with reinfections, including infections that break through vaccinations.

While we await a validated biomarker and effective treatments, what can we do about long COVID? First off, we can drop the skepticism and denial. Long COVID is real, and it takes a real toll. In the latest study, which followed patients and controls for an average of 400 days, there is a very close tracking of self-reported symptoms with objective markers — in fact 94%.

The recent relaxation of mitigation measures by the Centers for Disease Control and Prevention is premature, at a time when COVID hospitalizations are at a plateau for adults at more than 40,000, four times what they were in April, and still rising for children. Fortunately, children are at very low risk for long COVID, but the rare cases are linked with a doubling of some serious sequelae such as cardiovascular events.

For all ages, vaccination and booster rates in the U.S. are very low, even though it has been shown that vaccination helps minimize the chance of developing long COVID. Right now, our best chance to prevent long COVID is to not get COVID or to avoid getting it again. That's why it's vital to stay COVID-cautious now, and not capitulate to the notion that we should "live with COVID."

Too many people are indeed living with chronic COVID, detracting from their daily lives. As we eventually emerge from this pandemic, long COVID will be the enduring, major public health complication that we failed to address in a timely and aggressive manner. It's not too late to invest in understanding and combating it.

ERIC J. TOPOL is a professor of molecular medicine at Scripps Research and author of the newsletter Ground Truths.

Haul'

t linger for months

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The bias beneath drug dev

Questions, questions and no answers yet?

- What is Long COVID?

- Who is at risk?

- Causes of Long COVID?

- Comparison to other infections?

- What`s about fatigue?

- What about organic diseases?

- Return to work?

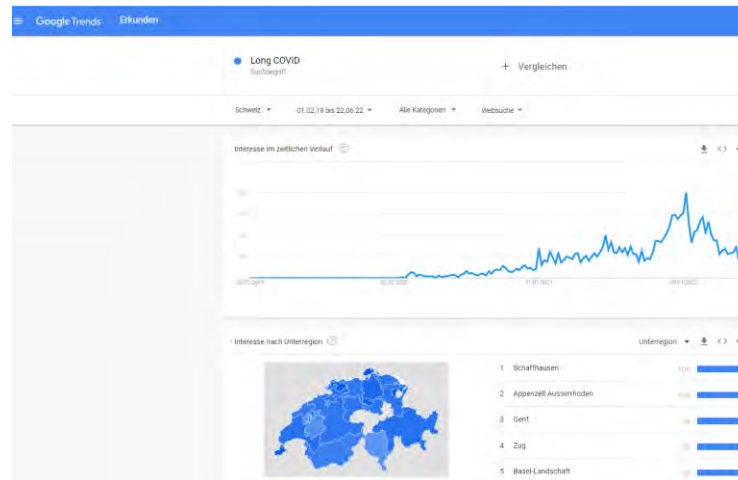- Treatment of Long COVID?

- State-of-the art of rehabilitation?

Despite vaccinations Long COVID is increasing

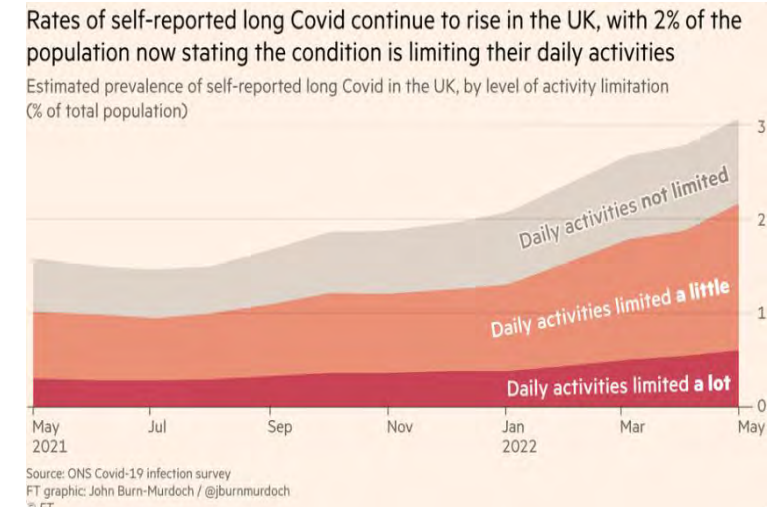## Social media hyped?

Synonyms

- Chronic COVID syndrome;

- Late sequelae of COVID-19;

- Long COVID;

- Long haul COVID;

- Long-term COVID-19;

- Post COVID syndrome;

- Post-acute COVID-19

- Short-term and long-term persistent post-acute sequelae of COVID-19 (PASC)

Google Trend (Switzerland)

Long COVID – self reported in UK

Rates of self-reported long Covid continue to rise in the UK, with 2% of the population now stating the condition is limiting their daily activities

Estimated prevalence of self-reported long Covid in the UK, by level of activity limitation (% of total population)

Daily activities not limited

Daily activities limited a little

Daily activities limited a lot

May 2021 — Jul — Sep — Nov — Jan 2022 — Mar — May

Source: ONS Covid-19 infection survey
FT graphic: John Burn-Murdoch / @jburnmurdoch

Proposal of a definition by WHO International Classification of Diseases (ICD) – ICD-10 U09

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A clinical case definition of post COVID-19 condition by a Delphi consensus

6 October 2021

World Health Organization

- 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

- which generally have an **impact on everyday functioning**.

- Symptoms may be **new onset**, following initial recovery from an acute COVID19 episode, or persist from the initial illness.

- Symptoms may also **fluctuate or relapse over time**

Vulnerability to COVID-19

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Source: https://alama.org.uk/covid-19-medical-risk-assessment/

Current age

| 45 |

If below 20, enter 20. If over 75, enter 75.

Sex ⓘ
○ Female ● Male

Ethnic background ⓘ   **BMI Group**

| Black or Black British ▾ | | Calculate | Greater t ▾ |

Asthma†   **Diabetes**

| Mild Asthma ▾ | | Type 2 and other - Hb ▾ |

Chronic kidney disease   **Heart conditions**

| None ▾ | | None ▾ |

Cancer: blood related†   **Cancer: non-blood related†**

| None ▾ | | None ▾ |

Other conditions
- ☑ Other chronic respiratory disease
- ☐ Hypertension
- ☐ Cerebrovascular disease
- ☐ Liver disease
- ☐ Chronic neurological disease other than stroke or dementia†
- ☐ Organ transplant recipient
- ☐ Spleen diseases†
- ☐ Rheumatoid Arthritis, Lupus or Psoriasis
- ☐ Other immunosuppressive condition†

Your Covid-age:

45 + 57 = 85+

In the absence of vaccination or previous infection, the probability that infection would be fatal is estimated to lie between 0.04 per 1000 and 0.1 per 1000

For Covid-ages less than 20, the risk of fatality may be even lower than indicated

Group	Variable	Modifier	Information
Ethnicity	Black	7	
BMI	Greater than 40	16	
Asthma	Mild	1	
Diabetes	Type 2 and other HbA1c greater than 58 mmol/mol in past year	20	
Other	Other chronic respiratory disease	13	
	Total	**57**	

Information

Estimates of personal vulnerability from the Covid-age

Who suffers form Long COVID?

Unvaccinated and vaccinated – the more reinfections the likelier

Extent to which ability to undertake day-to-day activities is reduced

Not at all	420,000
A little	478,000
A lot	196,000

Age breakdown

Age	Value
2-11 years	15,000
12-16 years	28,000
17-24 years	90,000
25-34 years	159,000
35-49 years	317,000
50-69 years	391,000
≥70 years	94,000

Source: Office for National Statistics

Still under investigation

- ICU >> hospitalized >> mild or asymptomatic COVID-19
- Being of older age
- Women > men
- Pre-existing chronic diseases
- Multiple SARS-CoV-2 infections
- Being vaccinated

Source: https://www.statista.com/topics/6112/coronavirus-covid-19-in-the-uk/

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Understanding Long Covid – a medical challenge

Most plausible explanations
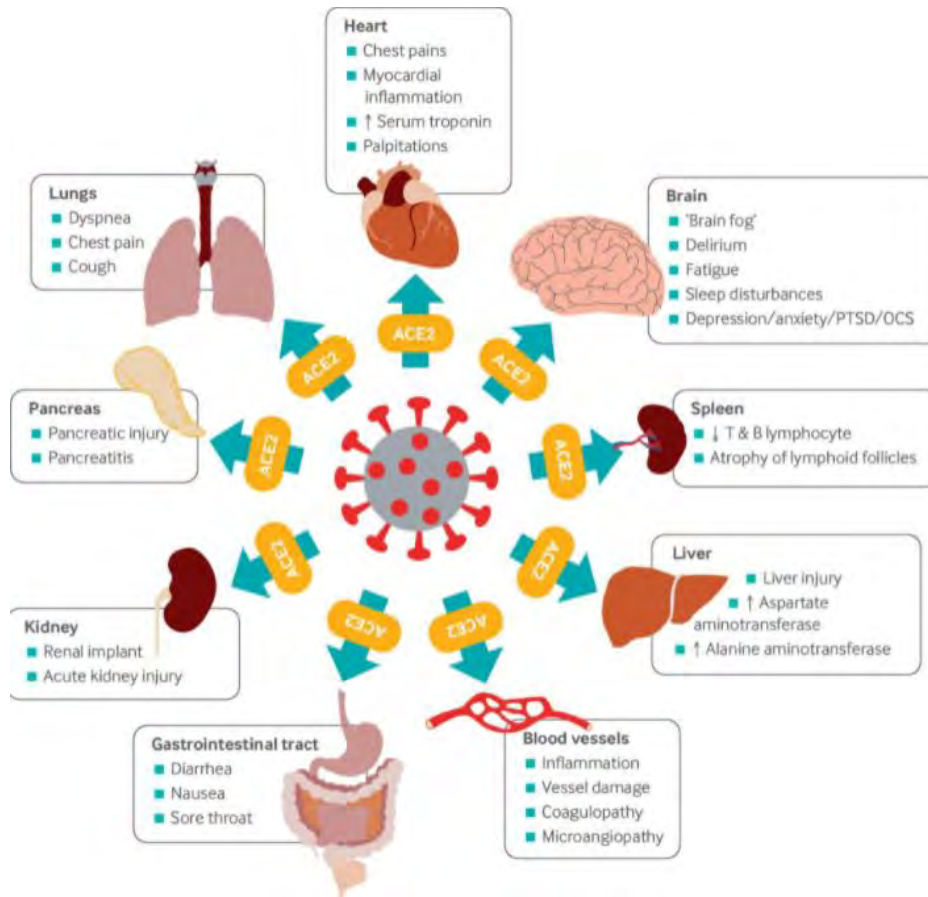
? **Persistent virus**, e.g. viral RNA in the stool, urine, blood plasma and autopsies

? Lingering tiny **blood clots**, e.g. lung, brain, vessels

? Haywire **immune system**; e.g. dozens of immune markers (exhausted T-cells, auto-antibodies)
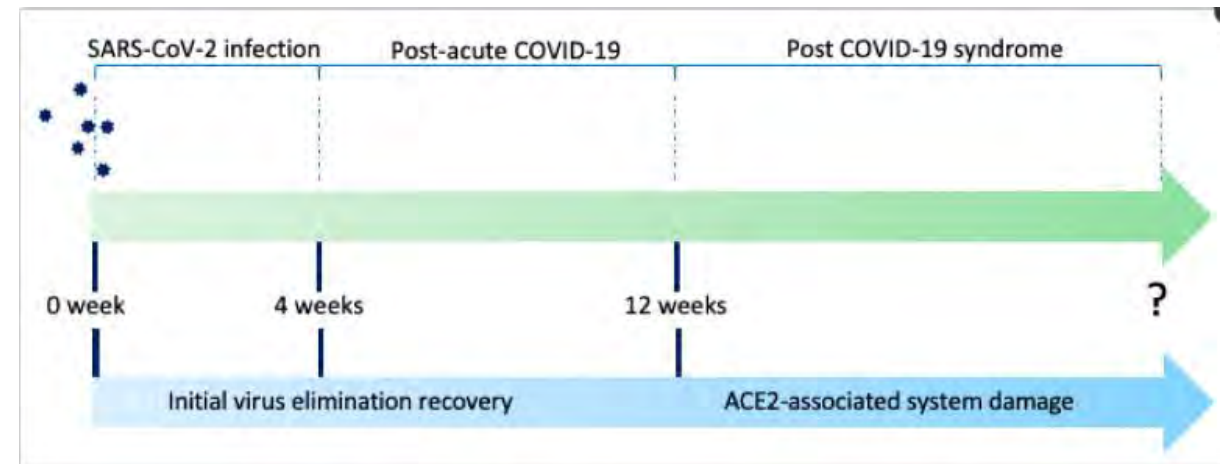
Source: *BMJ* 2021;374:n1648 and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8394513/

Persistence of somatic symptoms after COVID-19

- Multidisciplinary, **prospective**, Dutch population-based, observational cohort study

- Control-group: compared as to symptoms (severity) also prior SARS-CoV-2 infection!

