

Post-COVID-19 conditions 'Long Covid'

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For my Swedish GP colleagues

15 Oct 2020

Some definitions

not yet formalised

- Acute Covid: Weeks 0 - 3
- Post-acute Covid-19: Weeks 3 - 12
 - 10% have persisting, significant symptoms
 - Covid Symptom Study App (Kings College, London), daily completion by 4 million contributors
 - 3500 acute symptoms and PCR+ soon after ie confirmed cases (majority never hospitalised)
 - 10% report symptoms beyond 3 weeks
- Chronic Covid-19: > 12 weeks
 - estimates vary but 1% -10% seems likely
 - Covid Symptom Study App (Kings College, London)
 - 1-2% report symptoms beyond 12 weeks
 - Some now reporting > 6months
 - BMA Survey: 5650 respondents, 38% had COVID
 - of whom 30% left with fatigue, SOB and 18% cognitive problems



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PRACTICE POINTER

Management of post-acute covid-19 in primary care

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What you need to know

- Management of covid-19 after the first three weeks is currently based on limited evidence
- Approximately 10% of people experience prolonged illness after covid-19
- Many such patients recover spontaneously (if slowly) with holistic support, rest, symptomatic treatment, and gradual increase in activity
- Home pulse oximetry can be helpful in monitoring breathlessness
- Indications for specialist assessment include clinical concern along with respiratory, cardiac, or neurological symptoms that are new, persistent, or progressive

Box 1: A patient's account

My wife, kids, and I all had symptoms of presumed covid-19 in early April 2020. They were soon fine, but I was more unwell and ended up in bed extremely fatigued, lethargic, and without appetite for four days.

The only person whose symptoms persisted was myself, and the fatigue which I had experienced was still lingering in the background. From this point onwards, it became difficult to engage fully in day to day activities with my normal energy levels. Exercise, of which I do a fair amount, was not at all possible.

I continued to feel like this for another three weeks, before finally feeling completely overwhelmed. This happened very quickly and without warning, resulting in me heading for bed immediately as I felt so bad. For the next 72 hours, I felt unwell in a way that was bordering on not coping. I was feverish, soaked with sweat to the point of having to regularly towel myself down, and with a persistent headache that had no relief in spite of

Post-acute covid-19 ("long covid") seems to be a multisystem disease, sometimes occurring after a

Perspective

- Case fatality rate 1%
- Symptoms persisting 3-12 weeks: 10%
- Symptoms persisting > 12 weeks: 1-2%

‘long Covid’

Persistent symptoms 3 months after a SARS-CoV-2 infection:

the post-COVID-19 syndrome?

