



## PRACTICE POINTER

## Breathing difficulties after covid-19: a guide for primary care

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## What you need to know

- Breathing difficulties are common sequelae of covid-19
- Typically there are multiple contributing factors to breathing difficulties within an individual
- Breathing pattern disorder can be positively diagnosed from the history and clinical examination, but parallel investigations to rule out other causes may be necessary
- Self management support tools may help some patients regain a normal breathing pattern
- Further investigation and specialist respiratory physiotherapy should be considered when symptoms are not improving

Around one in four adults who were hospitalised with covid-19 and one in six who were not hospitalised experience persistent breathing difficulties beyond four weeks after SARS-CoV-2 infection,<sup>1,2</sup> and a cohort study in China demonstrated that breathlessness can persist beyond two years.<sup>3</sup> In long covid (defined as symptoms beyond four weeks<sup>4</sup>) breathing difficulties can be the predominant feature or be part of a multisystem presentation.<sup>5</sup> Cardiorespiratory complications after covid-19 include thromboembolic disease, interstitial lung disease, and heart failure and need to be excluded. This article predominantly focuses on other, more common causes of post-covid breathing difficulties that can be treated but are often less well understood.<sup>6</sup>

Definitive, evidence based protocols and treatment for persistent breathlessness after covid-19 are currently lacking. Until they exist, the pragmatic approach outlined here, including a careful history and examination and appropriate use of investigations, should help identify treatable conditions and improve symptoms. In particular, a positive diagnosis of breathing pattern disorder (box 2) can often be made in general practice. Self management resources (box 3) should be offered early. Timely referral to specialist services is needed for patients whose symptoms are severe or progressive.

## Presentation of breathing difficulties

Breathing difficulties can present in several ways, including breathlessness or pressure, tightness, soreness, and pain or burning in the chest. These symptoms can be associated with considerable distress. The general multisystem approach and investigation of breathlessness tends to be similar despite the interval between healthcare presentation and infection. Although there is some natural recovery in persisting symptoms between four to 12

weeks, it is difficult to predict at an individual level, and early support is often needed.<sup>7</sup> Box 1 describes a typical patient narrative.

## Box 1: Breathing difficulties after covid-19—a patient's story

I had covid-19 early in 2020. At the time of my initial illness, my breathlessness was not too bad, but about four weeks after and throughout the following months it became awful. I would be gasping for air and unable to speak, and my oxygen level would drop significantly. Over two and a half years later, I still experience breathlessness daily.

Initially, I didn't know what was wrong. It was frightening, but I couldn't get any investigations on the NHS. Many of us who were ill in the first wave were told to stay away from hospital unless having a heart attack or "turning blue." I can feel very breathless even whilst sitting down; it feels like I am breathing in through a straw that collapses and stops me from getting air in. I also feel breathless when speaking, even for a short time, and my chest can feel very sore, as if the air is grating on my windpipe.

It took over a year before I had a video appointment with a long covid clinic. Eventually I had a chest x ray (which was normal) and an echocardiogram. Although the echo showed the tachycardia I was also experiencing and revealed some other issues, I was told that these did not explain the severe ongoing breathlessness that was significantly impacting my whole life. I wasn't given any specific treatment, but I was referred to a respiratory physiotherapist. I had already been doing some breathing exercises so was sceptical, but it actually proved quite helpful and made me realise just how bad the way I was breathing had been.

I now use what I learnt from the physio every day and, although I still suffer from breathlessness, it helps me to control how I am breathing, to pace my breathing, and also helps my tachycardia. I underwent lung function testing in February 2023—nearly three years since I had covid-19.

Nikki Smith, person with lived experience of long covid, aged 51 years

## Pathophysiology of breathing difficulties after covid-19

Some patients with acute covid-19 develop pneumonitis, characterised on imaging by a variety of patchy or diffuse airspace opacities. Radiological changes generally clear over a few weeks, but breathing difficulties may persist. The pathophysiology of these and other manifestations of long covid remains poorly understood, but ongoing inflammation—including autoantibody response, clotting changes, and perfusion deficits—may play a role.<sup>8-12</sup>

Breathing difficulties may be compounded by pre-existing respiratory conditions such as asthma

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and by other symptoms of long covid, particularly those related to dysautonomia.<sup>13</sup> In non-covid breathlessness, even when there is clear involvement of a primary organ (such as heart failure or chronic obstructive pulmonary disease), the degree of exercise intolerance is not closely related to the severity of organ impairment.<sup>14</sup> Other factors such as deconditioning (loss of aerobic capacity), mood disturbance, and obesity contribute to breathlessness,<sup>15-17</sup> and may play a role in long covid. There are likely multiple contributing factors to breathing difficulties in long covid within an individual similar to non-covid related breathlessness.<sup>18</sup>

