## Post-acute sequalae of COVID-19

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ACI acknowledges the traditional owners of the land that we work on.

We pay our respect to Elders past and present and extend that respect to other Aboriginal peoples present here today.

#### Acute COVID-19 in 2022

Figure 1. Percentage of Flutracking participants nationally with fever and cough, 2020 to 17 July 2022.



https://info.flutracking.net/wp-

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#### **NSW hospitalisations with acute COVID-19 2022**

Figure 1. Daily seven-day rolling average of people with COVID-19 admitted to hospital within 14 days of their diagnosis, NSW, 1 January to 03 September 2022



Figure 3. Number of people in hospital with COVID-19 by day, NSW, 1 January to 03 September 2022



https://www.health.nsw.gov.au/Infectious/covid-19/Documents/weekly-covid-overview-20220903.pdf



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## Clinical practice guide for assessment and management of adults with post-acute sequelae of COVID-19

# Guidance for NSW health clinicians, ACI Clinical practice guide





- Publication due this week
- Document informed by clinical expertise and current evidence based including rapid evidence checks by CIU
- Intended for NSW health clinicians and primary care patient may present with symptoms in a variety of settings
- Symptoms persisting > 3 months post-diagnosis consistent with WHO and NICE definitions of PASC
- Lists the top 10 symptoms how they present, assessment tools, recommendations for management and referral. Includes where immediate or urgent referral required.
- To be integrated with the existing "Post-COVID-19 conditions" HealthPathway

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Clinical practice guide for assessment and management of adults with post-acute sequelae of COVID-19

Guidance for NSW health clinicians

This clinical practice guide is intended for use by clinicians in primary health networks and local health districts, as well as primary care practitioners across NSW who provide care to adults aged 16 years and older with a history of COVID-19 diagnosis, regardless of severity or COVID-19 variant of concern.

Contents		Definition of 'post-acute sequelae of COVID-19'
Intended audience and application	2	Post-acute sequelae of COVID-19 (PASC), also referred
Background	2	to as 'post-acute COVID-19 condition', 'post COVID-19
Methodology	3	the World Health Organization as:
Common symptoms of post-acute COVID-19 sequelae	4	"the condition that occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually:
Comprehensive patient assessment	4	• three months from the onset of COVID-19; AND
Patient reported outcome measures	4	<ul> <li>with symptoms that last for at least two months and</li> </ul>
Symptoms	6	cannot be explained by an alternative diagnosis.
Red flags	8	Common symptoms include fatigue, shortness of breath, coanitive dysfunction but also others and
Glossary	21	generally have an impact on everyday functioning.
Acknowledgements	22	Symptoms may be onset to lowing initial liness. Symptoms may also fluctuate or relapse over time"
Appendix A - Recommended services and clinicians for the establishment of		[emphasis added]. <sup>1</sup>
a dedicated PASC clinic	23	
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#### **Clinical Case Definitions**

- Acute COVID-19 Signs and symptoms for up to 4 weeks
- Ongoing symptomatic COVID-19 Signs and symptoms from 4 weeks up to 12 weeks
- Post COVID-19 Syndrome (also known as "long COVID", "post-COVID-19 condition" or "post-acute sequelae of COVID-19")

"the condition that occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, **usually three months from the onset of COVID-19 with symptoms that last for at least two months and cannot be explained by an alternative diagnosis**. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be onset following initial illness. Symptoms may also fluctuate or relapse over time" [emphasis added].

#### What we do (and don't) know about PASC

- The evidence base on the signs, symptoms and treatment of PASC is an evolving area which will continue to grow
- Research to date is largely limited to pre-Omicron strains (Omicron first reported in November 2021)
- Pre-Omicron, the reported rate of PASC ranged from 43-63% with a higher PASC estimated amongst those hospitalized during the acute phase of illness.
- Vaccination has a protective effect incidence and severity of PASC is reduced in vaccinated people.

#### **Factors that increase the risk of PASC**

- Hospitalisation or severity of symptoms during the acute phase of illness
- Age > 65
- Pre-existing frailty
- Comorbidities, particularly chronic lung disease and diabetes
- Obesity
- Vaccination status
- Increase of inflammatory markers during acute phase
- Female sex



### Why do people get ongoing symptoms?

- The mechanisms that lead to PASC are still poorly understood and under ongoing study may be singular or multifactorial.
- Possible causes include:
  - organ dysfunction as a consequence of the acute illness
  - a persistent hyper-inflammatory state
  - cerebrovascular disease
  - cerebral hypoxia
  - adverse effects of medications such as sedatives or neuromuscular blockade
  - physical deconditioning
  - pre-existing comorbidities and psychological sequelae.