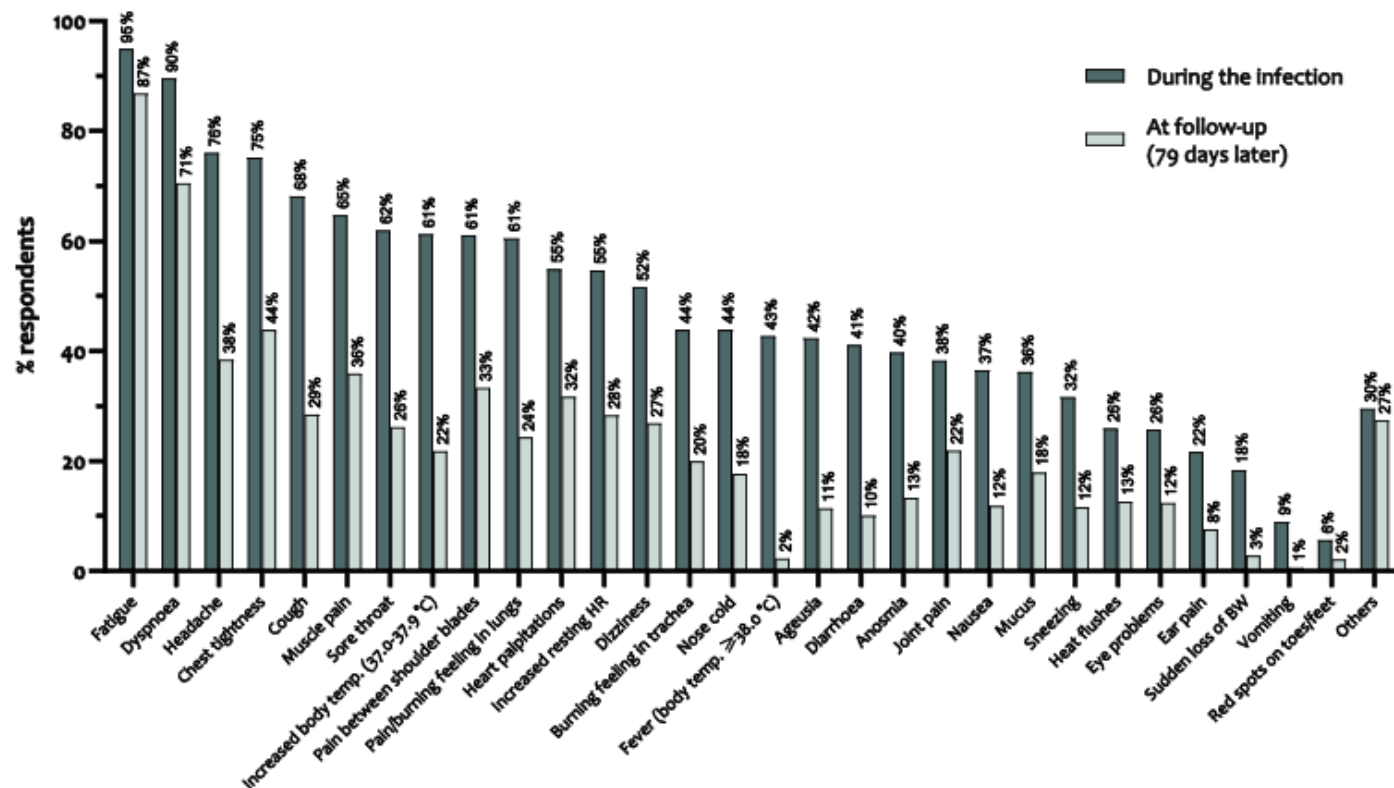
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	Whole sample (n=2113)	Hospitalized (n=112)	Non-hospitalized (confirmed COVID-19) (n=345)	Non-hospitalized (symptom-based COVID-19) (n=882)	Non-hospitalized (suspected COVID-19) (n=774)	p-value
Number of symptoms, median (IQR)	14.0 (11.0-17.0)	14.0 (9.3-17.0)	14.0 (11.0-18.0)	14.0 (11.0-18.0)	13.0 (10.0-17.0)	<0.001
Symptoms, n (%)						
Fatigue	2006 (94.9)	104 (92.9)	324 (93.9)	847 (96.0)	731 (94.4)	0.226
Dyspnoea	1892 (89.5)	100 (89.3)	300 (87.0)	827 (93.8)	665 (85.9)	<0.001
Headache	1605 (76.0)	80 (71.4)	273 (79.1)	682 (77.3)	570 (73.6)	0.097
Chest tightness	1588 (75.2)	68 (60.7)	248 (71.9)	709 (80.4)	563 (72.7)	<0.001
Cough	1438 (68.1)	89 (79.5)	235 (68.1)	620 (70.3)	494 (63.8)	0.002
Muscle pain	1367 (64.7)	60 (53.6)	245 (71.0)	578 (65.5)	484 (62.5)	0.003
Sore throat	1309 (61.9)	49 (43.8)	188 (54.5)	564 (63.9)	508 (65.6)	<0.001
Increased body temp. (37.0-37.9 °C)	1293 (61.2)	44 (39.3)	189 (54.8)	571 (64.7)	489 (63.2)	<0.001
Pain between shoulder blades	1289 (61.0)	53 (47.3)	216 (62.6)	584 (66.2)	436 (56.3)	<0.001
Pain/burning feeling in lungs	1279 (60.5)	53 (47.3)	178 (51.6)	587 (66.6)	461 (59.6)	<0.001
Heart palpitations	1159 (54.9)	44 (39.3)	191 (55.4)	521 (59.1)	403 (52.1)	<0.001
Increased resting HR	1154 (54.6)	58 (51.8)	199 (57.7)	519 (58.8)	378 (48.8)	<0.001
Dizziness	1091 (51.6)	46 (41.1)	171 (49.6)	490 (55.6)	384 (49.6)	0.006
Nose cold	928 (43.9)	38 (33.9)	169 (49.0)	363 (41.2)	358 (46.3)	0.006
Burning feeling in the trachea	927 (43.9)	37 (33.0)	121 (35.1)	428 (48.5)	341 (44.1)	<0.001
Fever (body temp. ≥38.0 °C)	903 (42.7)	94 (83.9)	178 (51.6)	380 (43.1)	251 (32.4)	<0.001

