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


Summary

Background Sleep disturbance is common following hospital admission both for COVID-19 and other causes. The clinical associations of this for recovery after hospital admission are poorly understood despite sleep disturbance contributing to morbidity in other scenarios. We aimed to investigate the prevalence and nature of sleep disturbance after discharge following hospital admission for COVID-19 and to assess whether this was associated with dyspnoea.

Methods CircCOVID was a prospective multicentre cohort substudy designed to investigate the effects of circadian disruption and sleep disturbance on recovery after COVID-19 in a cohort of participants aged 18 years or older, admitted to hospital for COVID-19 in the UK, and discharged between March, 2020, and October, 2021. Participants were recruited from the Post-hospitalisation COVID-19 study (PHOSP-COVID). Follow-up data were collected at two timepoints: an early time point 2–7 months after hospital discharge and a later time point 10–14 months after hospital discharge. Sleep quality was assessed subjectively using the Pittsburgh Sleep Quality Index questionnaire and a numerical rating scale. Sleep quality was also assessed with an accelerometer worn on the wrist (actigraphy) for 14 days. Participants were also clinically phenotyped, including assessment of symptoms (ie, anxiety [Generalised Anxiety Disorder 7-item scale questionnaire], muscle function [SARC-F questionnaire], dyspnoea [Dyspnoea-12 questionnaire] and measurement of lung function), at the early time point after discharge. Actigraphy results were also compared to a matched UK Biobank cohort (non-hospitalised individuals and recently hospitalised individuals). Multivariable linear regression was used to define associations of sleep disturbance with the primary outcome of breathlessness and the other clinical symptoms. PHOSP-COVID is registered on the ISRCTN Registry (ISRCTN10980107).

Findings 2320 of 2468 participants in the PHOSP-COVID study attended an early timepoint research visit a median of 5 months (IQR 4–6) following discharge from 83 hospitals in the UK. Data for sleep quality were assessed by subjective measures (the Pittsburgh Sleep Quality Index questionnaire and the numerical rating scale) for 638 participants at the early time point. Sleep quality was also assessed using device-based measures (actigraphy) a median of 7 months (IQR 5–8 months) after discharge from hospital for 729 participants. After discharge from hospital, the majority (396 [62%] of 638) of participants who had been admitted to hospital for COVID-19 reported poor sleep quality in response to the Pittsburgh Sleep Quality Index questionnaire. A comparable proportion (338 [53%] of 638) of participants felt their sleep quality had deteriorated following discharge after COVID-19 admission, as assessed by the numerical rating scale. Device-based measurements were compared to an age-matched, sex-matched, BMI-matched, and time from discharge-matched UK Biobank cohort who had recently been admitted to hospital. Compared to the recently hospitalised matched UK Biobank cohort, participants in our study slept on average 65 min (95% CI 59 to 71) longer, had a lower sleep regularity index (–19%; 95% CI –20 to –16), and a lower sleep efficiency (3.83 percentage points; 95% CI 3.40 to 4.26). Similar results were obtained when comparisons were made with the non-hospitalised UK Biobank cohort. Overall sleep quality (unadjusted effect estimate 3.94; 95% CI 2.78 to 5.10), deterioration in sleep quality following hospital admission (3.00; 1.82 to 4.28), and sleep regularity (4.38; 2.10 to 6.65) were associated with higher dyspnoea scores. Poor sleep quality, deterioration in sleep quality, and sleep regularity were also associated with impaired lung function, as assessed by forced vital capacity. Depending on the sleep metric, anxiety mediated 18–39% of the effect of sleep disturbance on dyspnoea, while muscle weakness mediated 27–41% of this effect.
Interpretation
Sleep disturbance following hospital admission for COVID-19 is associated with dyspnoea, anxiety, and muscle weakness. Due to the association with multiple symptoms, targeting sleep disturbance might be beneficial in treating the post-COVID-19 condition.