- Pre-Omicron: btw. March 31, 2020 - Aug 2, 2021

- 24 repeated measurements (questionnaires)

- **Follow-up 90–150 days**

- **12.7% or 1 in 8 people**

- No assessment of neuropsychiatric symptoms!
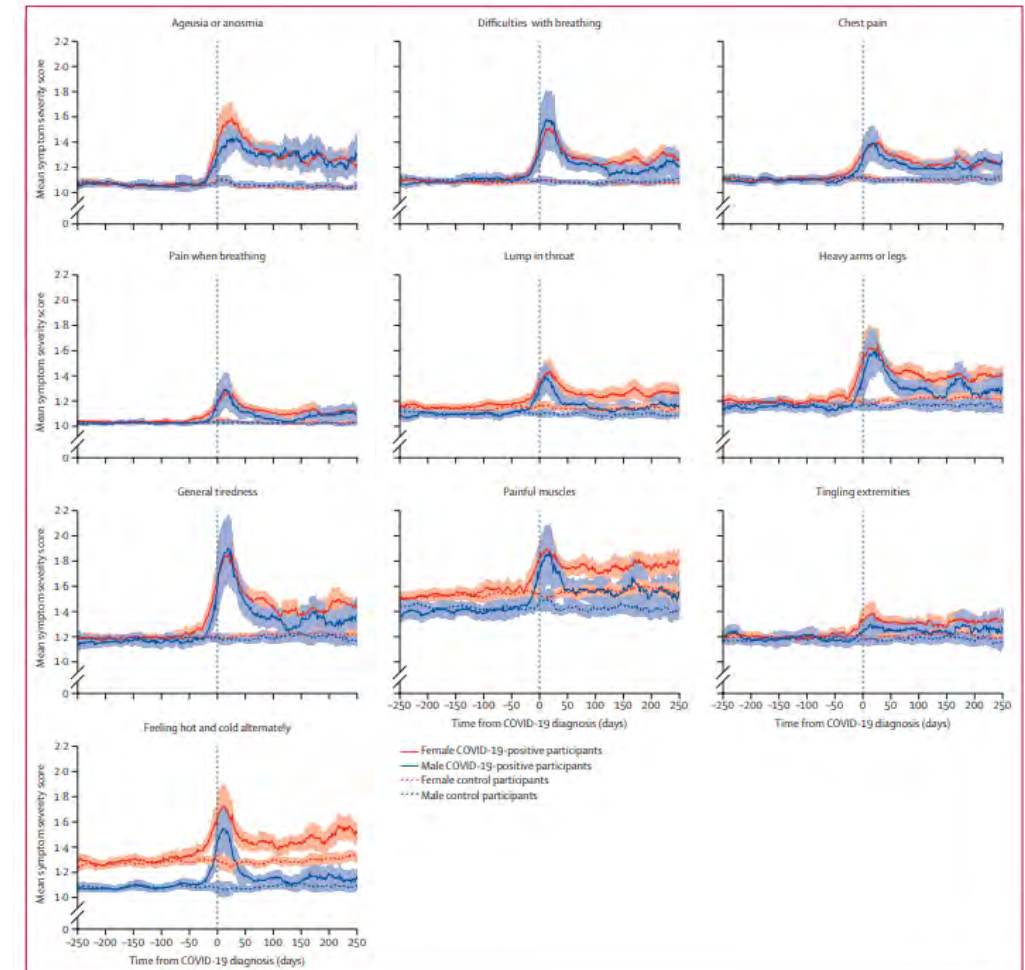
- ≥ 1 core symptom(s) (3-5 months):
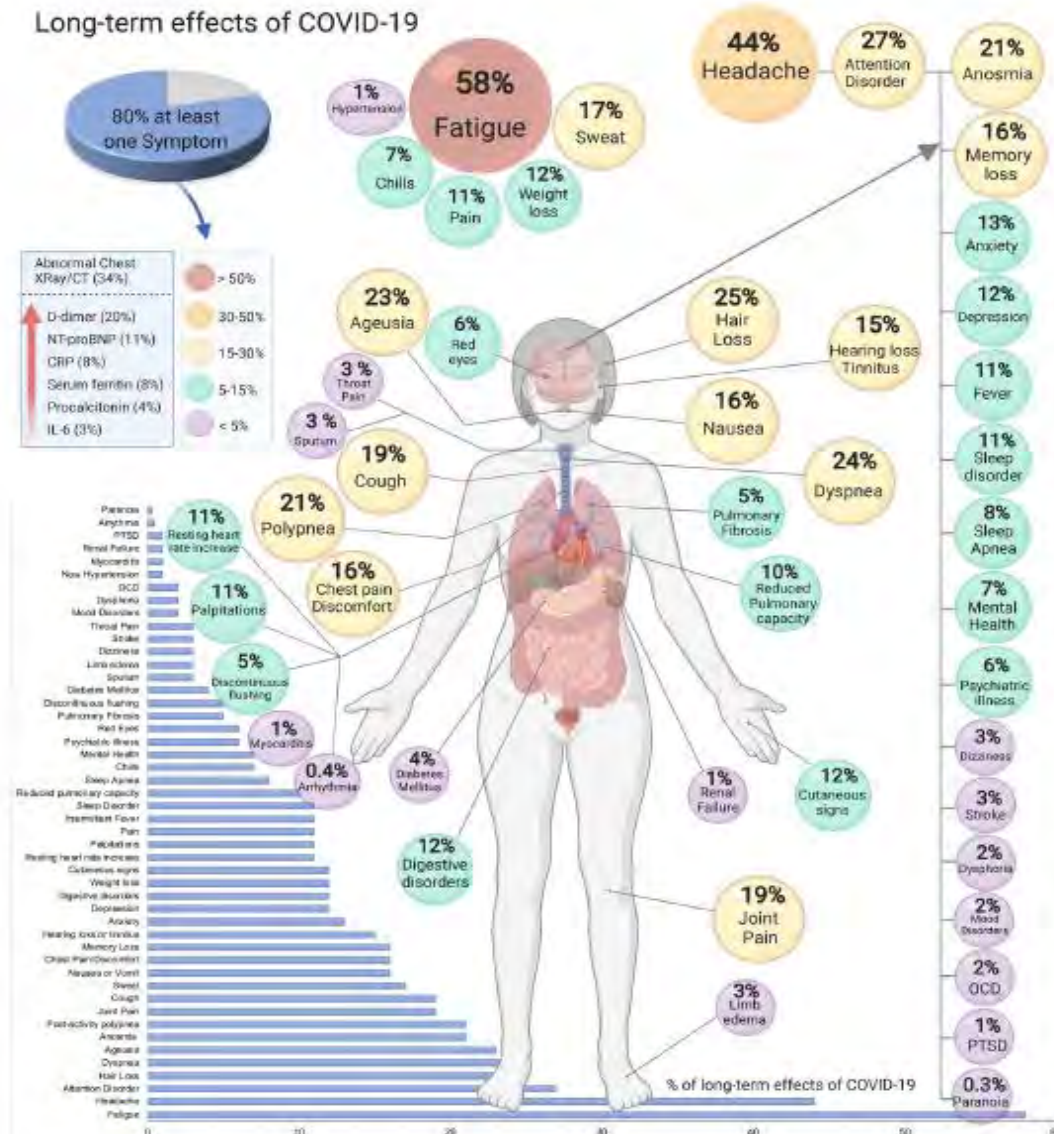 21.4% Covid group vs. 8.7% control group

Figure 2: Core symptoms

Source:https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01214-4/fulltext

Long COVID – a diagnostic chameleon!

> 200 various symptoms reported

Long-term effects of COVID-19

- **Many unspecific symptoms**
- Many subjective assessed
- Strong fluctuations
- **No routine lab, no routine imaging**
- Few organ specific

Source:: https://doi.org/10.1101/2021.01.27.21250617

Long COVID and evidence?

A clear dilemma: most limited and only small cohorts with short f-up

Table 1 | Findings from clinical studies on the prevalence of post-acute COVID-19 syndrome

	Carfi et al.[3]	Halpin et al.[24]	Carvalho-Schneider et al.	Chopra et al.[20]	Arnold et al.[22]	Moreno-Pérez et al.	Moreno-Pérez et al.	Garrigues et al.[26]	Huang et al.[5]
Site	Italy	United Kingdom	France	United States	United Kingdom	Spain	Spain	France	China
Number of participants	143	100	150	488	110	277	277	120	1,733
Follow-up Duration	2 months post-symptom onset	1-2 months post-discharge	2 months post-symptom onset	2 months post-discharge	3 months post-symptom onset	2-3 months post-COVID-19 onset	4 months post-COVID-19 onset	3-4 months post-admission	6 months post-symptom onset
Mode of follow-up evaluation	In person	Telephone survey	Telephone survey	Telephone survey	In person	In person	In person	Telephone survey	In person
Baseline characteristics									
Age (years)	Mean (s.d.) = 56.5 (14.6)	Median (ward/ICU) = 70.5/58.5	Mean (s.d.) = 45 (15)	NR	Median (IQR) = 60 (44-76)	Median (IQR) = 56 (42-67.5)	Median (IQR) = 56 (42-67.5)	Mean (s.d.) = 63.2 (15.7)	Median (IQR) = 57 (47-65)
Female (%)	37.1	46	56	NR	38.2	47.3	47.3	37.5	48
Acute COVID-19 features									
Oxygen therapy requirement (%)	53.8	78			75.4				75
Non-invasive ventilation (%)	14.7	30							6
Invasive ventilation (%)	4.9	1							1
ICU care (%)	12.6	32	0		16.4	8.7	8.7	20	4
Post-acute COVID-19									
≥1 symptom (%)	87.4		66	32.6	74	50.9			76
≥3 symptoms (%)	55.2								
General sequelae									
Fatigue (%)	53.1	64	40		39	34.8		55	63
Joint pain (%)	27.3		16.3		4.5	19.6			9
Muscular pain (%)						19.6			2
Fever (%)	0		0		0.9	0			0.1
Respiratory sequelae									
Dyspnea (%)	43.4	40	30	22.9	39	34.4	11.1	41.7	23
Cough (%)	~15			15.4	11.8	21.3	2.1	16.7	
Cardiovascular sequelae									
Chest pain (%)	21.7		13.1		12.7			10.8	5
Palpitations (%)			10.9						9
Neuropsychiatric sequelae									
Anxiety/depression (%)									23
Sleep disturbances (%)					24			30.8	26
PTSD (%)		31							
Loss of taste/smell (%)	~15		22.7	13.1	11.8	21.4		10.8-13.3	7-11
Headache (%)	~10				1.8	17.8	5.4		2
Gastrointestinal sequelae									
Diarrhea (%)					0.9	10.5			~5
Dermatologic sequelae									
Hair loss (%)								20	22
Skin rash (%)									3
Quality of life									
Scale	EuroQol visual analog scale	EQ-5D-5L			SF-36	EuroQol visual analog scale		EQ-5D-5L	EuroQol visual analog scale
Decline (percentage of patients reporting or yes/no)	44.1	Yes			Yes	Yes		Yes	Yes

IQR, interquartile range; NR, not reported; s.d., standard deviation; SF-36, 36-Item Short Form Survey.

