



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

## Sleep disturbances, dyspnoea, and anxiety in long COVID



Microgen Images/Science Photo Library

Although more than 6.8 million deaths have been attributed to COVID-19 worldwide, survivors of COVID-19 can be affected in numerous ways across multiple organ systems. The entity of long COVID has been controversial and remains poorly defined, but it is now clear that COVID-19 has a long-term impact in many individuals. The complaints among COVID-19 survivors are myriad but include fatigue, difficulty concentrating, sleep disturbance, anxiety, and dyspnoea. However, the causes of these complaints are unclear, with some studies suggesting a dissociation of objective abnormalities from subjective complaints.

Sleep disorders are also exceedingly common.<sup>1</sup> Obstructive sleep apnoea is thought to affect up to 1 billion people worldwide, with most cases remaining undiagnosed and untreated.<sup>2,3</sup> Insomnia is also a common problem affecting more than 10% of the adult population. Obstructive sleep apnoea is known to have major neurocognitive and cardiovascular sequelae, although the relative impact of obesity versus obstructive sleep apnoea on dyspnoea and exercise performance is less clear.<sup>2,4</sup>

In *The Lancet Respiratory Medicine*, Callum Jackson and colleagues<sup>5</sup> report the results of CircCOVID, a multicentre cohort study comprising more than 2000 participants who were admitted to hospital for COVID-19 in the UK. For this study, participants were recruited from the Post-hospitalisation COVID-19 study (PHOSP-COVID) and were compared with matched UK Biobank cohorts of more than 500 individuals (those who were recently hospitalised and those with pneumonia). The authors observed several important findings. The prevalence of sleep disturbance, anxiety, and dyspnoea (assessed by subjective measures of sleep quality) were exceedingly common among COVID-19 survivors compared with the recently hospitalised control group. In terms of objective measurements, some abnormalities in pulmonary function testing and actigraphy were observed. Based on actigraphy, the COVID-19 cohort had a greater rest time (a surrogate for sleep) but lower estimated sleep efficiency than the recently hospitalised control group. With regard to dyspnoea, there was an observed correlation between sleep quality and the severity of dyspnoea; however, this finding was not corroborated by actigraphy data. Additionally, patients reporting poor

sleep quality based on the Pittsburgh Sleep Quality Index reported greater anxiety than those who reported good sleep quality. In aggregate, these findings suggest that sleep disturbance, dyspnoea, and anxiety are common after COVID-19 and are associated with one another, although the underlying mechanisms remain unclear.

This study is an important addition to the literature, but a few potential limitations are noteworthy. First, since fewer than 50% of participants with COVID-19 provided follow-up data, a concern exists for participation bias, ascertainment bias, and recall bias (given that pre-existing abnormalities would be difficult to assess). Although the demographics of the participants resemble the overall CircCOVID cohort of more than 2000 participants, the findings clearly pertain only to the CircCOVID subcohorts studied. In theory, the most severely affected patients would be least likely to present for follow-up. Conversely, patients who are sometimes labelled as having psychosomatic complaints might be those most likely to seek follow-up care. Second, further data are required to investigate the degree of objective versus subjective abnormality in patients who have recovered from COVID-19. Although some patients might be labelled as having functional complaints, the observation of objective brain abnormalities after COVID-19 in previous studies might suggest an important neurological role in mediating symptoms.<sup>6</sup> Third, given the nature of this epidemiological study, the findings represent correlation rather than causation. For example, it is unclear whether sleep disturbance is causing anxiety or whether anxiety is contributing to poor sleep. Interventional studies are required to define the underlying causal pathways. Fourth, although some objective testing was available, gold standard polysomnography and full plethysmography were not provided. For the sleep disturbances, increased BMI in the cohort reporting poor sleep compared with those reporting good sleep might suggest underlying obstructive sleep apnoea, although this assertion is speculative. Thus, further mechanistic work is required to draw definitive conclusions.

Many questions remain both for researchers and for clinicians. For researchers, questions include whether the documented abnormalities in pulmonary microvasculature in previous studies are contributing

*Lancet Respir Med* 2023

Published Online  
April 15, 2023  
[https://doi.org/10.1016/S2213-2600\(23\)00138-8](https://doi.org/10.1016/S2213-2600(23)00138-8)

See Online/Articles  
[https://doi.org/10.1016/S2213-2600\(23\)00124-8](https://doi.org/10.1016/S2213-2600(23)00124-8)

to elevated dead space, yielding a risk of dyspnoea;<sup>7,8</sup> whether anxiety and dyspnoea are contributing to a low arousal threshold, which could contribute to disrupted sleep and a risk of obstructive sleep apnoea;<sup>9</sup> and whether pulmonary functional abnormalities are obstructive, restrictive, vascular, or mixed. For clinicians, questions include whether the observed abnormalities (eg, in dyspnoea score) are clinically significant, since the findings were quite modest, although statistically significant; whether therapies such as glucocorticoids, anticoagulants, or previous vaccinations mitigate the observed abnormalities during COVID-19 recovery; and whether recovery from respiratory infection due to COVID-19 is worse than that for other viral respiratory illnesses, such as influenza or adenovirus, which traditionally did not receive careful follow-up.<sup>10</sup>

Although we feel systematic screening of sleep and respiratory abnormalities following recovery from COVID-19 is not yet indicated, we applaud Jackson and colleagues<sup>5</sup> for their important contribution to this topic and welcome further research in this area.

AM is funded by the US National Institutes of Health, and reports income (medical education) from Zoll, Livanova, Jazz, and Eli Lilly. WCM and AKP declare no competing interests.

\*W Cameron McGuire, Alex K Pearce, Atul Malhotra  
wmcguire@health.ucsd.edu

Division of Pulmonary, Critical Care, Sleep Medicine, and Physiology, University of California, San Diego, La Jolla, CA 92037, USA

- 1 Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. *Lancet* 2014; **383**: 736–47.
- 2 Benjafield AV, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med* 2019; **7**: 687–98.
- 3 Heinzer R, Vat S, Marques-Vidal P, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *Lancet Respir Med* 2015; **3**: 310–18.
- 4 Veasey SC, Rosen IM. Obstructive sleep apnea in adults. *N Engl J Med* 2019; **380**: 1442–49.
- 5 Jackson C, Stewart ID, Plekhanova T, et al. Effects of sleep disturbance on dyspnoea and impaired lung function following hospital admission due to COVID-19 in the UK: a prospective multicentre cohort study. *Lancet Respir Med* 2023; published online April 15. [https://doi.org/S2213-2600\(23\)00124-8](https://doi.org/S2213-2600(23)00124-8).
- 6 Douaud G, Lee S, Alfaro-Almagro F, et al. SARS-CoV-2 is associated with changes in brain structure in UK Biobank. *Nature* 2022; **604**: 697–707.
- 7 Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *N Engl J Med* 2020; **383**: 120–28.
- 8 Harbut P, Prisk GK, Lindwall R, et al. Intrapulmonary shunt and alveolar dead space in a cohort of patients with acute COVID-19 pneumonitis and early recovery. *Eur Respir J* 2023; **61**: 2201117.
- 9 Edwards BA, Eckert DJ, McSharry DG, et al. Clinical predictors of the respiratory arousal threshold in patients with obstructive sleep apnea. *Am J Respir Crit Care Med* 2014; **190**: 1293–300.
- 10 Baskett WI, Qureshi AI, Shyu D, Armer JM, Shyu CR. COVID-specific long-term sequelae in comparison to common viral respiratory infections: an analysis of 17 487 infected adult patients. *Open Forum Infect Dis* 2023; **10**: ofac683.