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Introduction
Delayed recovery and persistent illness following hospital admission for COVID-19 have been recognised as constituting post-COVID-19 syndrome.1 Dyspnoea is a frequent symptom of this syndrome, with a recent study suggesting that 48% of patients admitted to hospital with COVID-19 in the UK have dyspnoea.2 Dyspnoea can arise from conditions that affect the respiratory, neurological, cardiovascular, and mental health systems.3 These systems are also affected by sleep disturbance,4 another phenomenon that has been frequently reported after COVID-19.5–14 The association between sleep disturbance and dyspnoea, however, has not been widely studied.

Sleep disturbance following hospital admission is common regardless of the original reason for admission.15 Despite its prevalence, the clinical implications of sleep disturbance during recovery from an acute illness are not well understood. In experimental settings, sleep disturbance is causally associated with two recognised causes of dyspnoea: anxiety and muscle weakness.16,17 Furthermore, epidemiological studies have suggested that sleep disturbance is associated with respiratory disease, which can cause dyspnoea.18 Whether these associations persist following acute sleep disturbance, such as after hospital admission, is yet to be established.

An accurate assessment of sleep disturbance is best carried out with a multimodal approach. Subjective assessments provide an overall score of sleep quality but might be affected by recall (reporting) bias,19 as well as questionnaire language. Subjective assessments also provide only limited insights into specific types of sleep disturbance. By contrast, device-based assessments of sleep quality such as actigraphy20 measure sleep disturbance more objectively. However, subjective methods such as after hospital admission, is yet to be established.

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Participants were recruited from the post-hospitalisation COVID-19 study (PHOSP-COVID) who were evaluated at the early timepoint and gave their consent for participation in the study. Sleep disturbance was evaluated with two types of measures (subjective and device-based). FVC=forced vital capacity. SARC-F=strength, assistance with walking, rising from a chair, climbing stairs, and falls. GAD7=Generalised Anxiety Disorder 7-item scale.

**Subjective assessment of sleep quality**
- 1141 participants did not attend an early follow-up visit at a centre administering the Pittsburgh Sleep Quality Index
- 1328 participants did not have device-based sleep measures available
- 285 completed both subjective and device-based measures after exclusions
- 79 participants provided device-based measures of sleep (actigraphy)
- 1375 particpants provided device-based measures of sleep (actigraphy)

**Device-based assessment of sleep quality**
- 2157 participants attended an early follow-up visit at a centre that collected actigraphy
- 163 participants did not attend an early follow-up visit at a Pittsburgh Sleep Quality Index centre
- 76 participants excluded
  - 6 pre-COVID-19 benzodiazepine
  - 67 pre-COVID-19 sleep comorbidities
  - 5 possible nosocomial COVID-19 infection
- 729 participants analysed
  - 703 Dyspnoea-12
  - 375 FEV1
  - 705 GAD7

**Figure 1: Consort diagram for participants included in the analysis**
- 2468 participants attended an early timepoint visit before Oct 6, 2021
- 148 excluded from analysis
  - 107 missing discharge or visit date
  - 10 early visit <62 days from discharge
  - 31 early visit >240 days from discharge
- 2320 participants attended an early follow-up
- 1179 participants attended an early follow-up visit at a centre administering the Pittsburgh Sleep Quality Index
- 367 participants did not complete the Pittsburgh Sleep Quality Index questionnaire
- 98 participants did not respond to the sleep quality numerical rating scale
valuable insights into sleep disruption, partially overcoming the limitations of individual approaches.31 Some studies have already reported altered sleep quality following hospital admission for COVID-19.3,13 The majority of these have been single-centre studies that were modest in size and only used subjective measures. Two studies to date have used a multimodal approach.22,23 In these studies, an association with anxiety was reported only with subjective but not device-based measures. Furthermore, no other clinical associations were reported. Moreover, the studies only used participants who had been admitted to critical care, thus limiting generalisation to the broader hospital cohort.

We aimed to characterise the prevalence, type, and clinical consequences of sleep disturbance in a broad cohort of patients who had been admitted to hospital for COVID-19 using a multimodal approach. We hypothesised that sleep disturbance would be associated with dyspnoea and that this relationship would be mediated by anxiety and muscle weakness.