### Breathing pattern disorder

Clinical and lived experience suggests long covid is commonly associated with breathing pattern disorder (dysfunctional breathing), supported by early study findings.<sup>6,19</sup> The term describes inefficient breathing which can present in a variety of ways (box 2). It can be precipitated and perpetuated by a range of factors and result in differing degrees of functional impairment. Breathing pattern disorder is not exclusive to covid-19, being reported in 8% of adults (14% of women, 2% of men), and 29% of people with asthma.<sup>24</sup> It may co-occur with other cardiorespiratory diseases.<sup>25</sup> The pathophysiology is still being elucidated but has broadly been described into three categories: biomechanical, neurocognitive, and biochemical.<sup>20-26-28</sup>

#### Box 2: Breathing pattern disorder

##### History

The features listed below can indicate breathing pattern disorder but may or may not be present and not all have to be present to support the diagnosis.

- Breathlessness characterised by
  - Excessive awareness of breathing
  - Air hunger (feeling unable to take a deep enough breath)
  - Feeling that breathing is no longer automatic
  - Feeling of pressure or heavy weight on chest
  - Disproportionately out of breath on exertion or at rest
  - Variability in how and when breathlessness occurs
- Classic hyperventilation symptoms
  - Dizziness
  - Blurred vision
  - Pins and needles in the extremities
  - Palpitations
  - Anxiety
- Other systemic symptoms including
  - Bloating
  - Muscle tension in the neck and shoulders
  - Headaches

##### Clinical features

- Thoracic dominant breathing (mostly in the upper chest with insufficient use of the diaphragm)
- Deep sighing and frequent yawning
- Mouth breathing

- Thoraco-abdominal asynchrony (work of ribcage and diaphragm are not aligned)
- Forced abdominal expiration (inappropriate and excessive abdominal muscle contraction in aid of expiration)
- A positive response to breathing retraining treatment makes the diagnosis of breathing pattern disorder more likely

##### Useful tools to aid clinical assessment

- Self-Evaluation of Breathing Questionnaire<sup>20</sup>
- Breathing Pattern Assessment Tool<sup>21</sup> (which seems to have reasonable sensitivity (89.5%) and specificity (78.3%) from one study when used in adults with long covid<sup>22</sup>)
- Other questionnaires
  - The Nijmegen Questionnaire is commonly used, but it was originally validated for hyperventilation and can miss other manifestations of breathing pattern disorder<sup>23</sup>

- Biomechanical:
  - Altered respiratory mechanics (such as basal pneumonia/pneumonitis during acute phase of covid-19) leading to rapid shallow breathing avoiding use of the diaphragm, which then becomes habitual
  - Chest wall pain from muscle tension or costochondritis.
- Neurocognitive:
  - Abnormal interoception (how the central and peripheral nervous systems receive and interpret information about changes to internal bodily processes)
  - Dysfunction of autonomic nervous system, including postural orthostatic tachycardia syndrome
  - Reactive affective impact on neurocognition.
- Biochemical:
  - Hyperventilation leading to hypocapnia and wider electrolyte imbalance.

### Questions patients may ask

Below, we address questions which patients with breathing difficulties after covid-19 might ask their general practitioner.

## 1. Do my breathing difficulties indicate a serious or life threatening problem?

Table 1 offers differential diagnoses from different features of the patient's history and clinical examination. While it is appreciated presentations can overlap, the most common or suggestive features for a particular condition are highlighted. Note the various "red flags," which suggest serious pathology.<sup>30-31</sup> Ask the patient to describe their breathing problem in their own words, paying particular attention to the trajectory.<sup>29</sup> In many cases the patient can be reassured that, although their persisting breathlessness is distressing and perhaps disabling, it does not indicate an underlying life threatening condition.