Ageusia	893 (42.3)	73 (65.2)	218 (63.2)	350 (39.7)	252 (32.6)	<0.001
Diarrhoea	869 (41.1)	49 (43.8)	150 (43.5)	374 (42.4)	296 (38.2)	0.225
Anosmia	839 (39.7)	67 (59.8)	223 (64.6)	308 (34.9)	241 (31.1)	<0.001
Joint pain	808 (38.2)	37 (33.0)	151 (43.8)	340 (38.5)	280 (36.2)	0.066
Nausea	772 (36.5)	51 (45.5)	124 (35.9)	341 (38.7)	256 (33.1)	0.021
Mucus	764 (36.2)	42 (37.5)	107 (31.0)	328 (37.2)	287 (37.1)	0.193
Sneezing	667 (31.6)	27 (24.1)	123 (35.7)	274 (31.1)	243 (31.4)	0.129
Heat flushes	548 (25.9)	18 (16.1)	90 (26.1)	224 (25.4)	216 (27.9)	0.061
Eye problems	542 (25.7)	20 (17.9)	76 (22.0)	245 (27.8)	201 (26.0)	0.045
Ear pain	459 (21.7)	12 (10.7)	74 (21.4)	210 (23.8)	163 (21.1)	0.015
Sudden loss of BW	388 (18.4)	42 (37.5)	81 (23.5)	165 (18.7)	100 (12.9)	<0.001
Vomiting	191 (9.0)	24 (21.4)	41 (11.9)	76 (8.6)	50 (6.5)	<0.001
Red spots on toes/feet	118 (5.6)	9 (8.0)	15 (4.3)	50 (5.7)	44 (5.7)	0.512
Others	623 (29.5)	19 (17.0)	87 (25.2)	284 (32.2)	233 (30.1)	0.002

Abbreviations: n = number; IQR = Interquartile range; temp. = temperature; HR = heart rate; BW = body weight

Patient outcomes after hospitalisation with COVID-19 and implications for follow-up; results from a prospective UK cohort.

Arnold DT^{1*}, Hamilton FW^{1*}, Milne A¹, Morley A¹, Viner J¹, Attwood M², Noel A², Gunning S¹, Hatrick J¹, Hamilton S¹, Elvers KT³, Hyams C¹, Bibby A¹, Moran E¹, Adamali H¹, Dodd J¹, Maskell NA¹, Barratt S¹

- n = 163 (110 @ 12 weeks)
- Post discharge, FU at 28 days and 12 weeks
- CXR, SpO2, 1min STS, Spirometry, QoL

Figure 2: Frequency of symptoms reported at 12-week follow-up compared to hospital admission.

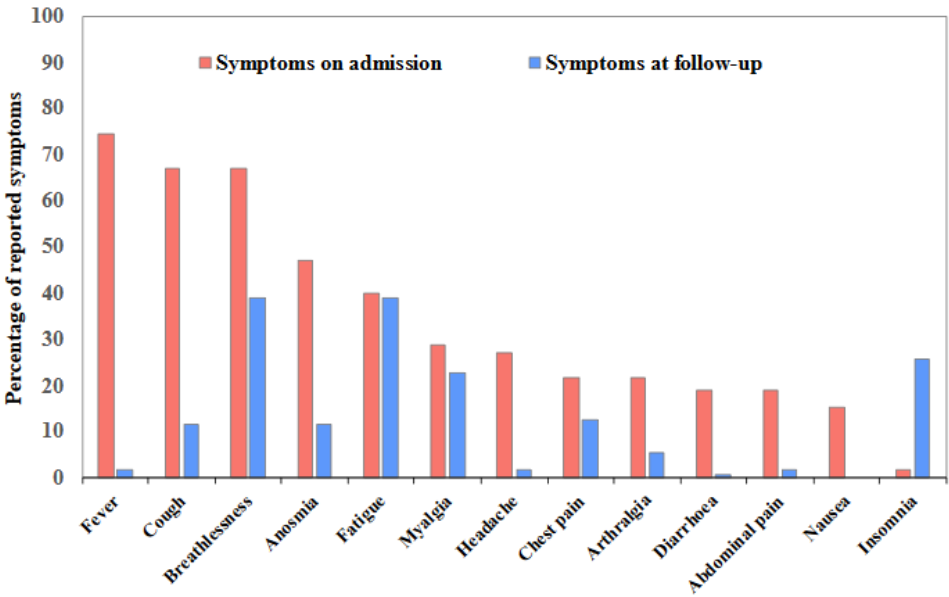


Figure 3: SF-36 results, mean and standard error, with age-matched population norm means.