Partner Re Research Database with published Long COVID studies

- Date
- Organ
- Country
- Sample
- Patient group
- Age, gender
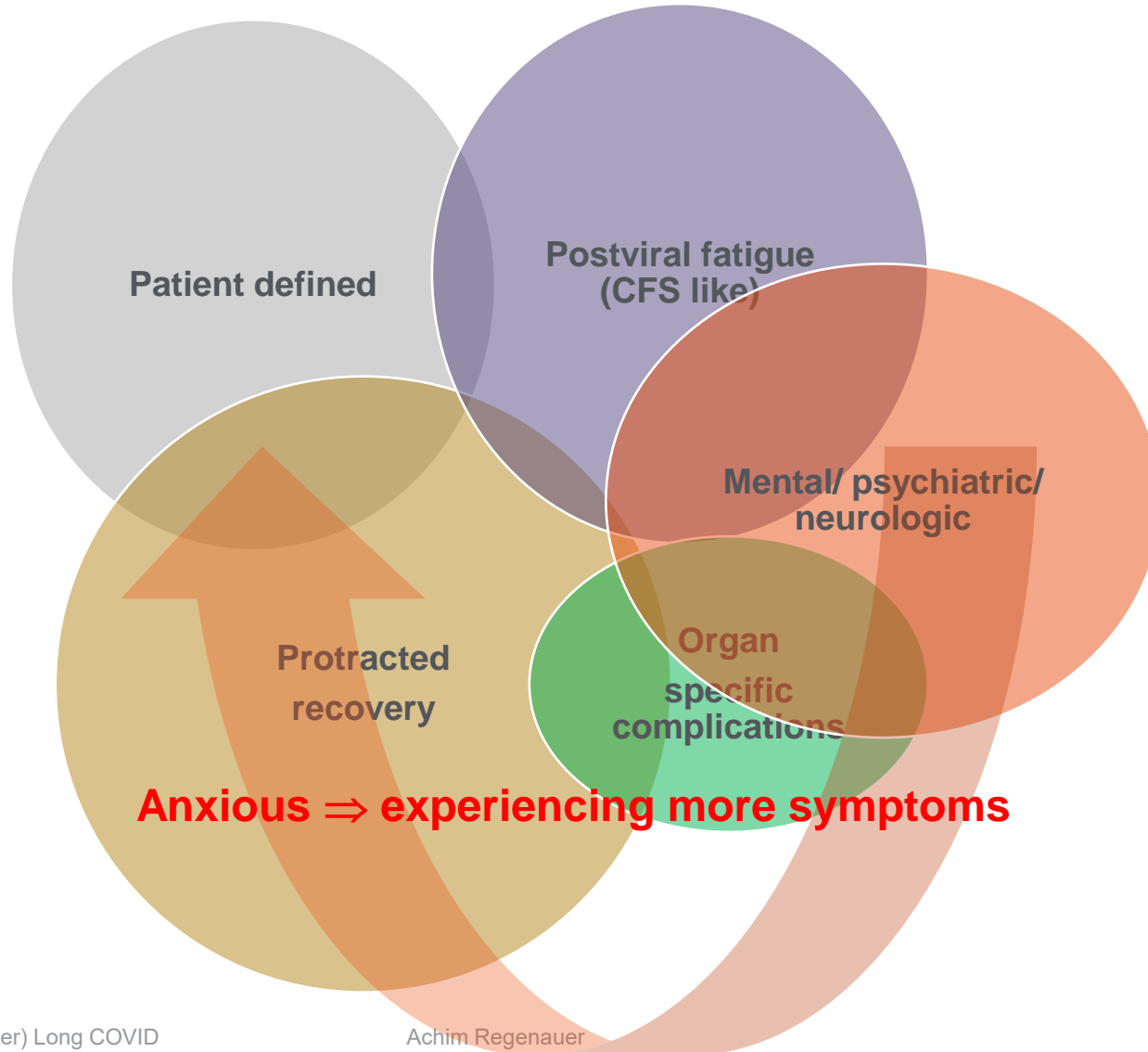- Preexisting diseases
- Follow-up
- Proportion of COVID severities

Long COVID or several Long COVIDs?

Synopsis of many studies (own hypothesis)

Patient defined

Postviral fatigue (CFS like)

Mental/ psychiatric/ neurologic

Protracted recovery

Organ specific complications

Anxious ⇒ experiencing more symptoms

Main features of Long-COVID

No clear biochemical or imaging features exist to aid diagnosis

Chronic fatigue syndrome Symptoms/Signs	Disease/Organ	Product
Extreme fatigue	Post viral-fatigue ? CFS	DI
Muscle weakness	Post viral-fatigue ?	
Low grade fever	Post viral-fatigue ?	
Joint pain	Joints	DI

Protracted recovery Symptoms/Signs	Disease/Organ	Product
Sleep difficulties	Post viral-fatigue ?	
Headaches	Brain affection? Post viral-fatigue ?	

Patient reported Symptoms/Signs	Disease/Organ	Product
	any	
XYZ	any	

Organ specific Symptoms/Signs	Disease/Organ	Product
Renal function tests	Kidney dysfunction	Life, CI, DI
Liver function rests	Liver dysfunction	Life, CI, DI
New onset of diabetes	Diabetes	
New onset of hypertension	Hypertension	Life, CI, DI
Shortness of breath,cough	Lung affection → lung fibrosis?	Life, CI, DI
Chest pains, palpitations	Heart affection, Cardiomyopathy, Chronic heart failure	Life, CI, DI

Mental/Neuro/Psych Symptoms/Signs	Disease/Organ	Product
Cognitive dysfunctions	Brain affection? "Brain fog" → Dementia	DI, LTC
Changes in mood	Brain affection?	DI

Unspecific symptoms fluctuate within hours or days

Specific symptoms or signs with objective metrics

Understanding (better) Long COVID   Achim Regenauer   August 31, 2022

Long COVID: here fatigue

Patient defined

Postviral fatigue
(CFS like)

Mental/ psychiatric/
neurologic

Protracted
recovery

Organ
specific
complications
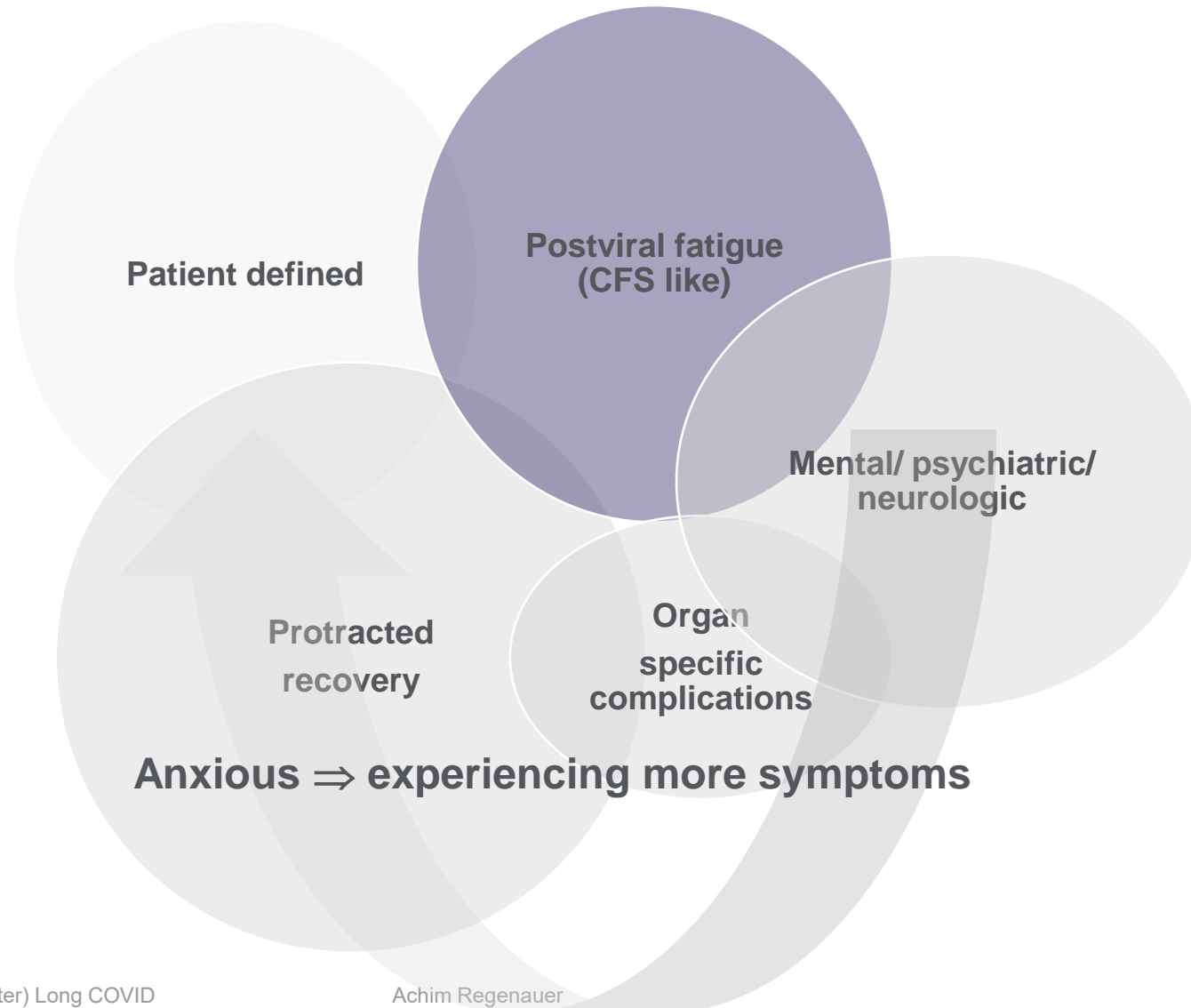
Anxious ⇒ experiencing more symptoms

Acute infectious diseases self-limiting events: resolution of symptoms or death ?
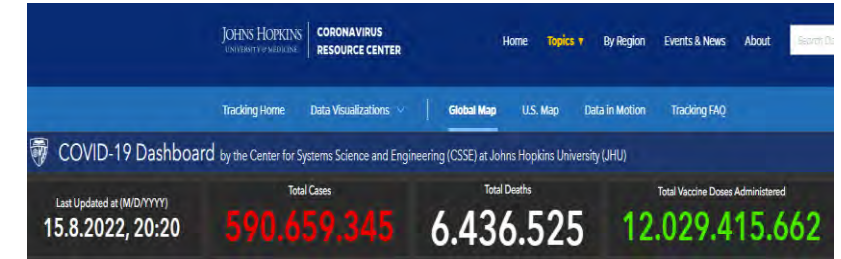
Historical perspective

Throughout recorded history, there have been at least 15 large pandemic events with at least 100,000 deaths.