Table 1 | Assessment and differential diagnosis of the patient with persistent breathlessness after covid-19 (Synthesised from various sources)

History	Clinical examination	Differential diagnosis
<b>Red flags</b>		
<ul style="list-style-type: none"> <li>Persistent, progressive breathlessness on exertion (and eventually at rest)</li> <li>Rapid deterioration</li> <li>Severe impairment (eg, too breathless to walk)</li> <li>Breathlessness with haemoptysis</li> <li>Significant smoking history in context of above</li> </ul>	<ul style="list-style-type: none"> <li>Unexplained hypoxia or exertional desaturation</li> <li>Altered mental status</li> <li>Persistent tachycardia</li> <li>Hypotension</li> <li>Signs of deep vein thrombosis</li> <li>Signs of cardiac strain (eg, heave, neck vein distension, additional heart sound, unexplained murmurs)</li> <li>Unstable cardiac arrhythmia</li> <li>Marked asymmetry in breath sounds</li> <li>True stridor (inspiratory, persistent)</li> </ul>	Identify or exclude serious conditions (due to covid-19 or other pathology) such as heart failure, arrhythmia, coronary artery disease, pulmonary emboli, pulmonary hypertension, pulmonary fibrosis, myocarditis/pericarditis, lung cancer, pleural effusion, pneumothorax or lung collapse, laryngeal obstruction
<b>Linked to previous covid-19</b>		
Breathlessness persisting after 4 weeks with ongoing trajectory of improvement	Elevated respiratory rate, hypoxia, generalised or focal crackles	Resolving covid pneumonitis (seen especially in patients hospitalised with acute covid-19)
Excessive awareness of breathing, pressure or tightness, air hunger	Thoracic breathing, sighing, yawning, mouth breathing, irregular breathing	Long covid and breathing pattern disorder (box 2)
Persistent or intermittent breathlessness with other symptoms (eg, fatigue, brain fog, joint pains)	Variable; there may be few or no abnormal findings	Long covid and investigate breathlessness in context of other symptoms. Breathing pattern disorder can occur in isolation or alongside multiple symptoms
Breathlessness with palpitations or fast heart rate, especially on standing	Sustained increase in heart rate on standing of 30 bpm or to >120 bpm, absence of hypotension	Long covid with dysautonomia or postural orthostatic tachycardia syndrome (covered in previous article in this series <sup>29</sup> )
Breathlessness and loss of voice with talking	Audible noisy breathing and wheeze (often variable)	Intermittent laryngeal obstruction or vocal cord dysfunction. Important to distinguish from true stridor, which requires urgent ENT referral
Exertional breathlessness may not be progressive	Variable; can be normal or have bilateral inspiratory crackles	Covid related interstitial lung disease or pulmonary fibrosis
<b>Non-covid causes</b>		
Intermittent breathlessness with familial or atopic history, nocturnal pattern, triggers	Variable; can be normal. Widespread wheezing, accessory muscle use, decreased breath sounds, pulsus paradoxus	Asthma: exclude acute severe or life threatening asthma
Persistent breathlessness with exacerbations, particularly in winter months	Variable; can be normal. Widespread wheezing, accessory muscle use, decreased breath sounds, pulsus paradoxus	Exacerbation of chronic obstructive pulmonary disease
Breathlessness, acutely unwell and deteriorating	Fever, crackles, bronchial breathing	Pneumonia
Sudden or progressive breathlessness and worsening exercise tolerance over days or weeks	Localised, decreased, or absent breath sounds	Pneumothorax (commonly starts with pain), pleural effusion, lung or lobar collapse
Progressive breathlessness and worsening exercise tolerance over weeks or months	Variable; can be normal. Fine end-inspiratory basal crackles Elevated JVP, 3rd or 4th heart sound, peripheral oedema Ejection systolic murmur over right carotid area	Interstitial lung disease or pulmonary fibrosis Heart failure (consider underlying coronary heart disease) Aortic stenosis
bpm = beats per minute. ENT = ear, nose, and throat. JVP = jugular venous pulse.		

## 2. Why do I feel anxious?

Persistent or chronic breathlessness is a complex symptom with multiple, interrelated contributing factors.<sup>32</sup> Breathlessness can trigger anxiety, and anxiety can exacerbate breathlessness. Patients with long covid often describe feeling “on-edge” or “stuck in fight or flight mode,” perhaps as part of dysautonomia in long covid,<sup>33</sup> and this can contribute to breathlessness. Furthermore, there may be concern about the underlying cause, delays in being investigated, and not being believed when seeking medical care. Breathlessness and long covid in general must be recognised as potentially disabling, distressing, even life changing, and deserving of an appropriately comprehensive clinical assessment.