### Methods

#### Study design and participants

CircCOVID was a prospective multicentre cohort sub-study designed to investigate the effects of circadian disruption and sleep disturbance on recovery after COVID-19. Participants were recruited from the Post-hospitalisation COVID-19 study (PHOSP-COVID). All participants were aged 18 years or older, admitted to 83 hospitals in the UK with either PCR-confirmed or clinically diagnosed COVID-19, and discharged between March, 2020, and October, 2021. The demographics and recruitment of participants into PHOSP-COVID have been described elsewhere2 and are briefly described in the appendix (p 24). COVID-19 severity during admission was assessed with the WHO clinical progression scale.24 Participants were excluded from the analysis on the basis of pre-existing conditions linked to sleep disturbance, medication, and nosocomial infections (appendix p 24). Written informed consent was obtained from all study participants. The study was approved by the Leeds West Research Ethics Committee (20/YH/0225). PHOSP-COVID is registered on the ISRCTN Registry (ISRCTN10980107).

#### Procedures

Two different methods were used to subjectively assess sleep quality after discharge from hospital. The first was the Pittsburgh Sleep Quality Index questionnaire.25 The second was the numerical rating scale assessment of sleep quality. Data for both methods were collected at an early timepoint 2–7 months after hospital discharge; for the numerical rating scale, data were also collected at a later timepoint 10–14 months after hospital discharge. For the device-based assessment of sleep quality, participants were invited to wear a wrist-worn accelerometer (GENEActiv Original, ActivInsights, Kimbolton, UK) on their non-dominant wrist for 24 h per day for 14 days. Details of data cleaning, analysis, and variable definitions are given in the appendix (p 25).

The UK Biobank26 was used as a pre-pandemic comparator cohort for actigraphy data. The UK Biobank recruited 502 540 participants aged 40–69 years who were...
invited to a baseline visit at one of 22 assessment centres between March, 2006, and July, 2010, during which their phenotypes were established with questionnaires, physical examination, and collection of biological samples. From this dataset, three subcohorts (non-hospitalised individuals, hospitalised individuals, and individuals hospitalised with pneumonia) were created for analysis, and are defined in the appendix (pp 26–28).

Outcomes
The Pittsburgh Sleep Quality Index questionnaire assesses sleep quality across seven components. A total score greater than 5 was defined as poor sleep quality and a score of 5 or less was defined as good sleep quality. The numerical rating scale assessment of sleep quality asked patients to rate their sleep quality (0–10, with zero being the worst sleep quality; appendix pp 24–25). Patients who rated their sleep quality as decreasing by one point or more were categorised as reporting deteriorated sleep quality.

The primary outcome for this analysis was breathlessness, assessed using the Dyspnoea-12 validated questionnaire. Other outcomes that were assessed were lung function, anxiety, depression, and muscle function. Details of each assessment are given in the appendix (pp 25–26).

Statistical analysis
Continuous values are presented as means (95% CIs) and ordinal values are presented as medians (IQRs). Unless specified elsewhere, participants with good sleep were compared to participants with poor sleep and participants whose sleep had deteriorated (ie, deterioration in sleep score compared to pre-COVID-19 baseline according to the numerical rating scale) were compared with those whose sleep was unaffected by COVID-19. The top and bottom quintiles were compared for sleep regularity, sleep efficiency, and sleep period duration. Sleep regularity was also analysed as a continuous measure; the results are reported in the appendix (p 18). All univariable and multivariable analyses of continuous data were analysed with ordinary least squares linear regression or multinominal logistic regression. The multivariable analyses adjusted for a minimally sufficient set of covariates: age, sex, BMI, number of days into the pandemic, number of days since discharge, pre-COVID-19 comorbidities, COVID-19 severity, and length of stay; participants with missing values for any variable were excluded. This set of covariates was identified on the basis of all interactions of interest. Patients with missing values for any variable were excluded. All univariable and multivariable analyses were adjusted for using the Bejamini-Hochberg procedure to control the false discovery rate (FDR). Mediation analysis was done as a post-hoc analysis to quantify the strength of the relationships between sleep disturbance, anxiety, muscle weakness, and dyspnoea. We conducted two sensitivity analyses; first, all regressions were repeated with continuous sleep exposures rather than dichotomised (appendix p 18). Second, when matching our cohort to UK Biobank, 25 distinct cohorts were matched and analysed to ensure the results were consistent (appendix p 27).