Event	Start	End	Deaths
Black Death	1331	1353	75,000,000
Italian Plague	1623	1632	280,000
Great Plague of Seville	1647	1652	2,000,000
Great Plague of London	1665	1666	100,000
Great Plague of Marseille	1720	1722	100,000
First Cholera Pandemic	1816	1826	100,000
Second Cholera Pandemic	1829	1851	100,000
Russia Cholera Pandemic	1852	1860	1,000,000
Global Flu Pandemic	1889	1890	1,000,000
Sixth Cholera Pandemic	1899	1923	800,000
Encephalitis Lethargica Pandemic	1915	1926	1,500,000
Spanish Flu	1918	1920	100,000,000
Asian Flu	1957	1958	2,000,000
Hong Kong Flu	1968	1969	1,000,000
H1N1 Pandemic	2009	2010	203,000

Sources: Alfani and Murphy (2017); Taleb and Cirillo (2020); and https://en.wikipedia.org/wiki/List_of_epidemics and references therein.

Source: Wikipedia

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Home Topics ▾ By Region Events & News About
Tracking Home Data Visualizations ▾ Global Map U.S. Map Data in Motion Tracking FAQ
COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)
Last Updated at (M/D/YYYY) 15.8.2022, 20:20
Total Cases 590.659.345
Total Deaths 6.436.525
Total Vaccine Doses Administered 12.029.415.662

Other **post-pandemic syndromes**:

1. Influenza **1892**: Neurasthenia, "grippe catalepsy"
   https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32134-6/fulltext

2. Influenza **1918**: «Encephalitis lethargica" ⟹ Parkinsonism https://pubmed.ncbi.nlm.nih.gov/18569452/

3. SARS-Co-V-1 **2003**: 10-20% still had chronic fatigue syndrome 12 years after
   https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/415378 and https://www.nature.com/articles/s41591-022-01810-6.pdf

Unexplained post-acute infection syndromes (PAIS)

What we know from non-SARS-CoV-2 infection

PAISs associated with infections

Pathogen	Name of PAIS
Viral pathogens	
SARS-CoV-2	Post-acute sequelae of SARS-CoV-2 infection (PASC) / Post-acute COVID-19 syndrome (PACS) / Long COVID
Ebola	Post-Ebola syndrome (PES) / Post-Ebola virus disease syndrome (PEVDS)
Dengue	Post-dengue fatigue syndrome (PDFS)
Polio	Post-polio syndrome (PPS)
SARS	Post-SARS syndrome (PSS)
Chikungunya	Post-chikungunya chronic inflammatory rheumatism (pCHIK-CIR) / Post-chikungunya disease
EBV	No name
West Nile virus	No name
Ross River virus[a]	No name
Coxsackie B[a]	No name
H1N1/09 influenza[a,b]	No name
VZV[a,b]	No name
Non-viral pathogens	
Coxiella burnetii	Q fever fatigue syndrome (QFS)
Borrelia[c]	Post-treatment Lyme disease syndrome (PTLDS)
Giardia lamblia[a,d]	No name

[a]Limited or very limited evidence base. [b]Association with increased use of ME/CFS diagnosis in health registry. [c]Contradicting or unclear evidence base. [d]Supporting evidence derives from a single outbreak in Norway.

Common features

- - 75% of ME/CFS cases infection-like episode preceding the onset

- Complex clinical **neurological** + **immunological** symptoms together with chronic fatigue

- **Un-/misdiagnosed**, disbelieved

- **Core symptoms**: lingering debilitating fatigue, post-exertional malaise, cognitive dysfunction

⇒ No diagnostic laboratory test – how to **objectify**?

- Unknown **therapy/prevention**

- **Prolonged** illness up to 15–40 yrs (**Post-polio**)

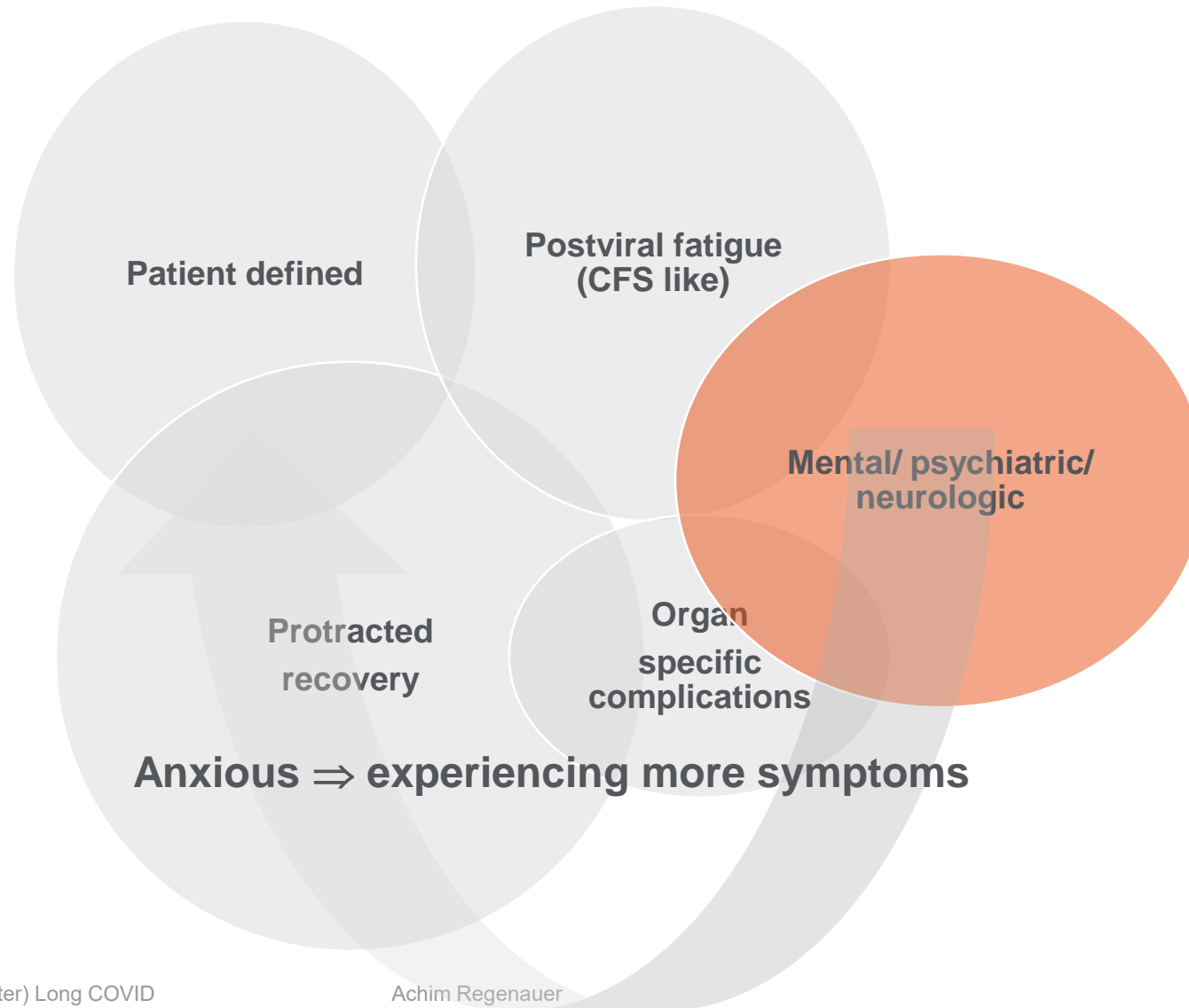- Shortage of prospective, well-powered **studies** with long-term follow-up examinations

Follow-up s after infectious mononucleosis
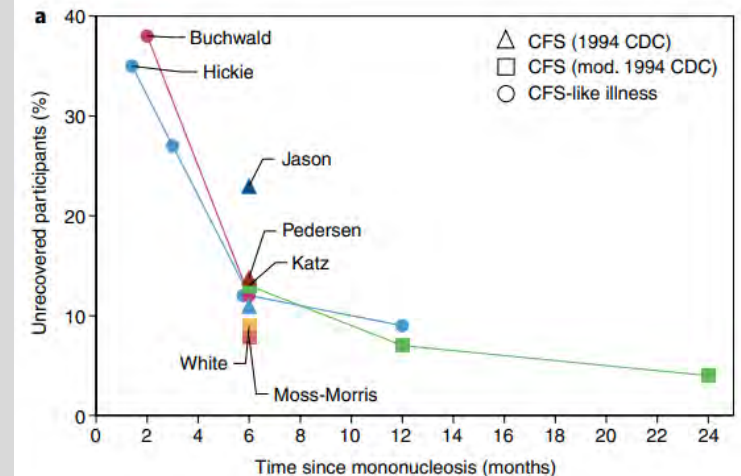
Source: Nature Medicine | VOL 28 | May 2022 | 911–923

Long COVID : here CNS

Patient defined

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Protracted
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Organ
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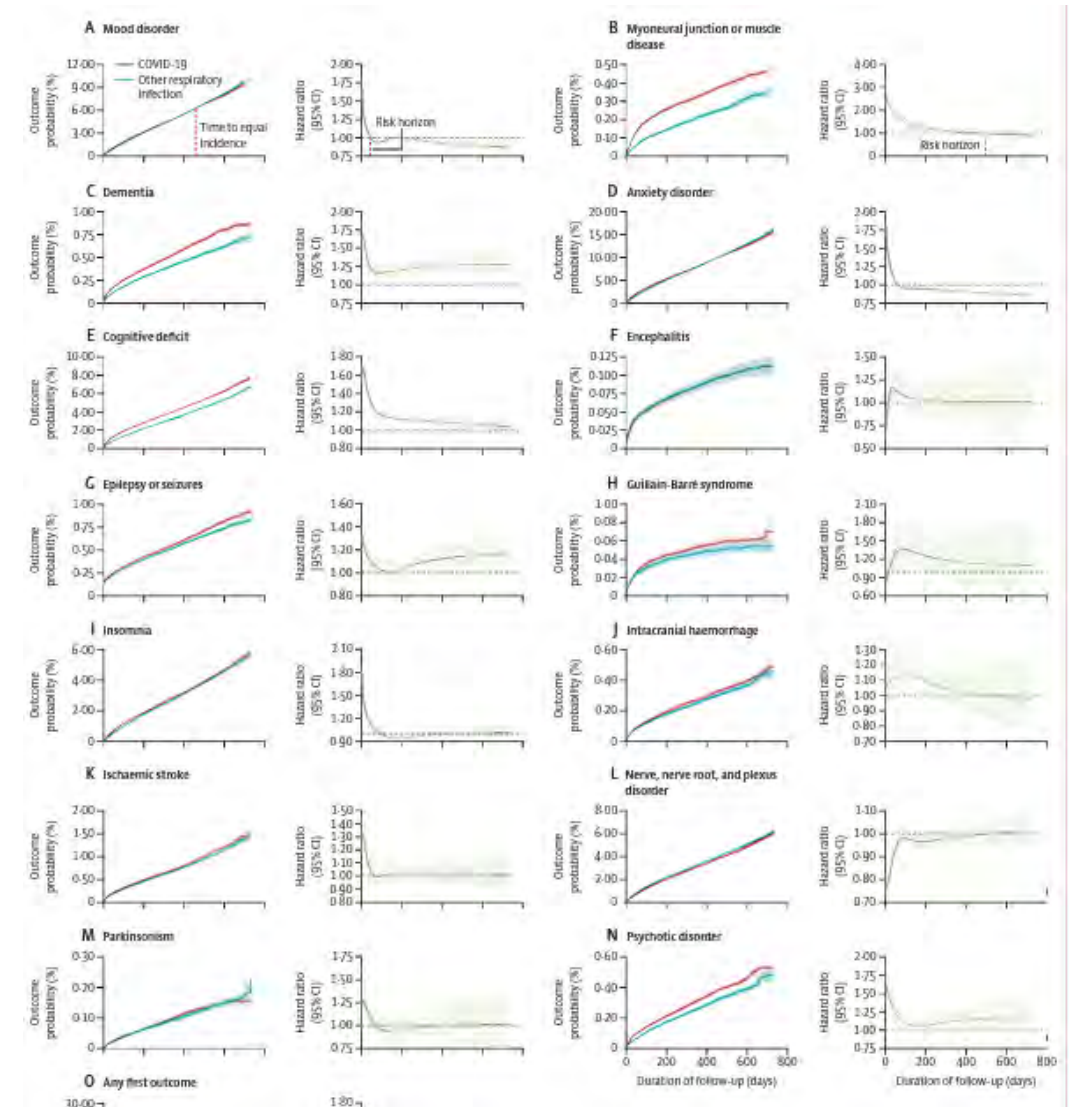complications