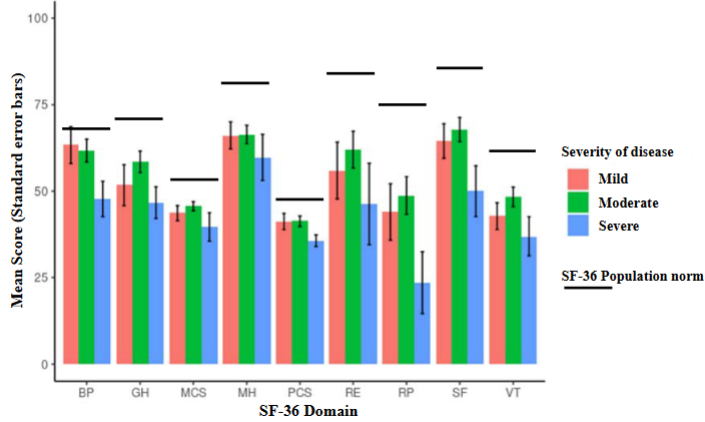


Figure 4: Summary of symptomatology and clinical results by disease severity.

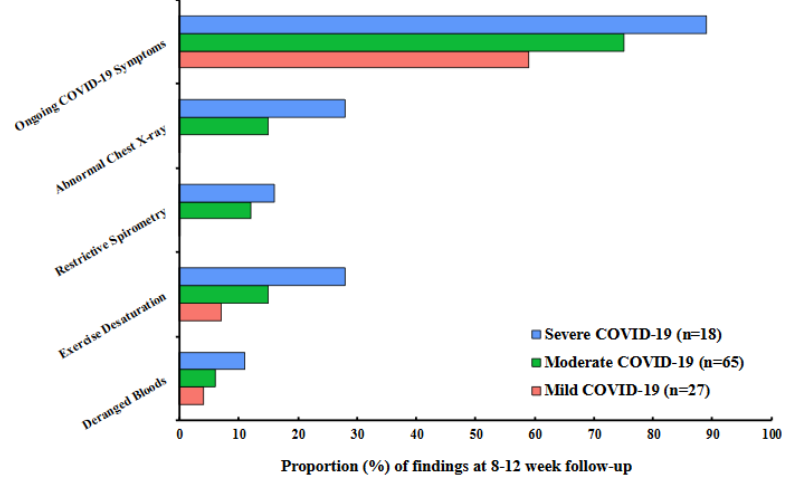
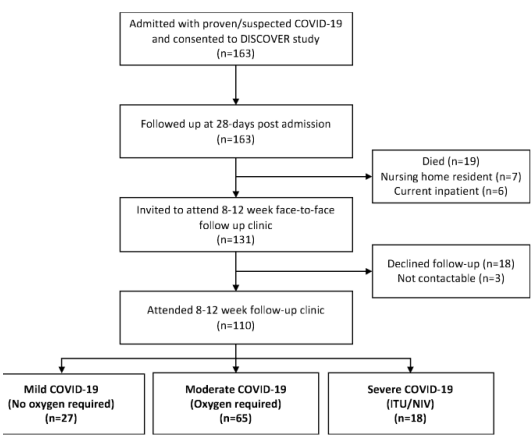


Figure 1: CONSORT diagram of the study



Implications for GPs of 'long COVID-19'