Role of the funding source
The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results
A total of 2468 participants were enrolled in PHOSP-COVID, of whom 2320 attended an early timepoint research visit a median of 5 months (IQR 4–6) following discharge from 83 hospitals in the UK. Subjective sleep quality was measured with both the Pittsburgh Sleep Quality Index questionnaire and the numerical rating scale. At the early timepoint, 1179 (51%) of 2320 participants attended an early follow-up at a centre offering the
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See Online for appendix.

Pittsburgh Sleep Quality Index questionnaire (figure 1). Of these, 714 (61%) of 1179 completed both the Pittsburgh Sleep Quality Index questionnaire and numerical rating scale at the early timepoint. A further 76 (11%) of 714 were excluded owing to suspected nosocomial infection or pre-COVID-19 sleep problems. At the late timepoint, 248 (39%) of 638 participants also completed the numerical rating scale (figure 1), a median of 12 months (IQR 11–13) after discharge. Device-based sleep quality was assessed by actigraphy in 829 (38%) of 2157 eligible participants who had not been admitted to hospital for COVID-19 and the at the time of assessment, during their early follow-up (median 5 months after discharge from hospital for COVID-19). Sleep quality was also assessed at a late follow-up (median 12 months after COVID-19 admission). The red line indicates median change; the black lines represent individual participants. *p<0.001, Dunn’s post-hoc test, Benjamini-Hochberg corrected p value.

Using a device-based approach, assessments were made for: (B) sleep period duration; (C) sleep regularity index; and (D) sleep efficiency. The post-COVID-19 cohort (blue shaded area) was matched (age, sex, BMI, and, if applicable, time from hospital discharge) to non-hospitalised UK Biobank participants (green shaded area) or recently hospitalised UK Biobank participants (red shaded area).

The prevalence of sleep disturbance following COVID-19 hospitalisation was then defined. A subjective assessment of sleep quality revealed that 396 (62%) of 638 participants reported poor sleep quality (assessed by the Pittsburgh Sleep Quality Index). Analysis of temporal changes in sleep quality by the numerical rating scale revealed that sleep quality deteriorated following hospital admission for COVID-19 in 338 (53%) of 638 participants. At the early timepoint, sleep quality fell by a median of 3 (IQR 0–4) points and at the late timepoint sleep quality fell by a median of 2 (0–4) points (figure 2A) compared to participants’ pre-COVID-19 scores.

The actigraphy traces of this cohort were then compared to two UK Biobank cohorts (non-hospitalised and recently hospitalised), as defined in the appendix (pp 26–27). Cohorts were matched for age, sex, BMI, and, if applicable, time from hospital discharge (appendix p 27). Participants admitted to hospital for COVID-19 slept on average 62 min (95% CI 56 to 68) longer (figure 2B), had a lower sleep regularity index (−21% [95% CI–19 to –23]; figure 2C), and a lower sleep efficiency (3·25 percentage points [95% CI 2.81 to 3.68]; figure 2D) than UK Biobank participants who had not been admitted to hospital.
Actigraphy traces of 91 participants in the UK Biobank who had recently been admitted to hospital with pneumonia (2–11 months before actigraphy; appendix p 27) were also compared to both UK Biobank cohorts defined above. No significant differences were observed for sleep duration or efficiency compared with either the non-hospitalised or recently hospitalised UK Biobank cohorts (appendix p 20). Participants recently hospitalised with pneumonia did, however, have a lower sleep regularity index (–19% [95% CI –20 to –16]; figure 2C), and a lower sleep efficiency (3·83 percentage points [95% CI 3·40 to 4·26]; figure 2D; p<0·0001 for all comparisons).