Anxious ⇒ experiencing more symptoms

Mental & neuropsychiatric symptoms 2 years after

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Most recent study with the longest follow-up

Study design:

- Analysis EHRs of 89 million patients

- USA mostly, but also Australia, the UK, Spain, Bulgaria, India, Malaysia, Taiwan

- Compilation of a **2-year retrospective** cohort studies matched
  - with patients with any other respiratory infection
  - Various cohort along 3 waves (alpha, delta, omicron variants)

- n = **1.25 million COVID-19** patients (∅ age 42.5) vs. cohort of patients with any **other respiratory infection**

- Jan 20, 2020 to April 13, 2022

- Investigation of 14 different neurological and psychiatric sequelae of COVID-19

Source: https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(22)00260-7/fulltext

Mental & neuropsychiatric symptoms 2 years after

Most recent study with the longest follow-up

- **Neuropsychiatric**: cognitive deficits, dementia, psychotic disorders, epilepsies remained elevated
  - part. ages 65+ years

- **Mental**: mood and anxiety disorders subsided after 1 to pre-pandemic levels (9.5% vs. 8.9%)
- Excess risk dropped within 2-3 months
- No overall excess over the 2 years

- Neuropsychiatric outcomes similar during **delta** and **omicron** outcomes (> alpha)
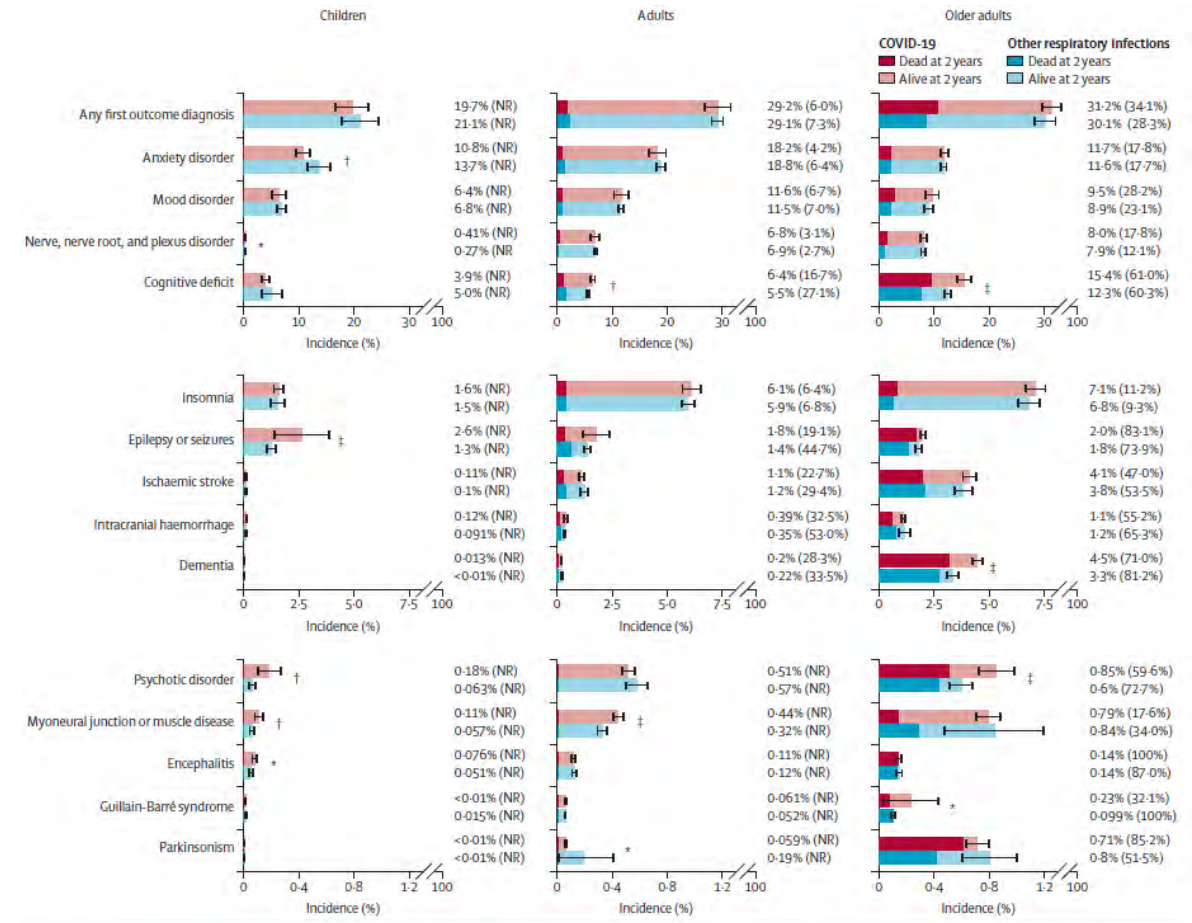
No tsunami on the horizon

Source: https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(22)00260-7/fulltext

Long COVID: here how often? How long?

Selection of some studies

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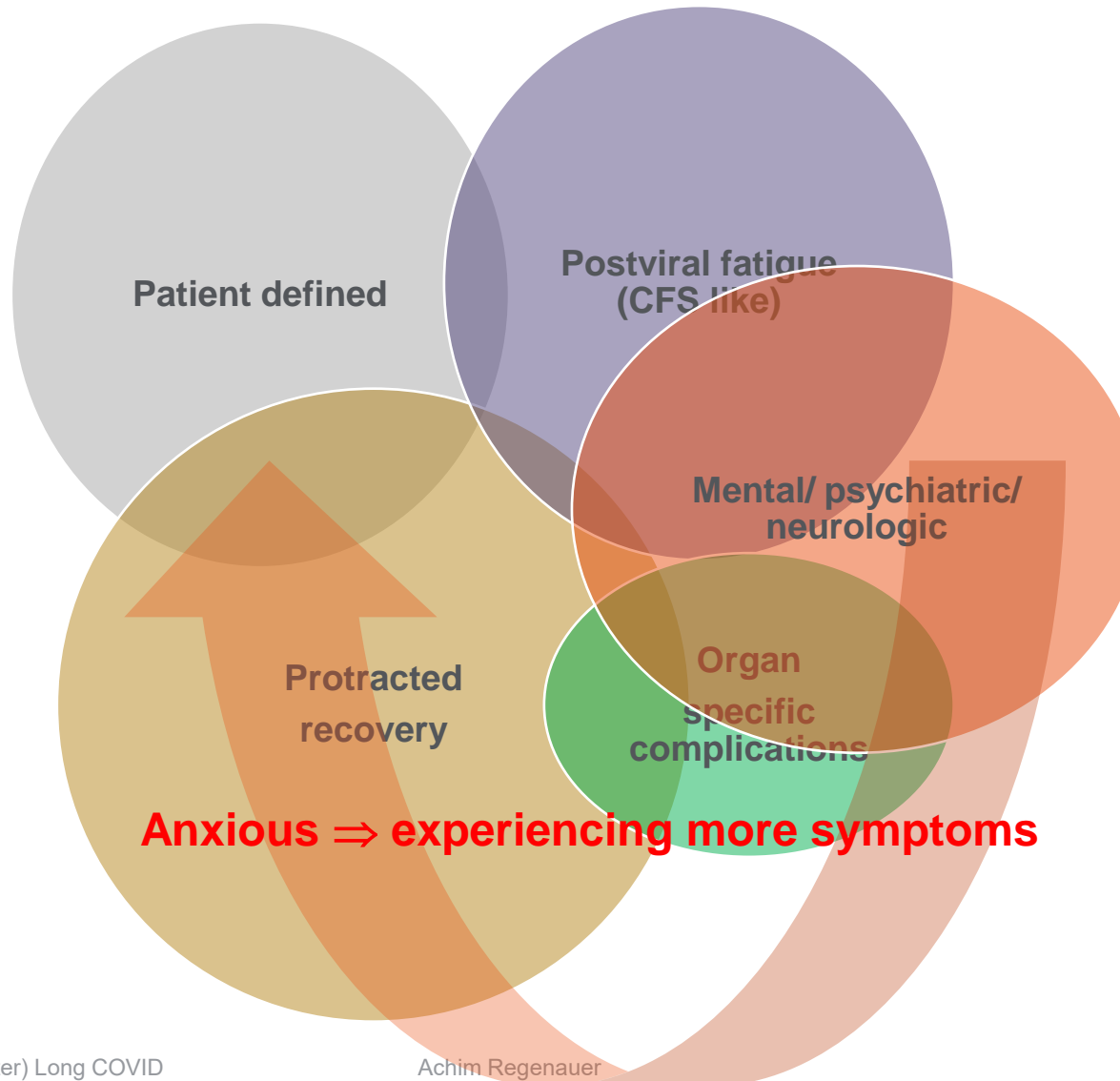
First "long" trial: for some, it may take years, not months

Study features

- Longitudinal cohort of **hospitalised** adult survivors of COVID-19
  - 70% Oxygen
  - 4% ICU n=
- 1,276 single-center study from **Wuhan**
- Time: January-May 2020 ("first cases")
- Follow-up: 6 months + 12 months
- ∅ age **59 years**
- Questionnaires on symptoms and examinations (subgroup)

6 months after - primary outcomes symptoms		
68%	≥ 1 symptom	Fatigue > muscle weakness > sleep…
30%	Dyspnea	Assessed by mMRC (Modified Medical Research Council)
23%	Anxiety or depression	questionnaires on health-related quality of life

12 months after - primary outcomes symptoms		
49%	≥ 1 symptom	Fatigue > muscle weakness > sleep…
26%	Dyspnea	Assessed by mMRC (Modified Medical Research Council)
26%	Anxiety or depression	questionnaires on health-related quality of life
12%	not yet returned to original work	