Symptoms may fluctuate and change in nature over time.



#### The top 10 most frequently reported symptoms

NB – prevalence varies between studies. Listed in no particular order

- 1. Fatigue
- 2. Breathlessness
- 3. Cough
- 4. Depression and anxiety
- 5. PTSD
- 6. Cognitive impairment ("brain fog")
- 7. Joint and muscle pain
- 8. Mobility impairment
- 9. Palpitations and chest pain
- 10. Loss of taste and/or smell



#### **PHOSP-COVID**

- 20 UK NHS trusts, from July 2020
- Analysis of 2320 at 5 months and 807 at 12 months
- Approx 40% of all admissions with COVID-19 (likely selection bias)

Recovered	5 months	12 months
Yes	25%	28.9%
Not sure	19.6%	22.4%
No	54.9%	48.8%

	One-year visit
Any symptoms	94.6%
Number of symptoms	9 (4-17)
Fatigue	60.1%
Aching in your muscles (pain)	54.6%
Physical slowing down	52.9%
Sleep disturbance	52.3%
Breathlessness	51.4%
Joint pain or swelling	47.6%
Slowing down in your thinking	46.7%
Pain	46.6%
Short term memory loss	44.6%
Limb weakness	41.9%

prative Group; Lancet Respir Med. 2022 Apr 22:S2213-2600(22)00127-8.

#### **Multidimensional face of PASC**



First 1000 assessed at 6 months.

The Lancet Respiratory Medicine 2021 91275-1287DOI: (10.1016/S2213-2600(21)00383-0)

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#### **Factors associated with worse recovery at 6 months**

	OK (95% CI)	p valu
Age at admission (years)		
<30	2.28 (0.83-6.29)	0.109
30-39	1.48 (0.73-2.97)	0.272
40-49	1.10 (0.64-1.88)	0.735
50-59	1 (ref)	
60-69	1.34 (0.85-2.12)	0.201
70-79	2.07 (1.13-3.80)	0.020
≥80	3.20 (1.44-7.14)	0.005
Sex at birth		
Male	1 (ref)	
Female	0.62 (0.43-0.92)	0.017
Ethnicity		
White	1 (ref)	
South Asian	1.54 (0.94-2.53)	0.085
Black	1.83 (0.99-3.39)	0.053
Mixed	1.69 (0.65-4.38)	0.279
Other	2.71 (1.32-5.59)	0.007
Index of multiple deprivation		
1 (most deprived)	1 (ref)	
2	1.17 (0.72-1.90)	0-522
3	0.85 (0.50-1.45)	0.550
4	1.22 (0.73-2.02)	0.450
5 (least deprived)	1.20 (0.73-1.99)	0.472
Number of comorbidities (factor)	(	- 17 -
None	1 (ref)	
1	0.97(0.62-1.51)	0.892
	0.65 (0.44-0.95)	0.026
PMI (2 lougis)	0.03 (0.44-0.93)	0.020
-20	1 (ref)	
- 30	0.74 (0.52, 1.04)	0.082
WHO divised progression scale	0.74 (0.53-1.04)	0.082
	1 (rof)	
Class 5-4	1 (rer)	
Class 5	1.11 (0.71-1.76)	0.640
	0.79 (0.43-1.45)	0.436
Class 7–9	0.54 (0.30-0.98)	0.034
Systemic (oral or intravenous) steroids	1 (6)	
	1 (ref)	
Yes	1.02 (0.70–1.49)	0.909
Antibiotic therapy		
	1 (ref)	
Yes	1.21 (0.77–1.90)	0.410
Therapeutic dose anticoagulation		
No	1 (ref)	
N/	0.78 (0.53, 4.45)	0.202

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The Lancet Respiratory Medicine 2021 91275-1287DOI: (10.1016/S2213-2600(21)00383-0)



#### **UK model integrated primary care**

Tier 1	on line support for self management of long covid symptoms
Tier 2	Management in General Practice with specialist phone support
Tier 3	GP/Specialist/Allied Health/Nursing run hospitals consults with presentation to a MDT of specialists from panel of specialists
Tier 4	only one Hospital in Greater Manchester super specialised panel with capacity to admit and specialty clinics eg CFS clinic (referral only from tier 3)
Overall principle	A single individual can be managed in a number of tiers simultaneously eMR

#### The importance of self-management





Support for Rehabilitation Self-Management after COVID-19-Related Illness

Name:

Discharge date:

Hospital where treated:

Healthcare professional providing leaflet:

Name and contact of local healthcare professional:





#### Where to now?

- 1. Structure and standardization;
  - a) Models of care that are themed to clinical problems (ie breathlessness, rehabilitation, cognition/neurological, psychosocial).
  - b) Evidence based approach to assessment and management
- 2. Access (A hierarchical approach)
  - a. Self management
  - b. Primary care and secondary care
  - c. Distribution and access to services
  - d. Challenges of social deprivation, chronic disease and minority groups
- 3. A culture to learn from experience and develop the evidence base for intervention.