Device-based measurements of sleep were then assessed: participants with the lowest sleep regularity scored higher on the Dyspnoea-12 questionnaire than those who did not have a deterioration in sleep quality (figure 3A). Associations were consistent following adjustments for a minimum set of covariates (age, sex, BMI, period into the pandemic, time since discharge, comorbidities, COVID-19 severity, and length of stay).

The relationship between sleep disturbance and dyspnoea was then investigated. Participants with poor sleep quality (assessed by the Pittsburgh Sleep Quality Index), scored higher on the Dyspnoea-12 questionnaire than those with good sleep quality (figure 3A). Sleep quality deterioration (assessed with the numerical rating scale) was also associated with dyspnoea. Those reporting a deterioration in their sleep quality scored higher on the Dyspnoea-12 questionnaire than those who did not have a deterioration in sleep quality (figure 3A). Associations were consistent following adjustments for a minimum set of covariates (age, sex, BMI, period into the pandemic, time since discharge, comorbidities, COVID-19 severity, and length of stay).

The associations between changes in sleep parameters were investigated for various clinical characteristics: (A) association with Dyspnoea-12 score; (B) association with predicted forced vital capacity; and (C) association with SARC-F score. Sleep quality (ie, poor vs good quality, assessed by the Pittsburgh Sleep Quality Index) is shown in black. Sleep quality deterioration (ie, those whose sleep deteriorated vs those whose sleep was unaffected by COVID-19), assessed by the numerical rating scale) is shown in light blue. Sleep regularity (ie, top vs bottom quintiles; dyspnoea only) is shown in red. Both unadjusted (circles) or multivariable (squares) effect estimates are shown alongside 95% CIs. In multivariable linear regression models, the association was adjusted for age, sex, BMI, comorbidities, COVID-19 severity, length of stay, number of days into the pandemic, and number of days since discharge. SARC-F=strength, assistance with walking, rising from a chair, climbing stairs, and falls.

### Table

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Figure 3: Clinical associations with sleep disturbance

The associations between changes in sleep parameters were investigated for various clinical characteristics: (A) association with Dyspnoea-12 score; (B) association with predicted forced vital capacity; and (C) association with SARC-F score. Sleep quality (ie, poor vs good quality, assessed by the Pittsburgh Sleep Quality Index) is shown in black. Sleep quality deterioration (ie, those whose sleep deteriorated vs those whose sleep was unaffected by COVID-19), assessed by the numerical rating scale) is shown in light blue. Sleep regularity (ie, top vs bottom quintiles; dyspnoea only) is shown in red. Both unadjusted (circles) or multivariable (squares) effect estimates are shown alongside 95% CIs. In multivariable linear regression models, the association was adjusted for age, sex, BMI, comorbidities, COVID-19 severity, length of stay, number of days into the pandemic, and number of days since discharge. SARC-F=strength, assistance with walking, rising from a chair, climbing stairs, and falls.
COVID-19 had a lower percentage predicted FEV₁ (–8.78%; 95% CI –14.94 to –3.78) and a lower percentage predicted FVC (–8.25%; 95% CI –14.38 to –3.56) than participants whose sleep quality had remained the same or improved. Associations were consistent following adjustments for the minimal set of covariates (figure 3B; appendix pp 18, 21).

Sleep regularity was then assessed. Participants with the lowest sleep regularity had a lower percentage predicted FEV₁ (–13.58%; 95% CI –24.86 to –4.84; appendix pp 18, 21) and a lower percentage predicted FVC (figure 3B) than participants with the highest sleep regularity. This association was also consistent following adjustment for a minimal set of covariates (figure 3B; appendix pp 18, 21).

Participants with the lowest sleep regularity had a lower maximum inspiratory pressure (–31.63 cmH₂O; 95% CI –58.47 to –3.29; appendix pp 18, 22) than participants with the highest sleep regularity. No similar association was observed with maximum inspiratory pressure. The small sample size (n=55) of this cohort precluded adjustment for a minimal set of covariates. No associations were observed for either maximum inspiratory pressure or maximum expiratory pressure and the subjective measures of sleep quality following hospital admission for COVID-19 (appendix pp 18, 22).