Secondary outcomes : Lung function + chest CT pattern

PartnerRe

	Scale 3: not requiring supplemental oxygen			Scale 4: requiring supplemental oxygen			Scale 5–6: requiring HFNC, NIV, or IMV		
	6 month	12 month	p value	6 month	12 month	p value	6 month	12 month	p value
Lung function									
Number of patients	59	56	..	125	118	..	70	70	..
FEV$_1$ <80%, % of predicted	4 (7%)	2 (4%)	0·32	2 (2%)	3 (3%)	0·56	10 (14%)	4 (6%)	0·014
FVC <80%, % of predicted	3 (5%)	2 (4%)	<0·0001	0 (0%)	2 (2%)	0·16	9 (13%)	6 (9%)	0·08
FEV$_1$/FVC <70%	5 (8%)	4 (7%)	0·32	11 (9%)	6 (5%)	0·10	2 (3%)	0 (0%)	0·16
TLC <80%, % of predicted	6/57 (11%)	3 (5%)	0·18	12/124 (10%)	8/117 (7%)	0·65	27/69 (39%)	20 (29%)	0·021
FRC <80%, % of predicted	4/57 (7%)	6 (11%)	0·32	5/124 (4%)	5/116 (4%)	1·00	14/67 (21%)	16 (23%)	1·00
RV <80%, % of predicted	12/57 (21%)	15 (27%)	1·00	18/124 (15%)	26/117 (22%)	0·050	34/69 (49%)	44 (63%)	0·11
DLCO <80%, % of predicted*	12/57 (21%)	13 (23%)	0·53	32/124 (26%)	36/117 (31%)	0·13	39/69 (57%)	38 (54%)	0·53
Chest CT									
Number of patients	33	28	..	56	52	..	39	38	..
At least one abnormal CT pattern	33 (100%)	11 (39%)	<0·0001	56 (100%)	21 (40%)	<0·0001	39 (100%)	33 (87%)	0·025
GGO	28 (85%)	11 (39%)	0·0047	52 (93%)	14 (27%)	<0·0001	32 (82%)	29 (76%)	0·56
Irregular lines	6 (18%)	6 (21%)	1·00	13 (23%)	12 (23%)	1·00	18 (46%)	23 (61%)	0·22
Subpleural line	5 (15%)	1 (4%)	0·10	1 (2%)	2 (4%)	0·56	3 (8%)	8 (21%)	0·06
Interlobular septal thickening	1 (3%)	0 (0%)	0·32	2 (4%)	1 (2%)	0·56	0 (0%)	4 (11%)	0·046
Reticular pattern	0 (0%)	0 (0%)	NA	0 (0%)	1 (2%)	0·32	1 (3%)	3 (8%)	0·16
Consolidation	0 (0%)	0 (0%)	NA	4 (7%)	0 (0%)	0·08	0 (0%)	1 (3%)	0·32

Data are absolute values, n (%), or n/N (%) when data are missing. HFNC=high-flow nasal cannula for oxygen therapy. NIV=non-invasive ventilation. IMV=invasive mechanical ventilation. FEV$_1$=forced expiratory volume in 1 s. FVC=forced vital capacity. TLC=total lung capacity. FRC=functional residual capacity. RV=residual volume. DLCO=diffusion capacity for carbon monoxide. GGO=ground glass opacity. NA=not applicable. *Carbon monoxide diffusion capacity was not corrected for haemoglobin.

Table 3: Lung function and chest CT among COVID-19 patients at 6-month and 12-month follow-up according to severity scale

- 349 patients with pulmonary function test (stratified disproportional random sampling)
- Lung diffusion impairment w/o improvement?
  - 20–30% of moderately ill patients
  - > 54% in critically ill patients
- Lung structural abnormality associated with lung diffusion impairment

Patient defined

Postviral fatigue (CFS like)

Mental/ psychiatric/ neurologic

Protracted recovery

Organ specific complications

Anxious ⇒ experiencing more symptoms

g (better) Long COVID   Achim Regenauer
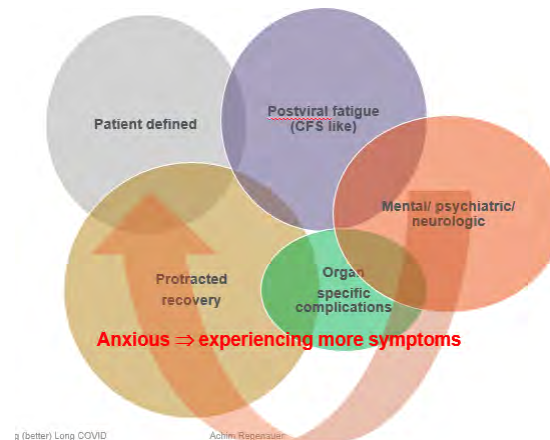
Source: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01755-4/fulltext
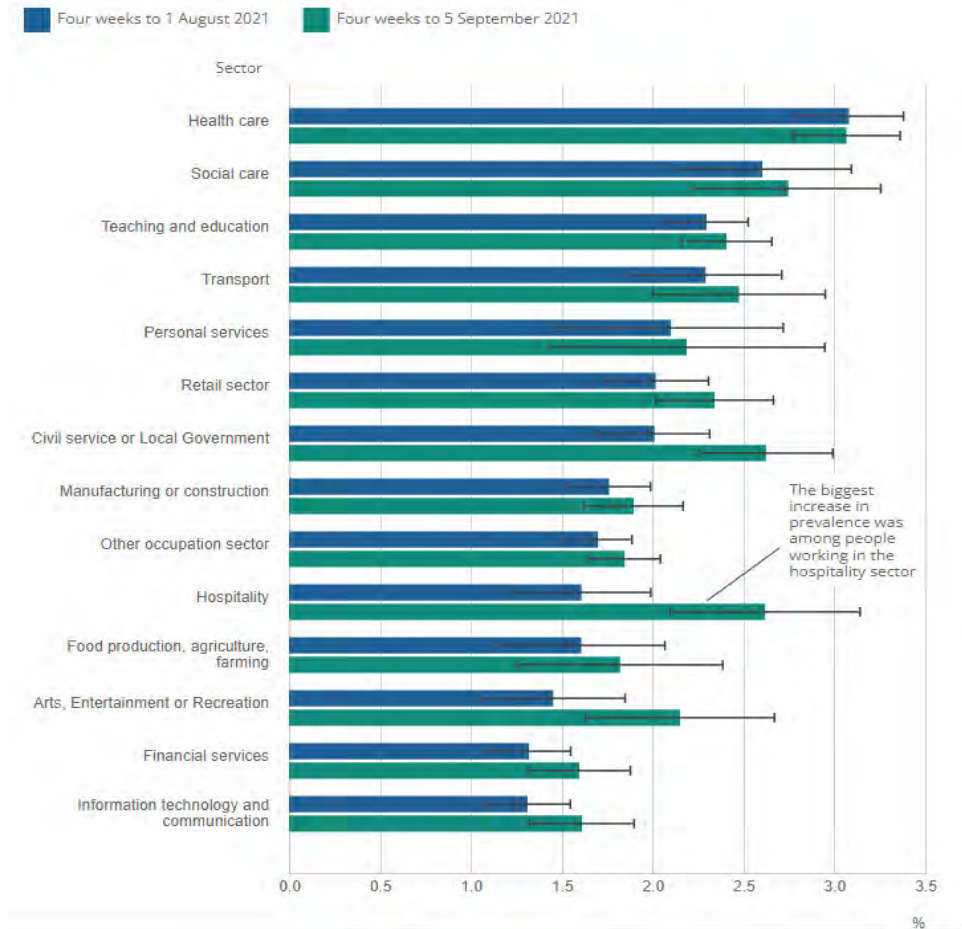
The largest: Coronavirus Infection Survey (CIS)

Last updated: 1 June 2022 -Based on self-classification

- Ongoing, large UK survey studies: population & community, swabs, antibodies, symptoms, vaccinated etc.

- Long COVID: ≈ 2.0 million (3.1% of population): Wuhan 30%, Alpha 12%, Delta 21%, Omicron 31%

- Of reported CIS: 826,000 > 1 year, 376,000 > 2 years

- Fatigue (55%), shortness of breath (32%), cough (23%), muscle ache (23%)

- More common among
  - Aged 35 to 69 years
  - Women
  - Deprived areas
  - Health or social care workers
  - with health condition or disability
- **20% reported ability day-to-day activities had been "limited a lot"**

Source: Office for National Statistics - Coronavirus Infection Survey

Estimated percentage of people living in private households with self-reported long COVID of any duration, stratified by employment sector, UK: four-week periods ending 1 August 2021 and 5 September 2021

■ Four weeks to 1 August 2021   ■ Four weeks to 5 September 2021

The biggest increase in prevalence was among people working in the hospitality sector

Risk of long COVID associated with delta versus omicron variants

Long covid risk with omicron may be half that of delta
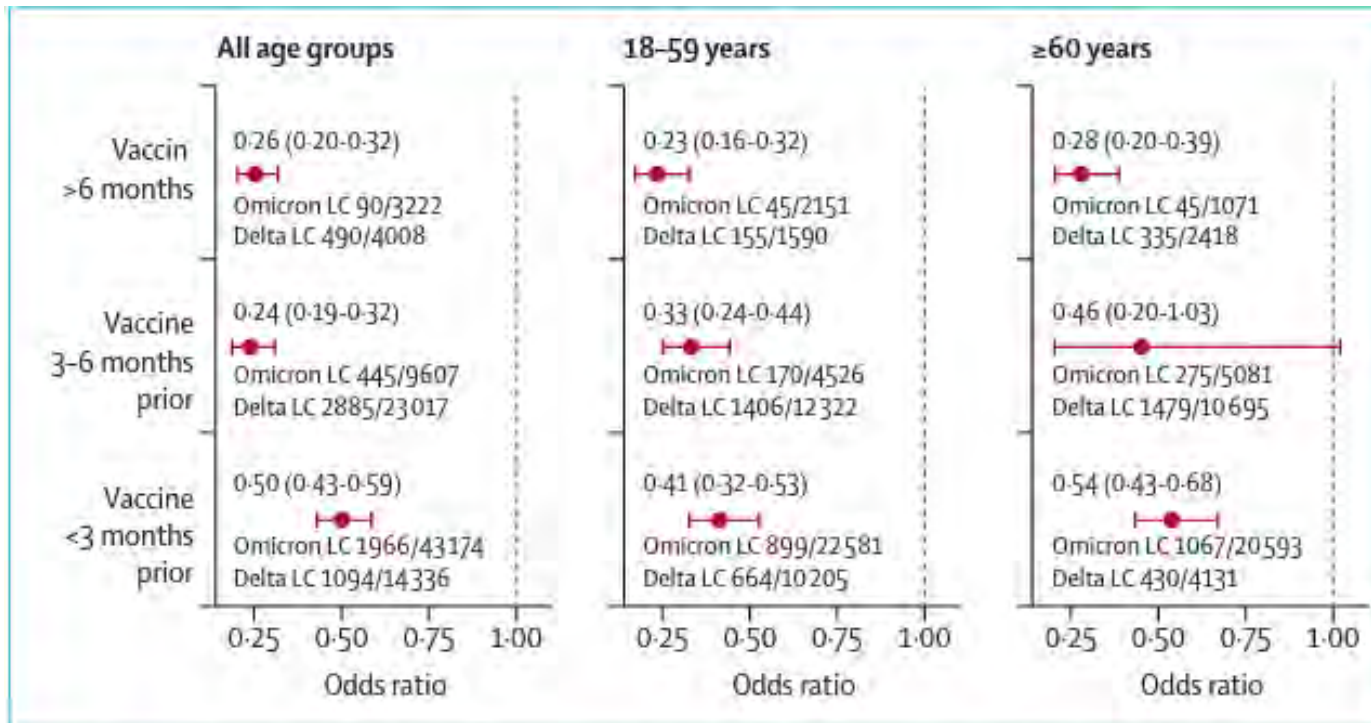
Figure: Odds ratio of long COVID (LC) adjusted by age, sex, body-mass index, Index of Multiple Deprivation, presence of comorbidities, and vaccination status

- Case-control observational study

- 56 003 UK adults Dec 2021 to March 2022

- **Omicron** cases 4.5% had long COVID

- **Delta** cases: 10.8% had long COVID

- Odds ⇓ of long COVID with omicron variant vs. delta variant of 0.24–0.50 depending on age and time since vaccination

- Insufficient data to estimate
  - Long COVID in **unvaccinated** individuals
  - **Longer durations** of long COVID (eg, >12 weeks)

How common is long COVID? Estimates of its prevalence can range from 5–50%....