## 3. What tests should I have?

Initial investigations should be informed by the specific clinical presentation. If there are no red flags, a reasonable starting point is pulse oximetry, blood tests, an electrocardiogram, and a chest radiograph (table 2) and low threshold for spirometry where airway diseases are considered.<sup>35</sup> Questionnaires to assess mood and physical activity<sup>35</sup> can inform decisions around treatment planning. Other respiratory conditions such as asthma may coexist with sequelae of covid-19, and other features of long covid such as dysautonomia may worsen breathlessness, so assessment for these should form part of the investigations.<sup>36</sup>

Table 2 | Investigations to consider for breathing difficulties after covid-19

Investigation	Reason
Oximetry (at rest and using 1-minute sit-to-stand test <sup>20</sup> )*	Unexplained resting hypoxia or exertional desaturation requires urgent investigation
Haemoglobin (and ferritin where indicated)*	Anaemia, iron deficiency
Chest x ray*	Post-covid interstitial lung disease, exclude other causes of breathlessness including malignancy
Electrocardiogram (with troponin, creatinine kinase, and C reactive protein tests where indicated)*	Arrhythmia, myocarditis, cardiomyopathy
Brain natriuretic peptide	Heart failure
NASA Lean Test or adapted Autonomic Profile <sup>34</sup>	Postural orthostatic tachycardia syndrome
Spirometry and bronchodilator reversibility	Commonly normal in long covid. May indicate obstructive (eg, asthma) or restrictive (eg, interstitial) lung disease
Fractional exhaled nitric oxide (FeNO) and review historical blood eosinophil counts	Where eosinophilic asthma or post-viral wheeze is considered and spirometry is normal
Patient Health Questionnaire 9 (PHQ-9), Generalised Anxiety Disorder 7 (GAD-7)	Assesses symptoms suggestive of depression and anxiety but need to interpret in context of any long term condition including long covid
Physical activity history, perhaps using GP Physical Activity Questionnaire (GPPAQ) <sup>35</sup>	Physical inactivity for impact of breathlessness and potential contributing factor of physical deconditioning
The Self Evaluation of Breathing Questionnaire <sup>20</sup>	Screening tool for breathing pattern disorder where a score >11 may indicate a problem

\* Should be considered in all patients with persisting breathlessness

#### 4. What if the tests don't show anything?

If initial tests are normal and the diagnosis remains unclear, further tailored investigation or referral to a specialist long covid clinic may be needed. It is important to let the patient know that long covid is by no means the only disabling condition in which standard medical investigations are unremarkable. Negative investigations alone are rarely enough to reassure or help the symptomatic patient. They require either an explanation of why they are breathless and what can be done in primary care, or a clear plan to further investigate or refer.

There are currently no specific biomarkers for breathing pattern disorder. For this reason, many clinicians believe that the diagnosis can only be made by exclusion of other conditions. However, several commonly occurring features in the history and physical examination can help to make breathing pattern disorder a positive clinical diagnosis (box 2).

#### 5. What can I do for myself?

If specialist services are unavailable locally or there is a wait for an appointment, primary care practitioners can signpost patients to relevant professional and self help websites for breathing pattern disorder (box 3). If the patient is physically inactive or overweight, increasing physical activity and weight management may help. However, fatigue and post-exertional symptom exacerbation can limit how much physical exertion a patient with long covid can tolerate; hence personalised pacing advice is recommended.<sup>13</sup> Randomised trials are lacking, but some people find the gentle movements and stretching, such as Tai Chi and some forms of yoga, are helpful, as can be developing a daily routine of using relaxation strategies (such as consciously relaxing the muscles around the neck and shoulders), consciously breathing through the nose, focusing on the stomach moving more than the chest during breathing, and being in well ventilated areas or using a handheld fan.<sup>26</sup>

#### Box 3: Resources for clinicians and patients

- SIGN guidelines for managing the long-term effects of COVID-19 (<https://www.sign.ac.uk/our-guidelines/managing-the-long-term-effects-of-covid-19/>)<sup>4</sup>
- Physio for BPD ([www.physiotherapyforbpd.org.uk](http://www.physiotherapyforbpd.org.uk))
  - Created by physiotherapists specialising in breathing pattern disorders. Contains information on breathing pattern disorder, the association with long covid, and advice on self management
- Long Covid Physio (<https://longcovid.physio/breathing-pattern-disorders/>)
  - Created by physiotherapists living with long-covid and respiratory physiotherapists. Contains step-by-step instructions to breathing retraining techniques
- Your COVID Recovery ([www.yourcovidrecovery.nhs.uk](http://www.yourcovidrecovery.nhs.uk))
  - Co-designed by patients and clinicians, advice on self management of breathlessness after covid-19 as well as other symptoms
- Long Covid Support (<https://www.longcovid.org>)
  - A charity formed by people with long covid, including people who work in the healthcare profession. Includes a peer support group, a programme of social and wellbeing activities including online yoga and opera breathing, and signposts to other useful information on long covid
- Yoga and Meditation for Covid Recovery (<https://www.youtube.com/c/YogaforLongCovidwithSuzyBolt36omind-bodysoul>)
  - A yoga teacher who has long covid has adapted gentle yoga and strength building classes for others with the condition
- The Long Covid Self-Help Guide. Green Tree, 2022<sup>26</sup>
- Spathis A, Booth S, Moffat C, et al. The breathing, thinking, functioning clinical model: a proposal to facilitate evidence-based breathlessness management in chronic respiratory disease. *NPJ Prim Care Respir Med* 2017;27:27<sup>32</sup>

