Rehabilitation post-COVID-19: cross-sectional observations using the Stanford Hall remote assessment tool

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ABSTRACT

Introduction The multisystem COVID-19 can cause prolonged symptoms requiring rehabilitation. This study describes the creation of a remote COVID-19 rehabilitation assessment tool to allow timely triage, assessment and management. It hypothesizes those with post-COVID-19 syndrome, potentially without laboratory confirmation and irrespective of initial disease severity, will have significant rehabilitation needs.

Methods Cross-sectional study of consecutive patients referred by general practitioners (April–November 2020). Primary outcomes were presence/absence of anticipated sequelae. Binary logistic regression was used to test association between acute presentation and post-COVID-19 symptomatology.

Results 155 patients (n=127 men, n=28 women, median age 39 years, median 13 weeks post-illness) were assessed using the tool. Acute symptoms were most commonly shortness of breath (SOB) (74.2%), fever (73.5%), fatigue (70.3%) and cough (64.5%); and post-acutely, SOB (76.7%), fatigue (70.3%), cough (57.4%) and anxiety/mood disturbance (39.4%). Individuals with a confirmed diagnosis of COVID-19 were 69% and 63% less likely to have anxiety/mood disturbance and pain, respectively, at 3 months.

Conclusions Rehabilitation assessment should be offered to all patients suffering post-COVID-19 symptoms, not only those with laboratory confirmation and considered independently from acute illness severity. This tool offers a structure for a remote assessment. Post-COVID-19 programmes should include SOB, fatigue and mood disturbance management.

INTRODUCTION

The COVID-19 pandemic has led to significant levels of mortality and morbidity. Some long-term effects were predicted in those who survived serious disease, using data from previous coronavirus epidemics and early data from COVID-19. However, it is apparent that those who have experienced mild to moderate disease may also have significant ongoing symptoms that may require rehabilitation.

Residual symptoms, often related to intrusive fatigue, cognitive dysfunction or ongoing shortness of breath (SOB), have potential to limit activities of daily living (ADLs) and prevent return to work. Rehabilitation can improve the course of post-COVID-19 illness with a focus on physical symptoms and pacing to avoid ‘boom and bust’, aiming for a symptom-titrated return to physical activity, while also offering psychological support such as patient education and peer support to reduce anxiety.

Not all patients who have suffered from COVID-19 will need the support of rehabilitation services; most will fully recover after a mild self-limiting illness. However, early indications suggested up to 50% of patients might need support with targeted COVID-19 rehabilitation.

The Defence Medical Rehabilitation Centre (DMRC) Stanford Hall has experience of managing patients with complex rehabilitation needs, including those with prolonged post-viral symptoms requiring specialist rehabilitation. DMRC Stanford Hall has been running such a service for COVID-19 since May 2020, including a 2-week residential multidisciplinary rehabilitation course. Other post-COVID-19 pathways have been developed by adapting existing programmes such as those for pulmonary rehabilitation, or creating new online patient education resources, such as ‘Your COVID-19 Recovery’ and ‘Post COVID-19 Hub’.

According to the guidance from the National Institute of Health and Care Excellence (NICE), patients with rehabilitation needs are likely to benefit from an early initial assessment using a multidisciplinary team (MDT) approach. The
use of telemedicine platforms to deliver virtual medical care has significantly increased during COVID-19. Virtual rehabilitation is known to be effective within the both civilian and military settings,19 20 with systematic reviews demonstrating similar outcomes and patient satisfaction to those delivered face-to-face, recognising the inability to perform examinations.21 22

A remote COVID-19 rehabilitation assessment tool was created by MDT clinicians at DMRC Stanford Hall to allow timely triage, assessment and management. A key consideration in the development of new services is the inclusion criteria for access to care. Patient groups have highlighted potential unmet need, particularly for those initially managed in the community.2 21 Anecdotally, a pattern of delayed presentation for those without laboratory-confirmed diagnoses was noticed and hypothesised that this may be associated with highly prevalent rehabilitation needs. As such, analysis was performed according to the availability of either antigen or antibody confirmation of COVID-19.

The current study aims to report its creation and outcomes in 8 months of clinical use, with a secondary aim to describe association of testing status to both timing of initial assessment and post-acute symptoms.

**METHOD**

In early April 2020, an MDT working group convened to develop the remote COVID-19 rehabilitation assessment tool. Led by a rehabilitation medicine consultant, and cognisant of video-teleconferencing (VTC) limitations, the team included: an occupational therapist, consultant pain nurse, physiotherapist and exercise rehabilitation instructor. The tool was modelled on the current understanding of COVID-19 using the experience of the rehabilitation and management of other post-viral syndromes, with reference to the International Classification of Functioning, Disability and Health domains.24 An initial draft of the tool was produced and reviewed within the DMRC Stanford Hall clinical delivery group, comprised of the clinical director and all head of services for allied health professionals. A final stage of adjustment by the panel of rehabilitation medicine consultants using the tool was subsequently performed.

The assessment tool (online supplemental file 1) incorporates a medical screening, identifying the acute course, severity and management of COVID-19. The existence of post-COVID-19 symptoms, including pain, fatigue, sleep and mood, and functional limitations such as SOB, exercise intolerance or cognitive problems on ADLs or occupation are identified. From this problem list, and in conjunction with the patient’s ideas, concerns and expectations, rehabilitation management was arranged.

The tool was introduced into clinical practice in late April 2020, using the NHSX-approved web-based VTC platform, Attend Anywhere (Attend Anywhere, Australia), the first such tool in clinical use in the UK. In parallel to the creation of the remote COVID-19 rehabilitation assessment tool, a pan-DMMC group also generated a patient information leaflet, of which 28 received ward-level care and 11 intensive care.