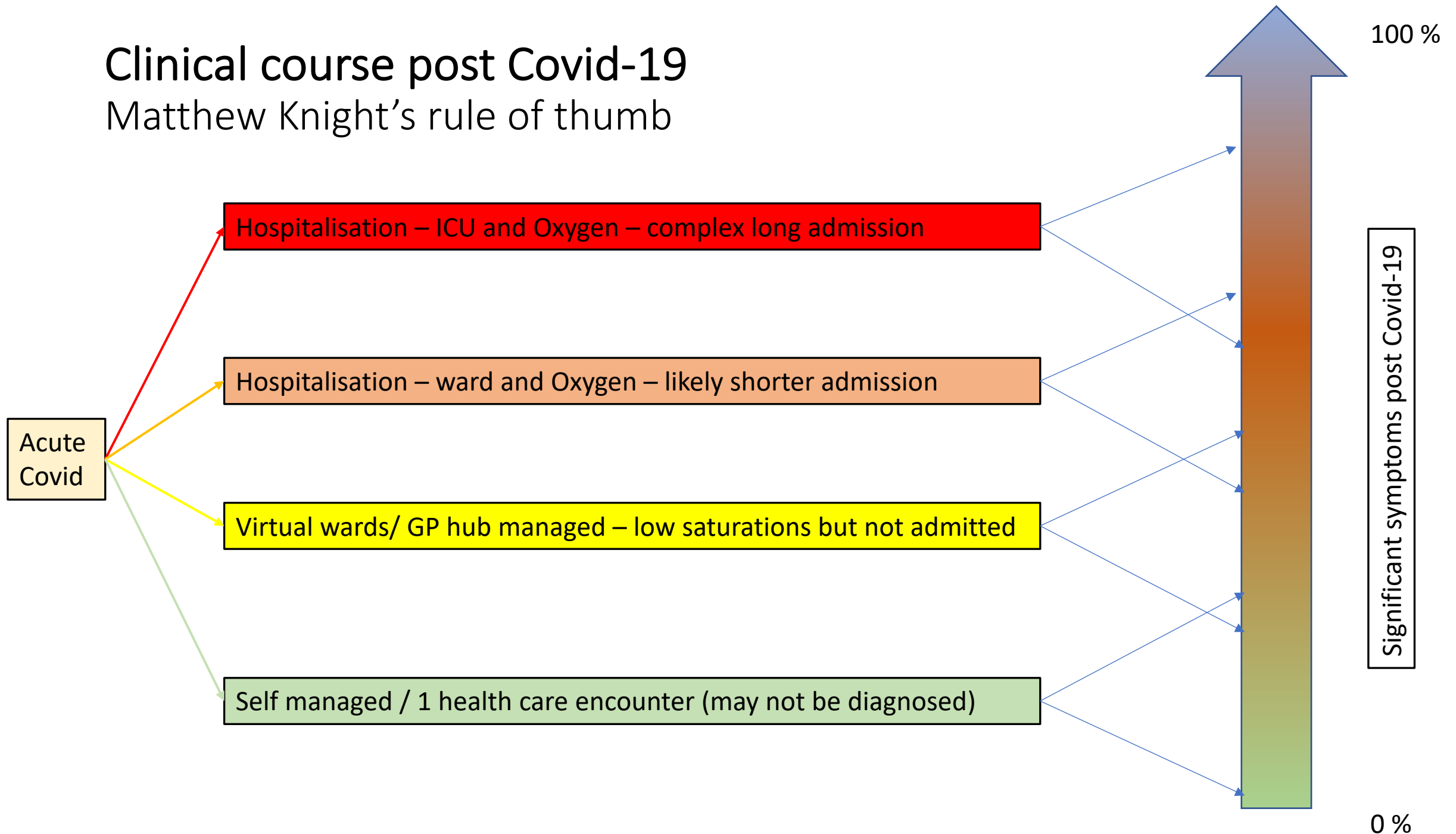
- Around 10% of all those infected with COVID-19 experience protracted symptoms beyond 3 weeks
 - much higher rate if were hospitalised ('74%' Bristol study)
 - 1%-2% beyond 3 months
- Many will not have a formal diagnosis of COVID-19
 - Early on (March-April) tests not available
 - False negative rate of 20% for current PCR tests
 - Some patient do not seroconvert (despite previous PCR positivity)
 - Many patients heeded self-isolation advice, self-managed, avoided testing

More about post COVID-19 symptoms

- Severity bears no relation to severity of acute illness (esp. non-pulmonary)
- Relapsing and remitting (in 80%*), sometimes unpredictable but often precipitated by exertion or by cognitive or emotional stress
- Multiple body systems and range of symptoms
 - respiratory: SOB, cough, chest tightness or pain, 'lung burn', severe sinus congestion, sore throat, hoarseness
 - cardiac: palpitations, high heart rate
 - neurological: headache, pain anywhere, paresthesiae (crawling, electric shock, vibrating sensation), insomnia, cognitive difficulties - 'brain fog', change/loss in smell/taste, sensory overload
 - gastrointestinal: nausea, diarrhea, acid reflux, decreased appetite, abdo pain
 - musculoskeletal: severe muscle aches, tightness or weakness
 - fatigue
 - exacerbation of pre-existing metabolic conditions

Clinical course post Covid-19

Matthew Knight's rule of thumb



Mechanisms?