The association between sleep disturbance and muscle function was then assessed. In the assessment of muscle function, participants with poor sleep quality (assessed by the Pittsburgh Sleep Quality Index) had a higher score on the SARC-F questionnaire (figure 3C) than those with good quality sleep. Those who reported sleep quality deterioration (assessed by the numerical rating scale) following hospital admission due to COVID-19 also reported higher scores on the SARC-F questionnaire (figure 3C) than participants whose sleep had not deteriorated. Associations were consistent following adjustments for a minimal set of covariates (figure 3C; appendix p 18). This association was also observed for sleep irregularity. Participants with the most irregular sleep had a higher SARC-F (figure 3C; appendix p 18) score than participants with the best sleep regularity, with similar results following adjustment.

The relationship between sleep disturbance and anxiety was then assessed. Participants with poor sleep quality (assessed by the Pittsburgh Sleep Quality Index) were more likely to have mild, moderate, or severe anxiety compared to participants who reported good quality sleep (figure 4A–C; appendix p 18). A similar association was observed between anxiety and sleep quality deterioration (assessed by the numerical rating scale) after admission to hospital for COVID-19. Participants who had sleep quality deterioration were more likely to have mild, moderate, and severe anxiety (figure 4A–C; appendix p 18) than participants who did not have any deterioration in their sleep quality. Following...
adjustment for the minimal sufficient set of covariates, the association was attenuated for severe anxiety, but the other associations remained unchanged.

Participants with the lowest sleep regularity were more likely to report moderate anxiety than participants with the highest sleep regularity (figure 4B; appendix p 18). By contrast, there was no association with mild or severe anxiety. Adjustment for the minimal sufficient set of covariates attenuated the effect with moderate anxiety.

Given that anxiety and altered muscle function are recognised causes of dyspnoea, mediation analysis was done (appendix p 30) to investigate the contribution of anxiety and altered muscle function in mediating the effect between sleep and dyspnoea after admission to hospital due to COVID-19. Anxiety following discharge from hospital mediated the effect of poor sleep quality on dyspnoea by 38.70% (95% CI 22.67–57.17) and reduced muscle function had a similar mediation effect (36.22% [95% CI 21.19–55.66]; figure 5A; appendix p 19).

For the relationship between sleep quality deterioration and dyspnoea, anxiety mediated the effect by 35.63% (95% CI 16.14–59.22) and reduced muscle function mediated the effect by 26.87% (3.91–52.34; figure 5B; appendix p 19). The relationship between sleep irregularity and dyspnoea was also mediated by both anxiety (17.69%; 95% CI 1.38–42.27) and reduced muscle function (40.62%; 15.15–72.34; figure 5C; appendix p 19).

**Discussion**

Using multimodal sleep evaluation done in a nationwide UK cohort, we have shown that sleep disturbance is prevalent following hospital admission for COVID-19. Moreover, sleep disturbance is likely to persist for at least 12 months, since subjective sleep quality hardly changed between early (5 months) and late (12 months) follow-up visits. Multimodal assessment of sleep disturbance revealed that three factors (sleep quality, degradation of sleep quality compared to baseline, and sleep regularity) were associated with dyspnoea and decreased lung function. Mediation analysis identified that reduced muscle function and anxiety, both recognised causes of dyspnoea, could partially mediate the association between sleep disturbance and dyspnoea.

Three different complementary methods (the Pittsburgh Sleep Quality Index, numerical rating scale, and device-based metrics) were used to assess sleep disturbance in our study. The Pittsburgh Sleep Quality Index is a well validated assessment tool that evaluates sleep quality at the time of administration. Additional evaluation of sleep quality with the numerical rating scale confirmed these associations occurred as a result of a deterioration of sleep quality following hospital admission for COVID-19, complementing the Pittsburgh Sleep Quality Index evaluation. Device-based metrics were then used to investigate specific aspects of sleep quality, revealing clinical associations with sleep irregularity. The gold standard device-based metric is polysomnography. However, this can be technically challenging and measures sleep quality over shorter timeframes. Instead, actigraphy was used, which accurately identifies many of the sleep traits captured by polysomnography. Analysis of the actigraphy traces revealed an association between dyspnoea and the sleep regularity index. Although this association has not previously been widely reported, the sleep regularity index has been associated with morbidity in other studies.