#### A complex problem with solutions

Identifying traits that are treatable



Agusti et al http://dx.doi.org/10.1136/thoraxjnl-2014-205507

- 1. Assess each individual and their multiple symptoms/impairments
- 2. Apply sensible diagnostics and investigations
- 3. Identify traits that are treatable and assess severity
- 4. A hierarchical approach to management
  - Self management
  - Leverage & refer to services
     currently available
  - Those most impaired dedicated specialist services

## Asessing breathlessness post COVID-19





#### The top 10 most frequently reported symptoms

NB – prevalence varies between studies. Listed in no particular order

- 1. Fatigue
- 2. Breathlessness
- 3. Cough
- 4. Depression and anxiety
- 5. PTSD
- 6. Cognitive impairment ("brain fog")
- 7. Joint and muscle pain
- 8. Mobility impairment
- 9. Palpitations and chest pain
- 10. Loss of taste and/or smell

Breathlessness and palpitations and chest pain most likely to present to ED



#### **Breathlessness**

- Ongoing breathlessness occurs in 14.2 37% of people
- May be continual or on exertion
- Does not always directly correlate with measures of respiratory function but can still be debilitating
- Considerations:
  - Severity of acute illness
  - Acute complications
  - Level of respiratory support required during the acute illness e.g. use of NIV
  - Review comorbid cardiac or respiratory disease



#### **Persistent breathlessness**

- Dyspnea 38 studies (median [IQR], 29.7%; [14.2%-37.0%]), and
- Cough 26 studies (median [IQR], 13.1% [5.3%-22.6%])
- Lung function abnormalities
  - Pulmonary diffusion abnormalities (DLCO) (4 studies; median [IQR], 30.3% [22.1%-38.5%])
  - Restrictive spirometry (3 studies; median [IQR], 10.0% [6.1%-24.1%])
  - Ground glass opacification (7 studies; median [IQR], 23.1% [19.7%-43.0%])

Goff et al JAMA 2021



#### HRCT changes and COVID-19

Serial CT scans 46yr woman with severe acute COVID-19. *A*–*C*, day 32 after symptom onset show multiple ground-glass opacities and interstitial thickening with mild cylindrical traction bronchiectasis

*D–F*, Scans obtained on day 198 show partial absorption of the abnormalities, reduced extension, traction bronchiectasis

<u>Six-month Follow-up Chest CT Findings after Severe COVID-19 Pneumonia</u> Xiaoyu Han, Yanqing Fan, Osamah Alwalid, Na Li, Xi Jia, Mei Yuan, Yumin Li, Yukun Cao, Jin Gu, Hanping Wu, and Heshui Shi Radiology 2021 299:1, E177-E186



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# Persistent breathlessness-HRCT chest should not be needed in most and can be misleading

#### **UKILD** cohort

- N=3702, 240 days post discharge
- Assessed spirometry, DLCO and CXR risk of ILD then HRCT
- 6.9% were at high risk ILD
- 85% CT scans demonstrated ILD
- Risk of an abnormal CT
  - Severe acute pneumonitis
  - DLCO<80pp
  - Abnormal CXR

https://www.medrxiv.org/content/10.1101/2022.03.10.22272081v1 NSW Agency for Clinical Innovation





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Reduced with discharge anticoagulation

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### New or worsened dyspnoea, Pulmonary embolism?

Li et al JAMA Netw Open. 2021;4(11):e2135397. doi:10.1001/jamanetworkopen.2021.35397

- N=2832, post hospitalized COVID-19
- Up to 90 days post discharge
- 1.3% post-discharge venous • thromboembolic events (16 PE, 18 DVT, and 2 portal vein thrombosis)
- Risk increased, ۲
  - history of PE/DVT ٠
  - Predischarge CRP>10 or d-• dimer>3.0.







PE? New or worsened breathlessness consider PE Assess pre-test clinical probability +d-dimer High probability or d-dimer>0.5mg/ml Low probability, d-dimer<0.5mg/ml CTPA PE confirmed treat PE excluded, consider alternate diagnosis Indeterminate consider ventilation lung scan

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