#### 6. Do I need to see a specialist?

Not all patients with persistent breathlessness after covid-19 need specialist referral. The primary care approach should include taking a history, tailored examination, and baseline investigations, offering empathy and explanation, managing treatable symptoms such as those from breathing pattern disorder and comorbidities, defining a clear baseline (including pre-existing breathlessness), and following up to monitor progress. Patients should be referred to a specialist cardiorespiratory or other appropriate service if red flag indicators are present; if symptoms are severe, unresolving, or negatively affecting daily life including occupation; or if the diagnosis is in doubt. If breathlessness is one symptom of many, referral to a multidisciplinary long covid service for holistic assessment and management is advised.<sup>37</sup> Covid rehabilitation programmes, many adapted from pulmonary rehabilitation models,<sup>38</sup> may also help.<sup>39</sup> Early results show potential for improvements in breathlessness,<sup>140</sup> and more formal research trials are under way.

## 7. Will breathing exercises help?

Self management and educational resources (box 3) can help patients learn about breathing pattern disorder and breathing retraining techniques. However, many patients benefit further from assessment by a specialist respiratory physiotherapist, who can provide a more bespoke treatment approach and help patients understand their particular presentation and how best to manage it. Key elements of treatment include restoring nose breathing rather than mouth breathing, reducing upper thoracic ventilation (often caused by overuse of the accessory muscles of breathing), and focusing on reducing tidal volume and respiratory rate. Typically, exercises are first taught in a semi-supine position, and progressed through sitting and standing into activities tailored to the individual patient. As emotions are closely linked to breathing, general relaxation techniques are also useful in restoring normal vagal tone and releasing abnormal muscle tension.<sup>41 42</sup> The Breathing, Thinking, Functioning model of breathlessness<sup>32</sup> is a useful tool to help health professionals understand and manage chronic breathlessness. The model explains why breathlessness happens and supports health professionals to provide personalised breathlessness management for their patients. It frames symptoms for patients in an understandable way, linking why breathlessness occurs and the impact of emotions and inactivity on breathlessness.

## 8. Will I get better—and what if I don't?

Breathing retraining has become an integral part of long covid management,<sup>37</sup> but research findings in long covid are currently limited. Efficacy has been evaluated in other long term respiratory conditions such as asthma, and breathing retraining improves health related quality of life when delivered face-to-face and via digital methods.<sup>43 44</sup> In long covid, a six week breathing and wellbeing programme delivered virtually improved some components of both quality of life and breathlessness in the short term.<sup>45</sup> Overall, clinical experience suggest symptoms can be improved, but unresolved symptoms merit specialist referral.

## 9. What research is ongoing?

Ongoing UK studies are assessing causes and treatment of breathlessness including lung damage using hyperpolarised magnetic resonance imaging,<sup>46</sup> management of ongoing venous thromboembolic pathology,<sup>47 48</sup> and multi-dimensional

rehabilitation programmes. Further research is needed to understand the epidemiology, trajectory, underlying mechanisms, and treatments for long covid breathlessness. Objective markers for breathing pattern disorder (covid and non-covid related) are urgently needed for diagnosis and response to treatment.

### How patients were involved in the creation of this article

Patients are members of the LOCOMOTION quality improvement collaborative. NS has lived experience of breathing difficulties, including breathing pattern disorder in long covid, and is networked with others with lived experience via the patient advisory group for LOCOMOTION, as well as to patient support groups, the Long Covid Support charity, and various other research studies. The paper was read by three additional patients with long covid and modified in response to their feedback.

### How this article was created

This article builds on a recent general introduction to long covid for primary care clinicians.<sup>13</sup> The authors are an interdisciplinary team with expertise in clinical management of long covid in primary and secondary care, specialist respiratory management of breathing disorders, systematic review, and lived experience of long covid.