‘We have no idea what is going on at the cellular level’ (Anthony Fauci)

*hypotheses
in no particular order
not mutually exclusive*

- A central nervous system sensitisation similar to ME/CFS or fibromyalgia
- Vasculitis (hence bizarre skin rashes, ‘Covid Toe’)
- Endothelial disorder* (so evident in acute severe COVID-19: thromboembolism, microthrombosis, alveolitis, serositis etc)
- Genetic predisposition/polymorphisms

* Libby P, Lüscher T. COVID-19 is, in the end, an endothelial disease. *Eur Heart J* 2020; **41(32)**: 3038–3044

What hope of some answers?

- PHOSP-COVID led by NIHR Leicester Biomedical Research Centre
 - Post-hospitalisation COVID-19 study
 - To recruit 10,000 patients, study for 1 year
 - Platform for developing care strategies
- ‘We cannot fight what we do not measure’
(N.Alwan. Assoc Prof in Public Health, Uni of Southampton)
 - whose responsibility?
 - Do GPs code on electronic medical record?



6 Oct 2020

Sources of data/information on post-Covid conditions

- Small body of literature emerging
- UK Based Covid Symptom Study (Smartphone App, Kings College London)
https://covid.joinzoe.com/post/covid-long-term?fbclid=IwAR1RxIcmmdL-EFjh_al-
- FaceBook: Long Covid Support Group
 - Created May 2020
 - 25K members Oct 20
 - Only join if you have experience of Long Covid This support group is for people who have had or are caring for someone with Long Covid (= symptoms for 3 weeks or more), not for those with new infections.
 - Researchers or journalists, please don't join the group, instead contact info@longcovid.org
 - No conspiracy, antivax, anti-mask, pseudoscience
 - No party politics please
 - No business promotion
 - Share your experience/don't tell others what to do

Who needs onwards specialist referral?

-suggestion from Dr Matthew Knight, respiratory physician, managed >1500 patients with Long COVID

- Persistent symptoms at 12 weeks
 - Predominantly fatigue (cause not known - but real)
 - Minority have measurable organ damage
- At any stage: severe symptoms
 - chest pain, syncope, dyspnoea at rest that does not settle
- Hypoxia or $\geq 4\%$ desaturation on an exertional exercise test
- When investigations suggest a need
 - E.g. elevated natriuretic peptide or D-dimer

COVID-19 and Cardiac considerations in the community

A'Court et al
BJGP, Nov 20

DOI:
<https://doi.org/10.3399/bjgp20X713141>

ACUTE MYOCARDIAL INJURY

Studies of patients hospitalised with COVID-19 have reported the prevalence of 'acute myocardial injury', defined as an acute rise of cardiac troponin T/I, to be 12%–36%.² The umbrella term 'acute myocardial injury' encompasses ischaemic causes, including Type 1 myocardial infarction (MI) due to atherosclerotic plaque disruption; and Type 2 MI due to microthrombosis, or to demand-perfusion mismatch. Non-ischaemic causes include myocarditis, stress cardiomyopathy, or right ventricular strain from pulmonary embolism (Figure 1).² Acute myocardial injury is associated with a worse prognosis in COVID-19, particularly in the older population and those with cardiovascular comorbidities.² The association with worse outcomes during

patients recovering from COVID-19, of whom only one-third had been hospitalised, suggests a large proportion (78%) have cardiac abnormalities when assessed at a single center with cardiovascular magnetic resonance (CMR) imaging.⁵ Subsequent debates⁶ highlight possible methodological and statistical issues, but similar high rates of CMR-detectable myocardial abnormalities were reported elsewhere in very small studies; namely 58% (15/26) of Chinese,⁷ 56% (9/16) of Hong Kong,⁸ and 66% (19/29) of UK⁹ study participants who were also recovering in the community.

While acute myocardial injury, defined as acute rise and fall of cardiac troponin, in hospitalised COVID-19 patients is associated with excess risk, the short-term clinical significance and long-term implication of

^aIncludes Troponin I and Troponin T.
NT-proBNP = N-terminal pro B-type natriuretic peptide.