Device-based sleep metrics following hospital admission for COVID-19 have predominantly been measured in participants admitted to critical care. Our cohort extends these findings, revealing altered sleep-based metrics in all participants who had been admitted to hospital regardless of critical care admission. Comparison with UK Biobank participants admitted to hospital for other causes suggested this could be partially due to COVID-19, given the comparatively modest effects seen with hospital admission for other causes.
Two previous device-based studies\textsuperscript{22,23} in the setting of COVID-19 revealed clinical associations between anxiety and subjective—but not device-based—assessments of sleep quality. These limited clinical effects are an apparent contradiction with experimental models in which sleep disturbance has several effects,\textsuperscript{19} with clinical studies outside the context of hospital admission,\textsuperscript{15} and the broad clinical effects reported in the present study. If sleep disturbance does have broad effects in this setting, this could also explain why the association between sleep disturbance and dyspnoea was only partially mediated by anxiety and muscle function. Therefore, other unidentified clinical or behavioural effects or a direct effect could explain the association between sleep disturbance and dyspnoea. Further studies will be needed to define this association further, since the association between sleep disturbance and dyspnoea is likely to be relevant to other respiratory diseases.

Strengths of our study include its size, multicentre design, and the use of different complementary assessment measures to evaluate sleep disturbance. Consistent clinical associations were also observed across each evaluation method. However, this study also has some limitations that should be considered when interpreting the results. First, the hypothesised directionality of effects in the directed acyclic graph (appendix pp 28–29, 32), used to identify the covariates in our models, cannot be confirmed by the data in this study. Other studies do support the hypothesised directions;\textsuperscript{24,25} however, bidirectionality relationships have been reported in other settings.\textsuperscript{16} Second, quantification of sleep quality deterioration based on the numerical rating scale relied upon participant recall and therefore could be affected by recall bias, also known as reporting bias.\textsuperscript{26} Last, selection bias could also affect the results. However, we minimised this bias by using bootstrapping combined with cohort matching.

In conclusion, this study provides insight into the prevalence and wider consequences of sleep disturbance following hospital admission for COVID-19. The associations described in this study between sleep disturbance and reduced muscle function, anxiety, and dyspnoea suggest that sleep disturbance could be an important driver of the post-COVID-19 condition. If this is the case, then interventions targeting poor sleep quality\textsuperscript{18} could be used to manage multimorbidity and convalescence following hospital admission for COVID-19, with the aim of potentially improving patient outcomes.

Contributors
The manuscript was initially drafted by CJ, IDS, MKR, and JFB, and further developed by the writing committee. CJ, IDS, NC, MKR, and JFB made substantial contributions to the conception and design of this work. CJ, IDS, JCP, AART, ALJ, PLM, RAE, and TP made substantial contributions to the acquisition of data. CJ, IDS, TP, PSC, ALH, BA-S, RA, CEB, TC, JDC, NC, ABD, GD, CLE, OE, NJC, NAH, VCH, EMM, EPH, LI-P, LI-W, LSH, CJJ, MGJ, OCL, KEL, NIL, MM, HJCMc, MAMc, BVP, KP-H, KP, BR, MR, PB-O, SLR-J, AVR, AVS, JTS, MS, AMS, AS, ASI, SCS, MT, DGW, TY, RGG, SJ, WD-CM, CEBR, LVW, JCP, AART, AH, PLM, RAE, SEJ, MKR, and JFB made contributions to the analysis or interpretation of data for this work. CJ, IDS, RAE, and TP verified the underlying data. All authors contributed to data interpretation and critical review and revision of the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Data sharing
The PHOSP-COVID study protocol, consent form, definition, and derivation of clinical characteristics and outcomes, training materials, regulatory documents, information about requests for data access, and other relevant study materials are available online. UK Biobank information can be released once necessary approvals have been obtained. Other data (eg, the R code and protocol) will be made available on reasonable request to the corresponding author.

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