The idea for the paper emerged from a long covid quality improvement collaborative (part of the NIHR-funded LOCOMOTION study<sup>49</sup>), which brought together 30 clinicians from 10 long covid services in the UK to share case histories and analyse service provision; patients attended parts of some of these meetings. Clinical experiences and literature known to participants were shared and discussed at the collaborative.

A targeted literature search was conducted with specialist librarian support, with a primary focus on breathing difficulties (breathlessness/dyspnoea) following covid-19 but also including selected seminal articles on breathlessness and breathing pattern disorders more generally. Around 2000 articles were retrieved from Embase and Medline, and 100 were considered relevant. Specialists in this condition were contacted and asked to suggest additional references. We also took account of patient-facing literature and websites. Published sources, clinical experiences (both patient and clinician), and patient expertise were combined by narrative synthesis.

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- 1 European Centre for Disease Prevention and Control. Technical report. Prevalence of post COVID-19 condition symptoms: a systematic review and meta-analysis of cohort study data, stratified by recruitment setting. 2022. <https://www.ecdc.europa.eu/sites/default/files/documents/Prevalence-post-COVID-19-condition-symptoms.pdf>.
- 2 Zheng B, Daines L, Han Q, et al. Prevalence, risk factors and treatments for post-COVID-19 breathlessness: a systematic review and meta-analysis. *Eur Respir Rev* 2022;31:220071. doi: 10.1183/16000617.0071-2022 pmid: 36323418
- 3 Huang L, Li X, Gu X, et al. Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study. *Lancet Respir Med* 2022;10:76. doi: 10.1016/S2213-2600(22)00126-6 pmid: 35568052