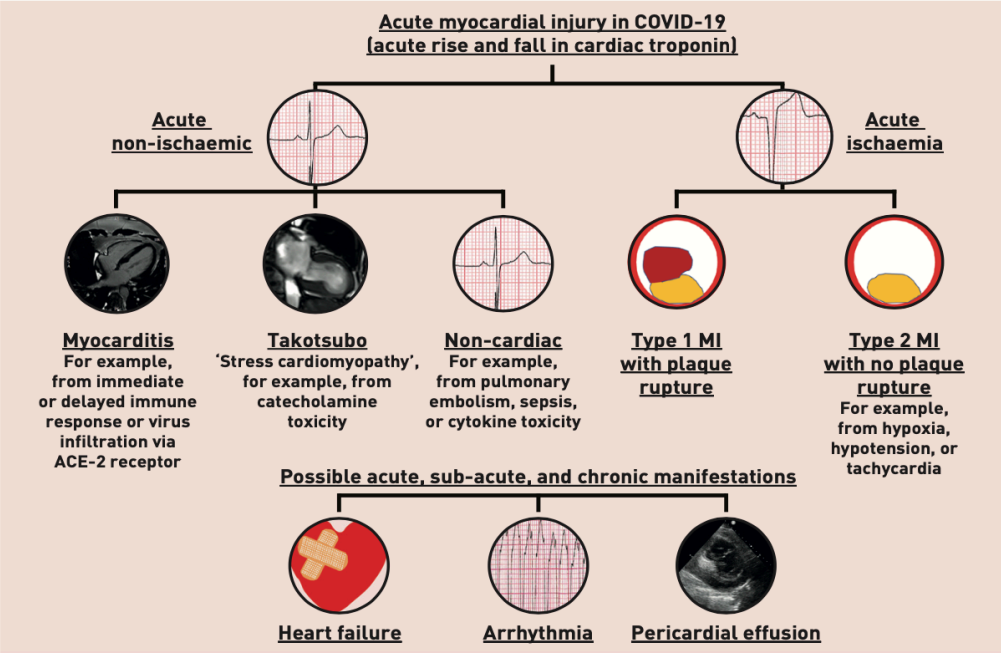
CMR abnormalities in recovering patients are unknown.⁶ Nor is it apparent to what extent cardiorespiratory pathophysiology explains the persistent fatigue, dyspnoea, or chest pain in up to 74% of patients 2–3 months post-admission.^{1,10} Large population based multi-organ studies are underway to address these questions. Perhaps we should be reassured that most of the patients in the CMR studies had normal ventricular function, N-terminal pro B-type natriuretic peptide (NT-proBNP) levels, and cardiac troponin levels at the time of the scan. This suggests that, at around 1–2 months after presentation with COVID-19, heart failure was not a complication of the abnormalities seen on CMR. Despite speculation,^{5,6} progression to future heart failure is as yet unproven.

Theoretically, myocardial injury can present at any stage after a viral infection.^{3,6,11} Myocardial injury during a viral respiratory illness is not surprising as it was reported during the avian influenza A(H7N9), SARS, and MERS pandemics.^{11,12} Influenza infection is associated with a doubling of short-term acute myocardial infarction rates.¹³ Myocarditis can be driven by immediate and delayed immune responses, with some patients progressing to develop dilated cardiomyopathy.^{11,14}

DIAGNOSTIC CHALLENGES FOR GPs

Pending longitudinal studies, GPs need to reassure the majority of post-COVID-19 patients but be alert to the development of acute myocardial injury in the early weeks, or delayed complications (for example, pericardial effusion, arrhythmias, and heart failure) (Figure 1).^{3,4,8} While most suspected cases would merit referral to

Figure 1. Acute myocardial injury in COVID-19. COVID-19 is defined by an acute rise and fall in cardiac troponin. Possible mechanisms and clinical manifestations are shown. MI = myocardial infarction. ACE-2 = angiotensin converting enzyme 2.





ESC

European Society
of Cardiology

European Heart Journal (2019) 40, 19–33

doi:10.1093/eurheartj/ehy730

SPECIAL ARTICLE

Sports cardiology

Recommendations for participation in competitive and leisure time sport in athletes with cardiomyopathies, myocarditis, and pericarditis: position statement of the Sport Cardiology Section of the European Association of Preventive Cardiology (EAPC)