…….depends on how you measure it

Understanding (better) Long COVID   Achim Regenauer   August 31, 2022
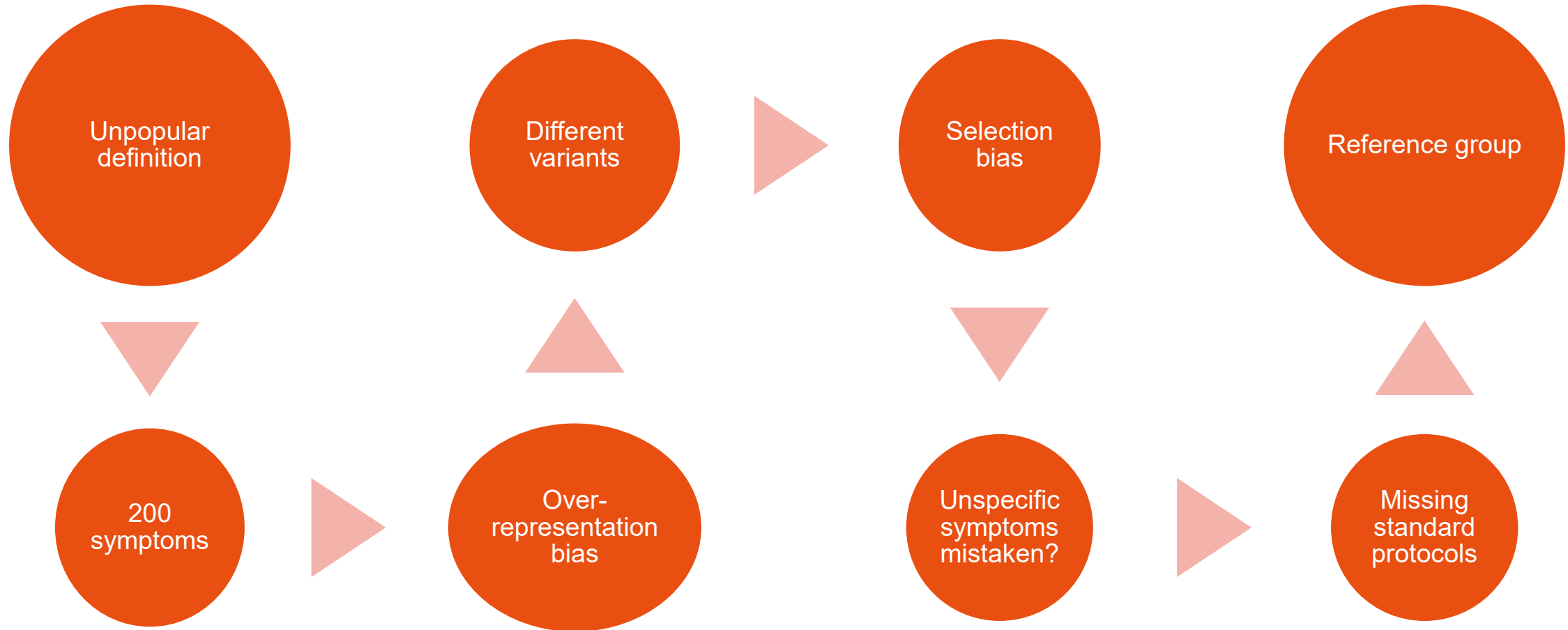
How frequent is Long COVID?

Well it depends, but not neglegible
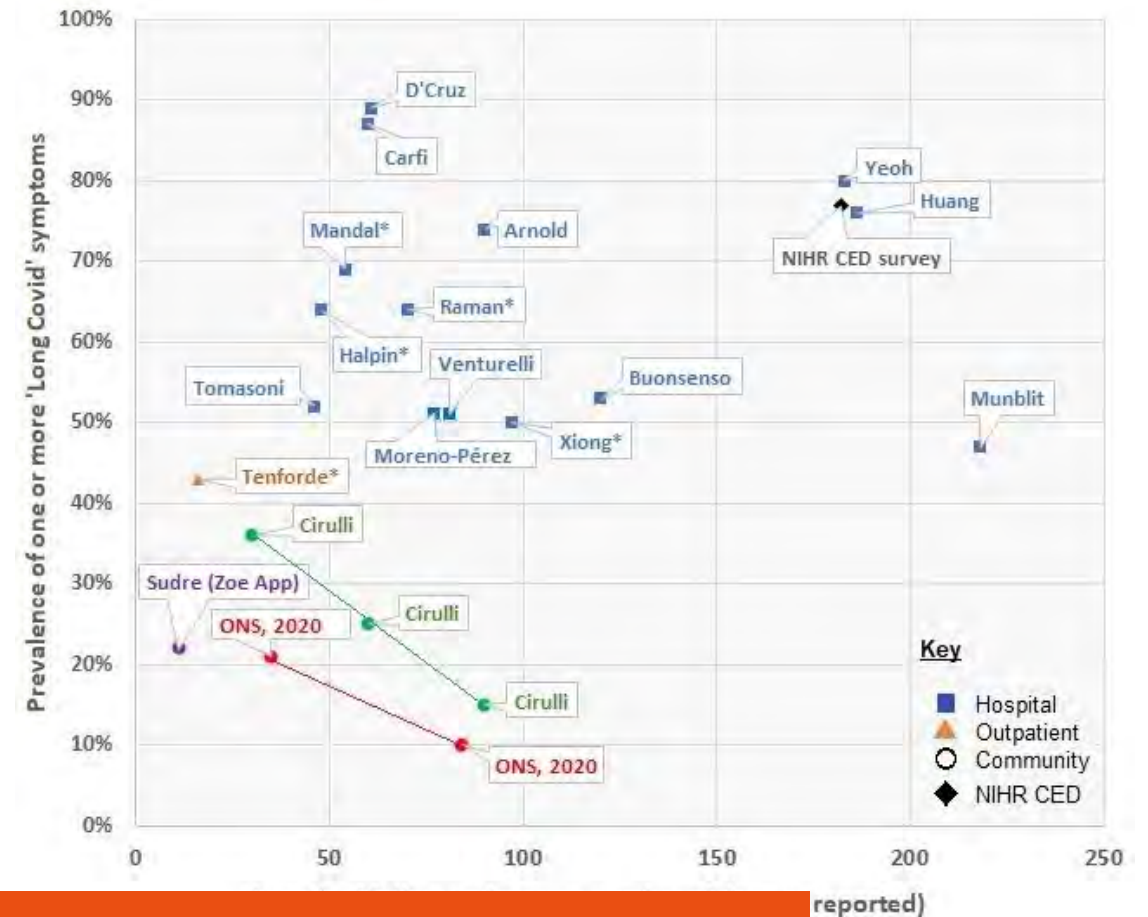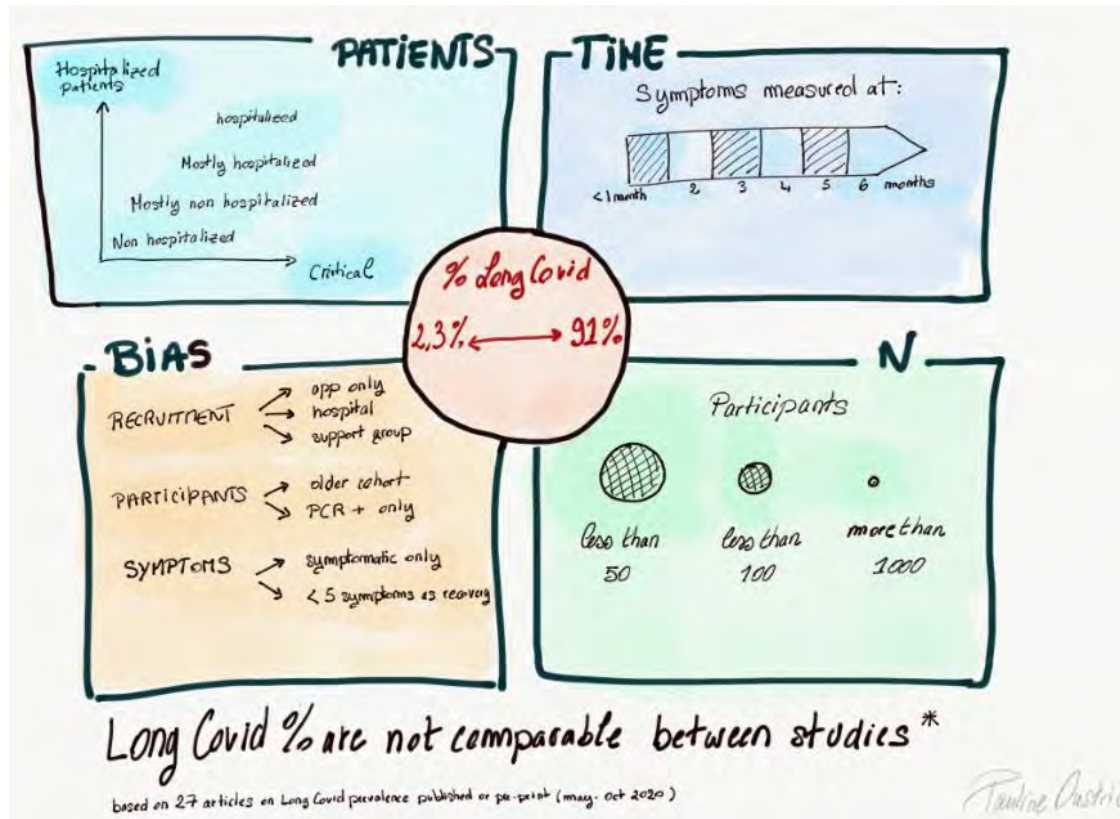
Longitudinal studies with control cohorts (RECOVER; PHOSP-COVID) will tell us more

Medical treatment of Long COVID?

TRIALS TAKE OFF

At least 26 randomized trials are under way to test therapies for long COVID. Many candidates target symptoms such as inflammation or clots. Some, such as the antidepressant fluvoxamine, act on different symptoms. Some researchers are repurposing drugs already approved for other conditions.

- ● Anti-inflammatory
- ● Cell-based therapy
- ● Antithrombotic
- ● Dietary supplement
- ● Steroid
- ● Other

Phase I

Phase II

Phase III

Approval not needed

- 26 different randomized trials

- **Potpourri** of steroids, other anti-inflammatory agents, cell-based therapies, anti-clotting drugs, dietary supplements

- Currently **no therapies** for Long Covid that have been **validated**

- Covid is a **mosaic** but no cluster specific approach by now

Treatment/Rehabilitation of Long COVID

A challenge for disability claim managers and occupational health

- Identify and treat what is treatable **as early as is feasible** (30 days)
- Wide variety of **rehabilitation programmes** (6-8 weeks)
- **Multimodal**: Bio-psycho-social
- Clinical therapy specialised to e.g cardiology, respiratory, neurology, gastroenterology etc
- Case managed rehabilitation and vocational rehabilitation
- **Slow phased** return or alternative work

But

- **Mental health service** access already difficult pre-pandemic?
- **Job Loss**, significant financial stress, subsequent recession?