- 4 National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19 (NICE guideline NG188). 2021. <https://www.nice.org.uk/guidance/ng188>.
- 5 Whitaker M, Elliott J, Chadeau-Hyam M, et al. Persistent COVID-19 symptoms in a community study of 606,434 people in England. *Nat Commun* 2022;13. doi: 10.1038/s41467-022-29521-z pmid: 35413949
- 6 Heightman M, Prashar J, Hillman TE, et al. Post-COVID-19 assessment in a specialist clinical service: a 12-month, single-centre, prospective study in 1325 individuals. *BMJ Open Respir Res* 2021;8:e001041. doi: 10.1136/bmjresp-2021-001041 pmid: 34764200
- 7 Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of long COVID. *Nat Med* 2021;27:31. doi: 10.1038/s41591-021-01292-y pmid: 33692530
- 8 Grist JT, Collier GJ, Walters H, et al. Lung abnormalities detected with hyperpolarized <sup>129</sup>Xe MRI in patients with long COVID. *Radiology* 2022;305:17. doi: 10.1148/radiol.220069 pmid: 35608443
- 9 Acosta-Ampudia Y, Monsalve DM, Rojas M, et al. Persistent autoimmune activation and proinflammatory state in post-coronavirus disease 2019 syndrome. *J Infect Dis* 2022;225:62. doi: 10.1093/infdis/jiac017 pmid: 35079804
- 10 Rojas M, Rodríguez Y, Acosta-Ampudia Y, et al. Autoimmunity is a hallmark of post-COVID syndrome. *J Transl Med* 2022;20. doi: 10.1186/s12967-022-03328-4 pmid: 35296346
- 11 Glynne P, Tahmasebi N, Gant V, Gupta R. Long COVID following mild SARS-CoV-2 infection: characteristic T cell alterations and response to antihistamines. *J Investig Med* 2022;70:7. doi: 10.1136/jim-2021-002051 pmid: 34611034
- 12 Knight R, Walker V, Ip S, et al. COVID-UK/COVID-IMPACT Consortium and the Longitudinal Health and Wellbeing COVID-19 National Core Study. Association of COVID-19 with major arterial and venous thrombotic diseases: a population-wide cohort study of 48 million adults in England and Wales. *Circulation* 2022;146:906. doi: 10.1161/CIRCULATIONAHA.122.060785 pmid: 36121907
- 13 Greenhalgh T, Sivan M, Delaney B, Evans R, Milne R. Long covid-an update for primary care. *BMJ* 2022;378:e072117. doi: 10.1136/bmj-2022-072117 pmid: 36137612
- 14 Gosker HR, Lencer NH, Franssen FM, van der Vusse GJ, Wouters EF, Schols AM. Striking similarities in systemic factors contributing to decreased exercise capacity in patients with severe chronic heart failure or COPD. *Chest* 2003;123:24. doi: 10.1378/chest.123.5.1416 pmid: 12740256
- 15 Kersten J, Hoyo L, Wolf A, et al. Cardiopulmonary exercise testing distinguishes between post-COVID-19 as a dysfunctional syndrome and organ pathologies. *Int J Environ Res Public Health* 2022;19. doi: 10.3390/ijerph19181421 pmid: 36141693
- 16 Ahmadi Z. The burden of chronic breathlessness across the population. *Curr Opin Support Palliat Care* 2018;12:8. doi: 10.1097/SPC.0000000000000364 pmid: 29927754
- 17 Mahler DA, Fierro-Carrion G, Baird JC. Evaluation of dyspnea in the elderly. *Clin Geriatr Med* 2003;19:33. v. doi: 10.1016/S0749-0690(02)00050-2 pmid: 12735113
- 18 Sandberg J, Olsson M, Ekström M. Underlying conditions contributing to breathlessness in the population. *Curr Opin Support Palliat Care* 2021;15:25. doi: 10.1097/SPC.0000000000000568 pmid: 34610625
- 19 Frésard I, Genecand L, Altarelli M, et al. Dysfunctional breathing diagnosed by cardiopulmonary exercise testing in 'long COVID' patients with persistent dyspnoea. *BMJ Open Respir Res* 2022;9:e001126. doi: 10.1136/bmjresp-2021-001126 pmid: 35354589
- 20 Courtney R, Greenwood KM. Preliminary investigation of a measure of dysfunctional breathing symptoms: The Self Evaluation of Breathing Questionnaire (SEBQ). *Int J Osteopath Med* 2009;12:7. doi: 10.1016/j.ijosm.2009.02.001.
- 21 Todd S, Walsted ES, Grillo L, Livingston R, Menzies-Gow A, Hull JH. Novel assessment tool to detect breathing pattern disorder in patients with refractory asthma. *Respirology* 2018;23:90. doi: 10.1111/resp.13173 pmid: 28905471
- 22 Hylton H, Long A, Francis C, et al. Real-world use of the Breathing Pattern Assessment Tool in assessment of breathlessness post-COVID-19. *Clin Med (Lond)* 2022;22:9. doi: 10.7861/clinmed.2021-0759 pmid: 35760447
- 23 Boulding R, Stacey R, Niven R, Fowler SJ. Dysfunctional breathing: a review of the literature and proposal for classification. *Eur Respir Rev* 2016;25:94. doi: 10.1183/16000617.0088-2015 pmid: 27581828
- 24 Thomas M, McKinley RK, Freeman E, Foy C, Price D. The prevalence of dysfunctional breathing in adults in the community with and without asthma. *Prim Care Respir J* 2005;14:82. doi: 10.1016/j.pcrj.2004.10.007 pmid: 16701702
- 25 Law N, Ruane LE, Low K, Hamza K, Bardin PG. Dysfunctional breathing is more frequent in chronic obstructive pulmonary disease than in asthma and in health. *Respir Physiol Neurobiol* 2018;247:3. doi: 10.1016/j.resp.2017.08.011 pmid: 28870869
- 26 Specialists at the Post-Covid Clinic Oxford. *The Long Covid Self-Help Guide*. Green Tree, 2022.