Table 10 Recommendations for athletes with myocarditis

	Class/level of evidence
1. General consensus exists that athletes with diagnosis of myocarditis should be restricted from exercise programmes for a period of 3–6 months, according to the clinical severity and duration of the illness, LV function at onset, and extent of inflammation on the CMR. This time period is considered appropriate to ensure clinical and biological resolution of the disease. ^{3,4,105,118–120}	Class IIb/Level C
2. Individuals with previous myocarditis have an increased risk for recurrence and silent clinical progression of the disease. Therefore, athletes with previous myocarditis should undergo a periodical re-assessment, particularly within the first 2 years.	Class IIa/ Level C
3. It is reasonable for athletes to resume training and competition after a myocarditis if all of the following criteria are met: (1) LV systolic function has returned to the normal range. (2) Serum biomarkers of myocardial injury have normalized. (3) Clinically relevant arrhythmias, such as frequent or complex repetitive forms of ventricular or supraventricular arrhythmias are absent on 24-h ECG monitoring and exercise test.	Class IIa/ Level C
4. The clinical significance of persistent LGE in an asymptomatic athlete with clinically healed myocarditis is unknown, however, myocardial scar is a potential source of ventricular tachyarrhythmias. ^{111–113} At present, it seems reasonable for these athletes to resume training and participate in competitive sport if LV function is preserved and in the absence of frequent or complex repetitive forms of ventricular or supraventricular arrhythmias during maximal exercise and on 24-h ECG monitoring (including session of training/competition). Asymptomatic athletes with LGE, however, should remain under annual clinical surveillance.	Class III/ Level C

What to expect after severe COVID-19 FAQs

- What FU?
 - if improving, just watch and wait. No indication for routine D-dimer, ferritin, CRP unless worrying symptoms.
 - Ferritin should be < 500 (and definitely <1000)
 - Patients that required O2 should get FU CT @12 weeks.
 - Expect abnormal CT for at least 6-8 weeks after
- What treatments?
 - No formal guidance but anticoagulants often given for 10 days post hospital admission: no longer
 - Ibuprofen for symptomatic use only eg myalgia, pleuritis (no evidence that dampens cytokine storm etc)
 - Steroids: not routine, individualized specialist decision
 - eg relapsing fevers and severe malaise (having ruled out sepsis/other inflammation/autoimmune etc)
 - Chronic pericarditis resistant to low dose colchicine +/- NSAIDS
- Flu jabs?
 - to be avoided in acute COVID-19 (definite) and post-acute (probably)

What therapies for long Covid without tangible disease (the majority)?

- Validation: patients need to be heard, believed, not dismissed
- Cognitive approaches
 - Recognise harmful mindsets, cognitive distortions that hamper recovery
 - Manage excess worry or preoccupation with physical symptoms by distraction or mindfulness
- Manage fatigue
 - Energy conservation techniques: pacing, planning & prioritisation. 'Chunking'
 - V. gradual, sensitive exercise increase, heeding fatigue, avoiding boom & bust
 - Good quality rest (NB activity can be cognitive, emotional, physical)
 - Healthy diet
 - Find some fun - fun recharges the battery (Prof Tim Peto)
 - Phased return to work over 8-12 weeks, work from home
- [Yourcovidrecovery.nhs.uk](https://yourcovidrecovery.nhs.uk)



Misapprehensions and corrections

- Mild/Moderate COVID-19 will recover quickly
 - Symptoms persist > 28 days in 10%, and > 3 months in 1-2%
 - *‘mild acute COVID-19 more likely to have strange protracted symptoms that come and go over a more extended period’* (Prof, Tim Spectre, on Covid Symptom Study, App)
- Exercise improves everything
 - Worsens those with post exertional fatigue/malaise
 - Potentially fatal in myocarditis
- The main myocardial complication in acute COVID-19 is myocarditis
 - ‘acute myocardial injury’ is heterogenous, and consequences uncertain
- ‘Man flu’ is a joke.....

Press release accompanying BMJ article on long Covid

- Dr Matthew Knight (@mjknight0380), a respiratory physician who has managed more than 1500 patients with long COVID in his virtual clinic:
 - “Whilst some patients with long COVID should be referred to specialists and investigated for serious complications, many will slowly get better by carefully pacing themselves with support from their primary care team and peers.”
- Prof Greenhalgh (@trishgreenhalgh), a retired GP:
 - “I think the medical profession needs a new word, to say to people with #longcovid..... It would mean ‘I believe you, I witness your suffering, I share my uncertainty with you, I can't cure you but I will not abandon you’.”

Anosmia

- Background (non COVID) olfactory dysfunction is common.
 - Point prevalence 19% of gen population partial/complete loss of smell(80% > 75s)
 - Rhinitis, Alzheimer's, Parkinsons'
- In acute COVID-19
 - Loss of smell in 55% (meta-analysis, CI 38-70%)
 - Impaired taste in 42% patients
 - Anosmia is only symptom in 16%
 - Loss of smell is usually severe and sudden in onset
 - 9/10 recover smell within 4 weeks
 - Try intranasal steroid spray/oral CS (if other symptoms resolved) or omega-3 -supplements
 - >3months refer

*Anosmia & loss of smell during the covid-19 pandemic.
Walker et al. BMJ 25 Jul 20*