

# COVID-19 and what comes after?

Nicholas S Hopkinson <sup>1</sup>, Gisli Jenkins <sup>2</sup>, Nicholas Hart<sup>3</sup>

At the end of January 2020, the WHO declared the SARS-CoV-2 outbreak a public health emergency of international concern, its highest level of alarm. Although measures in the UK to reduce spread and 'protect the NHS' did prevent a complete collapse of the acute health-care system, delay in the implementation of a lockdown until 23 March led to tens of thousands of excess deaths and, by December, more than 220,000 COVID-19 hospital admissions, with effects for many individuals persisting beyond hospital discharge (<https://coronavirus.data.gov.uk/healthcare>).<sup>1-5</sup>

The SARS-CoV-2 targets the respiratory epithelium and has a myriad of clinical consequences ranging from asymptomatic illness, through to mild, moderate and severe disease. Although the initial illness leads primarily to respiratory symptoms, many patients will have physical, cognitive and psychological disability that will require long-term management. In this edition of *Thorax*, four Brief Communications from the UK and Canada report the short-term to medium-term post-discharge outcome of hospitalised COVID-19 patients, identifying a pattern of five key persisting symptoms: breathlessness, cough, fatigue, muscle and joint pain and poor sleep quality.<sup>6-9</sup> Mandal and colleagues recruited 384 patients from three large London hospitals.<sup>6</sup> A median 54 days after discharge, approximately half of the patients reported persistent breathlessness with a third reporting an ongoing cough. Two-thirds of patients described persistent fatigue and poor sleep with 15% reporting scores consistent with depression. Biomarkers of ongoing inflammation (D-dimer and CRP) were commonly elevated. Only 11% of patients reported an absence of all four of these key symptoms. Of note, although respiratory disease was a common comorbidity in hospitalised patients, the MRC Dyspnoea Score at follow-up was not different between those with and without

pre-existing respiratory disease (both median (IQR) 2 (1-3)).

Arnold and colleagues in Bristol<sup>8</sup> report the follow-up of 110 patients at a median of 83 days following their hospital admission. In this study, almost three-quarters of patients reported at least one ongoing symptom with 39% describing breathlessness, 39% fatigue and 24% insomnia. Persisting symptoms were more common in those who had a more severe initial illness. Importantly, even in the group that did not require supplemental oxygen during admission, 26% reported ongoing breathlessness and fatigue with poor sleep quality.

In a third study by Hall and colleagues in London,<sup>7</sup> the investigators screened patients by telephone prior to clinic and reported that one third of patients had returned to baseline functional level and declined clinic attendance, one third were unsuitable for clinic due to their clinical status or were uncontactable and one third had persistent symptoms. Although breathlessness was a prominent feature in the 200 individuals with persistent symptoms who were reviewed, with a median MRC Score of  $2.6 \pm 1.2$ , 31% of patients had not required oxygen on admission during the acute illness. Of the 170 patients who underwent a 6-minute walk test, one third of patients had an oxygen desaturation of greater than 4% and 27% and 44% of patients studied demonstrated a reduction in lung volumes and gas transfer, respectively. Persistent radiological abnormalities on chest imaging were observed in a third of patients followed up.

In Vancouver, Shah and colleagues<sup>9</sup> conducted a prospective post-discharge study in 60 patients reviewed 12 weeks following symptom onset. Pulmonary function abnormalities were common, with reduced gas transfer in 52% and a reduction in total lung capacity in 45%. Persistent CT changes were almost universal; 83% of patients had areas of ground glass and 65% areas of reticulation, while only 12% had neither imaging abnormality. There was a strong association between days on oxygen supplementation during the acute phase of COVID-19 and both reduction in gas transfer and CT abnormalities at follow-up. Despite this, only 20% of participants reported persisting breathlessness.

These observational data highlight the need for systematic follow-up in this patient population<sup>10</sup> but further studies are necessary to detail the nature and mechanisms of the sequelae of SARS-CoV-2 infection—pulmonary, systemic and psychological. A substantial proportion of hospitalised patients have radiological or physiological changes consistent with interstitial abnormalities and there is an urgent need to define the trajectory of this lung pathology. Whether these changes resolve or progress, will have a profound impact on service provision in the coming years.

Long-term studies should also investigate the effect of disruption of the brain–heart–lung–kidney–skeletal muscle axis with the development of physiological imaging and include both physical and psychological impacts so that we can develop clinical strategies to manage post-traumatic stress disorder and other psychological morbidities. Interestingly, the only study reporting on cognitive impairment<sup>7</sup> determined that the test used was inappropriate for this cohort of patients. It will be important to ensure that appropriate tools are used for this crucial area of assessment. The multicentre PHOSP-COVID Study ([www.phosp.org/](http://www.phosp.org/)) which will recruit 10 000 patients who have been hospitalised with COVID-19 across the UK, is an example of this comprehensive approach, embedding physical, psychological and cognitive areas of investigation. Over 12 months, research assessments will provide mechanistic and clinical observational data on the trajectory of recovery of post hospitalisation COVID-19 patients to provide greater knowledge of the longer term health outcomes impact.