Physical capacity

Social functioning

Mental capacity

(Long) COVID recovery

What we currently know

- **Physical, mental and cognitive** symptoms quite common
- **New symptoms** after asymptomatic infection: unknown
- **Persistent symptoms** are unlikely to **worsen**
- May even improve following **vaccination**

- **Longer recovery** course depends upon
  - premorbid risk factors
  - severity of the acute COVID-19
  - spectrum of symptoms
  - patients with medical complications
  - older patients
  - Pats with prolonged stay in hospital or ICU

Type, proportion, and duration of persistent COVID-19 symptoms*

Persistent symptom¶	Proportion of patients affected by symptom	Approximate time to symptom resolution△
Common physical symptoms		
Fatigue	15 to 87%[1,2,6,9,14,16]	3 months or longer
Dyspnea	10 to 71%[1,2,6-9,14]	2 to 3 months or longer
Chest discomfort	12 to 44%[1,2]	2 to 3 months
Cough	17 to 34%[1,2,9,12]	2 to 3 months or longer
Anosmia	10 to 13%[1,3-5,9,11]	1 month, rarely longer
Less common physical symptoms		
Joint pain, headache, sicca syndrome, rhinitis, dysgeusia, poor appetite, dizziness, vertigo, myalgias, insomnia, alopecia, sweating, and diarrhea	<10%[1,2,8,9,11]	Unknown (likely weeks to months)
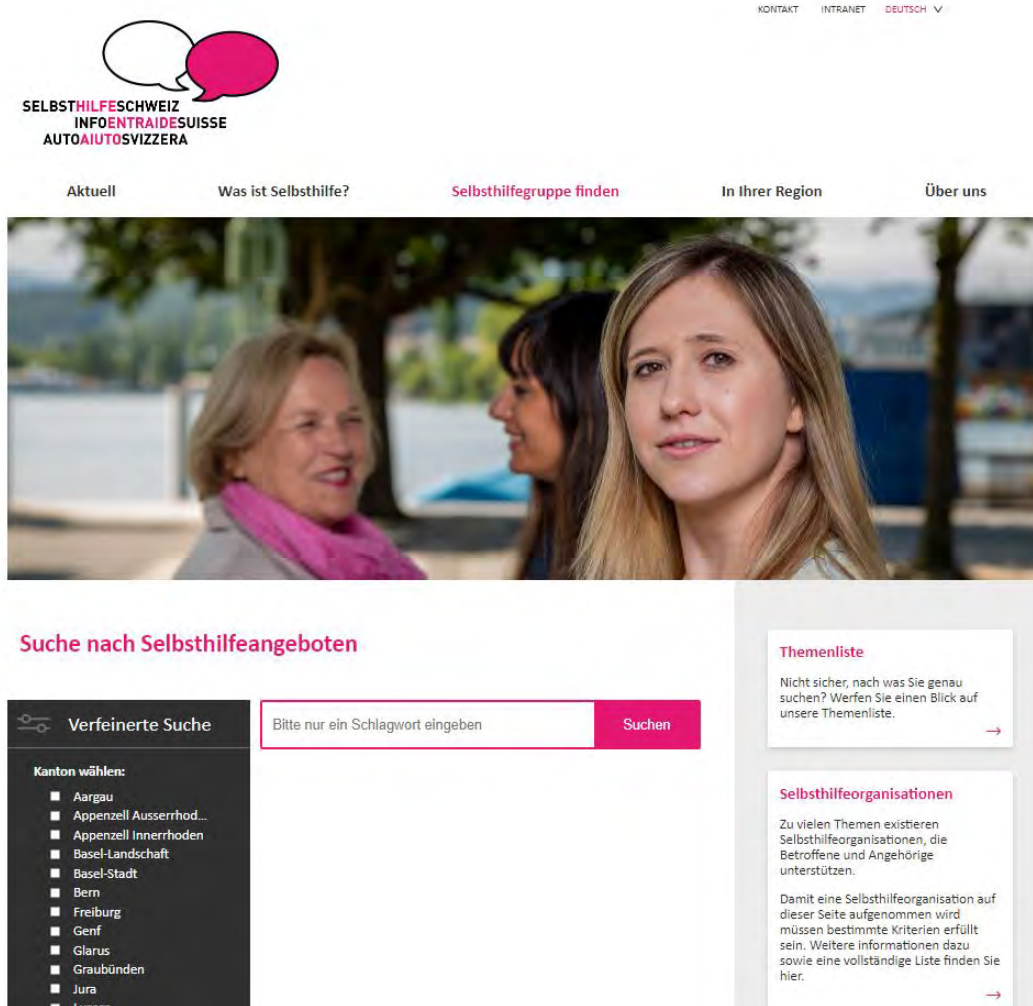
Source: Uptodate

- Data examining the outcome of rehabilitation utmost limited
- Optimal timing of follow-up evaluation unknown
- 10-20 % require **rehospitalization** within 30- 60 days

Affinity/Pressure groups Long COVID

Example Switzerland and Germany

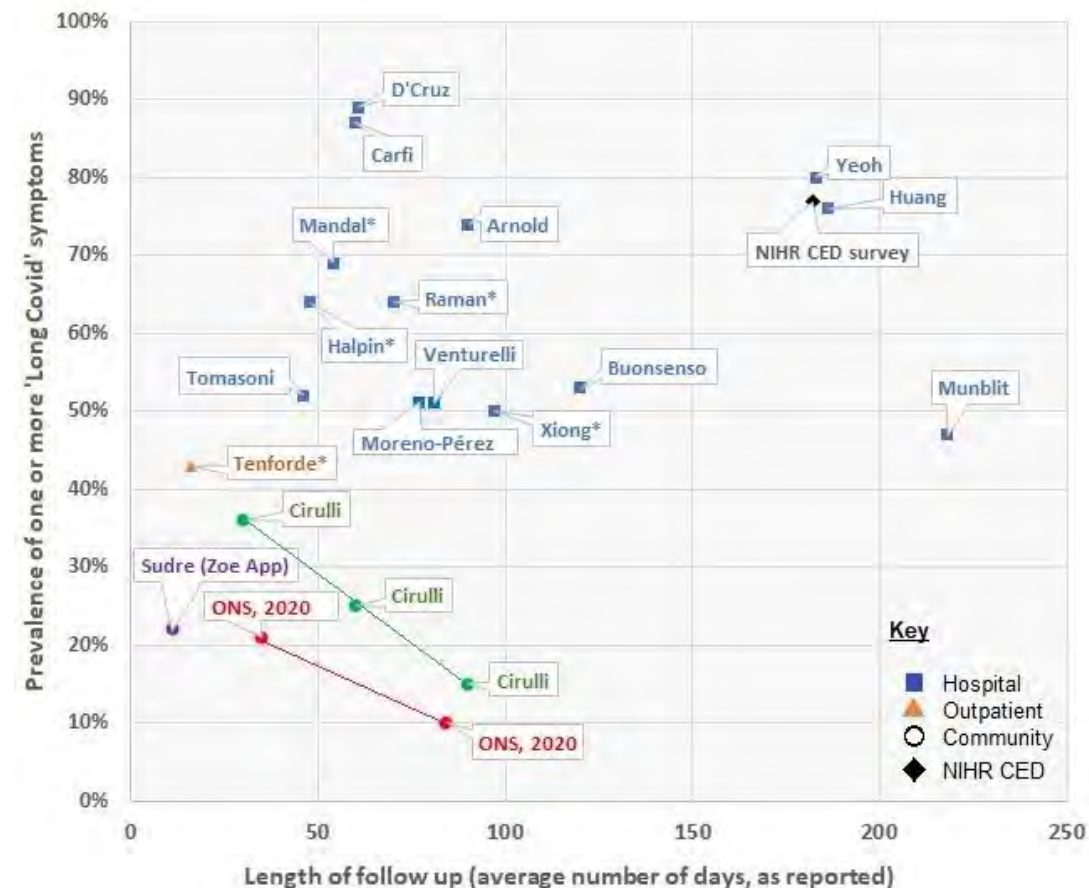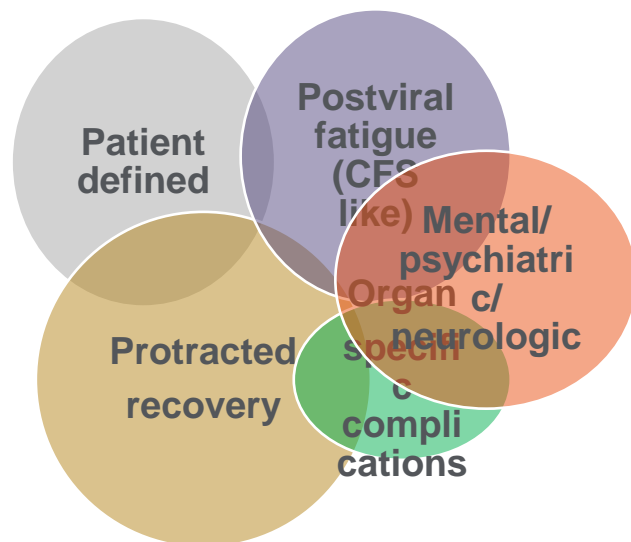| Ort	Thema	Beschreibung	Weitere Informationen
München	Long-Covid-Erkrankte	„Post-Covid-Erkrankte – Selbsthilfegruppe zur Bearbeitung der Folgen einer Corona-Erkrankung" Gruppe in Gründung	Selbsthilfezentrum München: https://www.shz-muenchen.de/gruppeninitiativen/marktplatz
München	Trauer, Angehörige von an Covid-19-Verstorbener	Trauernde Angehörige von an Covid-19 Verstorbene	Selbsthilfezentrum München: https://www.shz-muenchen.de/
München	einsame Menschen	Selbsthilfe im Lockdown und für Betroffene von Kontaktbeschränkungen	Selbsthilfezentrum München: https://www.shz-muenchen.de/
München	Angehörige von Verschwörungsgläubigen	Selbsthilfegruppe für Angehörige von Coronaleugnern, Coronaverharmlosern, Verschwörungstheoretikern	Selbsthilfezentrum München: https://www.shz-muenchen.de/
Neu-Ulm/Ulm	Long-Covid-Erkrankte	Gruppe in Gründung	KORN Ulm (auch für Neu-Ulm= Bayern): https://www.selbsthilfebuero-korn.de
Nürnberg	Angehörige von Verschwörungsgläubigen	Verquere Welten (Angehörige von Corona-Leugnern) Gruppe in Gründung	KISS Nürnberg: https://kiss-mfr.de
Nürnberger Land	Long-Covid-Erkrankte	„Long Covid, genesen, aber mit Spätfolgen" bestehende Onlinegruppe	KISS Nürnberger Land: https://kiss-mfr.de/kontaktstelle-nuernberger-land/
Regensburg, Oberpfalz	Long-Covid-Erkrankte	4 bestehende Gruppen	KISS Regensburg: https://www.kiss-regensburg.de/
Schwabach	Long-Covid-Erkrankte	bestehende Gruppe	KISS Roth-Schwabach: https://kiss-mfr.de/neue-selbsthilfegruppen/
Traunstein	Long-Covid-Erkrankte	bestehende Gruppe	Selbsthilfezentrum Traunstein: https://selbsthilfe-traunstein.de/
Weiden / Nordoberpfalz	Trauer, Angehörige von Covid-19-Verstorbenen	Einzelperson gibt Auskunft	Selbsthilfekontaktstelle Nordoberpfalz: https://seko-nopf.de/index.htm
Weilheim	Long-Covid-Erkrankte	bestehende Gruppe	Selbsthilfebüro Landkreis Weilheim-Schongau: https://www.weilheim-schongau.de/landkreis/gesundheit-im-landkreis/gesundheitsamt/selbsthilfebuero/

https://www.selbsthilfeschweiz.ch/shch/de/aktuell/virtuelle-selbsthilfe.html
https://www.nakos.de/aktuelles/corona/

"But there aren`t that many Long COVID claims"

- Unspecific symptoms – no diagnosis yet

- Scarcity of multidisciplinary centres

- Claims management affected

- Healthcare system – delayed treatments

- Era of uncertainty

- Socio-economic classes

- Delayed return to offices

- Economic recession

- Claims presented with non-COVID diagnoses but SARS-CoV-2 +

Long Covid → BMI 40, CFS, COPD, Corona infection 9/21

Wrap up

Extent to which ability to undertake day-to-day activities is reduced
- Not at all — 420,000
- A little — 478,000
- A lot — 196,000

Age breakdown
- 2-11 years: 15,000
- 12-16 years: 28,000
- 17-24 years: 90,000
- 25-34 years: 159,000
- 35-49 years: 317,000
- 50-69 years: 391,000
- ≥70 years: 94,000

Source: Office for National Statistics

- Patient defined
- Postviral fatigue (CFS like)
- Mental/psychiatric/neurologic
- Organ specific complications
- Protracted recovery