- 27 Burton C, Dalton C, Dawes H. Associations between symptoms and of symptoms with activity in long covid: an intensive longitudinal study. *J Psychosom Res* 2022;157:110832. doi: 10.1016/j.jpsychores.2022.110832.
- 28 Faull OK, Subramanian HH, Ezra M, Pattinson KTS. The midbrain periaqueductal gray as an integrative and interoceptive neural structure for breathing. *Neurosci Biobehav Rev* 2019;98:44. doi: 10.1016/j.neubiorev.2018.12.020 pmid: 30611797
- 29 Greenhalgh T, Koh GCH, Car J. Covid-19: a remote assessment in primary care. *BMJ* 2020;368. doi: 10.1136/bmj.m1182 pmid: 32213507
- 30 Kalin A, Javid B, Knight M, Inada-Kim M, Greenhalgh T. Direct and indirect evidence of efficacy and safety of rapid exercise tests for exertional desaturation in Covid-19: a rapid systematic review. *Syst Rev* 2021;10. doi: 10.1186/s13643-021-01620-w pmid: 33726854
- 31 Baxter N, Loneragan P. Primary Care Respiratory Update. The differential diagnosis of the breathless patient. 2020. <https://www.pcrs-uk.org/resource/differential-diagnosis-breathless-patient>.
- 32 Spathis A, Booth S, Moffat C, et al. The breathing, thinking, functioning clinical model: a proposal to facilitate evidence-based breathlessness management in chronic respiratory disease. *NPJ Prim Care Respir Med* 2017;27. doi: 10.1038/s41533-017-0024-z pmid: 28432286
- 33 Espinosa-Gonzalez AB, Master H, Gall N, Halpin S, Rogers N, Greenhalgh T. Orthostatic tachycardia after covid-19. *BMJ* 2023;380:e073488. doi: 10.1136/bmj-2022-073488 pmid: 36828559
- 34 Sivan M, Corrado J, Mathias C. The Adapted Autonomic Profile (Aap) home-based test for the evaluation of neuro-cardiovascular autonomic dysfunction. *Adv Clin Neurosci Rehabil* 2022; doi: 10.47795/QKBU6715.
- 35 National Institute of Health and Care Excellence. Clinical Knowledge Summary. Breathlessness. 2022. <https://cks.nice.org.uk/topics/breathlessness/>.
- 36 Nurek M, Rayner C, Freyer A, et al. Delphi panellists. Recommendations for the recognition, diagnosis, and management of long COVID: a Delphi study. *Br J Gen Pract* 2021;71:25. doi: 10.3399/BJGP.2021.0265 pmid: 34607799
- 37 NHS England. National commissioning guidance for post COVID services. 2022. <https://www.england.nhs.uk/publication/national-commissioning-guidance-for-post-covid-services/>.
- 38 Lacasse Y, Brosseau L, Milne S, et al. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2002;(3):CD003793. pmid: 12137716
- 39 World Health Organisation. COVID-19 clinical management: living guideline (15th September 2022 update). 2022. <https://www.who.int/publications/item/WHO-2019-nCoV-Clinical-2022.2>.
- 40 Fugazzaro S, Contri A, Esseroukh O, et al. Regional Emilia COVID-19 Working Group. Rehabilitation interventions for post-acute COVID-19 syndrome: a systematic review. *Int J Environ Res Public Health* 2022;19. doi: 10.3390/ijerph19091855 pmid: 35564579
- 41 Holloway EA, West RJ. Integrated breathing and relaxation training (the Papworth method) for adults with asthma in primary care: a randomised controlled trial. *Thorax* 2007;62:42. doi: 10.1136/thx.2006.076430 pmid: 17573445
- 42 Bradley D. Physiotherapy in rehabilitation of breathing pattern disorders. In: *Recognizing and treating breathing disorders*. Elsevier, 2014: -96. doi: 10.1016/B978-0-7020-4980-4.00017-4.
- 43 Thomas M, McKinley RK, Mellor S, et al. Breathing exercises for asthma: a randomised controlled trial. *Thorax* 2009;64:61. doi: 10.1136/thx.2008.100867 pmid: 19052047
- 44 Bruton A, Lee A, Yardley L, et al. Physiotherapy breathing retraining for asthma: a randomised controlled trial. *Lancet Respir Med* 2018;6:28. doi: 10.1016/S2213-2600(17)30474-5 pmid: 29248433
- 45 Philip KEJ, Owles H, McVey S, et al. An online breathing and wellbeing programme (ENO Breathe) for people with persistent symptoms following COVID-19: a parallel-group, single-blind, randomised controlled trial. *Lancet Respir Med* 2022;10:62. doi: 10.1016/S2213-2600(22)00125-4 pmid: 35489367
- 46 Gleeson F. ISRCTN14304264. An investigation to explore the use of a type of MRI scan using an inhaled gas in identifying lung damage associated with long COVID sufferers. *ISRCTN Registry* 2022. <https://www.isrctn.com/ISRCTN14304264>.
- 47 ClinicalTrials.gov. NCT04801940. HELPing Alleviate the Longer-term Consequences of COVID-19 (HEAL-COVID). 2022. <https://clinicaltrials.gov/ct2/show/NCT04801940>.
- 48 Ramasawmy M, Mu Y, Clutterbuck D, et al. STIMULATE-ICP Consortium. STIMULATE-ICP-CAREINEQUAL (Symptoms, Trajectory, Inequalities and Management: Understanding Long-COVID to Address and Transform Existing Integrated Care Pathways) study protocol: defining usual care and examining inequalities in Long Covid support. *PLoS One* 2022;17:e0271978. doi: 10.1371/journal.pone.0271978 pmid: 35969597
- 49 Sivan M, Greenhalgh T, Darbyshire JL, et al. Locomotion consortium. Long Covid Multidisciplinary consortium Optimising Treatments and services across the NHS (LOCOMOTION): protocol for a mixed-methods study in the UK. *BMJ Open* 2022;12:e063505. doi: 10.1136/bmjopen-2022-063505 pmid: 35580970