The work described so far in hospitalised patients excludes two important groups. The first is those individuals who were infected with SARS-CoV-2 and had moderate to severe disease but avoided hospitalisation, and the second is people with 'Long COVID-19' who have persisting debilitating symptoms after what may have been a comparatively mild acute phase.<sup>4</sup> Long-term outcomes in different populations are likely to vary. Thus, among participants in the Zoe Symptom Study,<sup>11</sup> in 4182 incident cases of COVID-19 who reported testing positive for SARS-CoV-2 by PCR and logged their symptoms prospectively, 13.9% of whom had attended hospital because of COVID-19, 13.3% had symptoms lasting >28 days, 4.5% for >8 weeks and 2.3% for >12 weeks.<sup>12</sup> 43.9% of those with symptoms at 8 weeks had attended hospital. Stavem and colleagues<sup>13</sup> studied symptoms and their determinants 1.5–6

<sup>1</sup>National Heart and Lung Institute, Imperial College London, London, UK

<sup>2</sup>Centre for Respiratory Research, University of Nottingham, Nottingham, UK

<sup>3</sup>Lane Fox Respiratory Service, Guy's & St Thomas' NHS Foundation Trust, London, UK

**Correspondence to** Dr Nicholas S Hopkinson, National Heart and Lung Institute, Imperial College London, London, UK; [n.hopkinson@ic.ac.uk](mailto:n.hopkinson@ic.ac.uk)

months after symptom onset in a Norwegian non-hospitalised population with confirmed COVID-19. Fifty three per cent of women and 67% of men were symptom-free, while 16% reported dyspnoea, 12% loss/disturbance of smell and 10% loss/disturbance of taste. A greater burden of symptoms during the initial illness was associated with a greater symptom burden at follow-up, suggesting a link to disease severity.

Given the persistence of symptoms including breathlessness, cough, fatigue, muscle and joint pain and poor sleep quality following COVID-19, there is a need for a rehabilitation approach to address physical and psychological issues in a holistic way and British Thoracic Society guidance is set out on its website ([www.brit-thoracic.org.uk](http://www.brit-thoracic.org.uk)). The structured self-management approach that has been shown to be effective in the treatment of post-polio syndrome can also provide a model for this.<sup>14</sup> The COPD assessment test score, an established measure to assess response to pulmonary rehabilitation, has been repurposed as a tool to evaluate post-COVID symptoms.<sup>15</sup>

Even prior to COVID-19, the provision of pulmonary rehabilitation services to support people limited by breathlessness was inadequate to meet the level of need<sup>16</sup> and the ongoing pandemic has further limited the capacity to provide face to face services. People with long-term conditions who are clinically vulnerable to COVID-19 have been advised to practice strict social isolation and have also experienced a disruption in their access to healthcare.<sup>17 18</sup> The pandemic has highlighted the effect of inequalities and structural racism on healthcare outcomes.<sup>19</sup> It is to be hoped that understanding and recognising the needs of people recovering from the illness will in turn lead to a greater appreciation of the importance of rehabilitation across the healthcare system.

**Twitter** Nicholas S Hopkinson @COPDdoc and Nicholas Hart @NickHartThorax

**Contributors** NSH wrote the first draft, to which NH and GJ contributed. All authors approved the final manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Patient consent for publication** Not required.

**Provenance and peer review** Commissioned; externally peer reviewed.

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**To cite** Hopkinson NS, Jenkins G, Hart N. *Thorax* 2021;**76**:324–325.

Accepted 23 November 2020

Published Online First 15 February 2021



- ▶ <http://dx.doi.org/10.1136/thoraxjnl-2020-215818>
- ▶ <http://dx.doi.org/10.1136/thoraxjnl-2020-216086>
- ▶ <http://dx.doi.org/10.1136/thoraxjnl-2020-216308>
- ▶ <http://dx.doi.org/10.1136/thoraxjnl-2020-216377>
- ▶ <http://dx.doi.org/10.1136/thoraxjnl-2020-215861>

*Thorax* 2021;**76**:324–325.

doi:10.1136/thoraxjnl-2020-216226

#### ORCID iDs

Nicholas S Hopkinson <http://orcid.org/0000-0003-3235-0454>

Gisli Jenkins <http://orcid.org/0000-0002-7929-2119>

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