COVID-19-laboratory confirmation was available for 60 patients at the time of assessment (Table 2). Those with laboratory confirmation had a VTC sooner following the onset of referral criteria: an acute illness characterised by either persistent cough, fever or anosmia in association with ongoing rehabilitation needs as assessed by their general practitioner.

In December 2020, a reviewer coded all remote COVID-19 rehabilitation assessment VTC consultations performed from April to November 2020 using the electronic health record system, Defence medical information capability programme. Anonymised data were extracted, compiled and analysed using SPSS (IBM, V27) and independently reviewed. Continuous data for age and time-to-VTC were tested for normality using the Shapiro-Wilk test. Time-to-VTC data were not normally distributed and therefore compared between those with/without laboratory confirmation using the Mann-Whitney U test. All other data were binary coded.

Levels/location of treatment were entered into separate binary logistic regression models with laboratory confirmation (y/n) as the dependent variable. Laboratory confirmation was then switched to the independent variable to assess association with post-acute symptoms. For the most prevalent post-acute symptoms (>30%), further independent variables were tested as predictors initially using univariate binary logistic regressions. Where significant associations were found, these were entered into a hierarchical multiple model in order of effect size (OR) and the four most common acute symptoms. To accommodate eight variables (age, time-to-VTC, laboratory confirmation, location of treatment and the four most common acute symptoms) assuming a 50% ratio for the dependent variable (presence/absence of symptoms at VTC), a sample size of 80–144 was sought to allow for five to nine events per predictor in the smaller group.26 This threshold was reached in November 2020.

There was no patient involvement in the initial working group which predated receipt of referrals with this novel condition, however feedback was used from patients to tailor the ongoing use of the tool.

**RESULTS**

Rehabilitation VTC assessments were completed for 155 patients (n=127 men and n=28 women, median age of 39 years), between April and November 2020, at a median of 13 weeks of follow-up (Table 1). Thirty-nine patients were admitted to hospital, of whom 28 received ward-level care and 11 intensive care.

| Table 1 | Demographics of 155 patients at the point of video-teleconference (VTC) |
| --- | --- |
| **Age (years)** | 39* (17) |
| **Gender (m/f)** | 81.9%/18.1% (n=127/28) |
| **Time-to-VTC (weeks)** | 13† (12) |
| **Proportion of patients with either Ab or Ag positive** | 38.7% (n=60) |
| **Proportion of patients Ag tested** | 62.6% (n=97) |
| **Proportion of patients Ab positive** | 34.2% (n=53) |
| **Proportion of patients Ab tested** | 9.68% (n=15) |
| **Proportion of patients Ab positive** | 5.8% (n=9) |

*Median data with IQR presented as data not normally distributed; W(155)=0.936, p=0.006.†Median data with IQR presented as data not normally distributed; W(155)=0.975, p=0.005.

Ab, antibody; Ag, antigen.
symptoms than those without (median 8.5 vs 16 weeks, respectively, U=1574.0, p<0.01).

Patients who self-managed at home (n=100, 64.5%) were 75% less likely to receive laboratory confirmation (OR 0.25 (0.12 to 0.50), p<0.01) (Table 2). Patients admitted to hospital wards and intensive care unit were more likely to receive laboratory confirmation (OR 4.43 (1.84 to 10.63), p<0.01 and OR 4.72 (1.20 to 18.56), p=0.03, respectively).

Symptoms during the acute illness were most commonly SOB (n=115, 74.2%), fever (n=114, 73.5%), fatigue (n=109, 70.3%) and cough (n=100, 64.5%) (Table 3). Post-acute, at the time of VTC assessment, 119 patients complained of SOB, occurring in 10 patients at rest, 62 on mild activity and 47 on moderate activity. Fatigue (n=109, 70.3%), cough (n=89, 57.4%) and anxiety/mood disturbance were also prevalent (n=61, 39.4%) across the whole cohort. Patients who received a laboratory confirmation for COVID-19 were 69% less likely to experience anxiety/mood disturbance and 63% less likely to experience pain than those who did not receive laboratory confirmation (OR 0.31 (0.15 to 0.64), p<0.01, and OR 0.37 (0.15 to 0.92), p=0.03) (Figure 1), respectively. When admission to hospital was included along with laboratory confirmation as a predictor of anxiety/mood disturbance, the step change was not significant (χ²=0.956, p=0.33) hence the univariate model was retained (Table 4). Other univariate tests were not significant for association with anxiety/mood disturbance including age, time-to-VTC, acute SOB, fever, fatigue or cough (online supplemental data).

In the remaining univariate analyses, acute SOB was associated with post-acute cough (OR 2.61 (1.25 to 5.45), p=0.01), and increased time-to-VTC was associated with SOB on moderate activity (OR 1.04 (1.00 to 1.08), p=0.04) (online supplemental data).

Ninety-nine (63.8%) patients were recommended for residential rehabilitation after their VTC assessment. Of those not admitted for residential rehabilitation following assessment, 15.5% (24 of 155) required a further VTC to determine if symptoms had resolved satisfactorily with the self-help pack and 16.8% (26 of 155) required no further input from rehabilitation services. A further three patients declined further rehabilitation input, and three patients had no outcome recorded. Given the uncertainty of the clinical course of post-COVID-19 syndrome, patients were reassured that re-referral from primary care was welcomed where necessary. Further involvement of specialist services, including dietitians, psychology or DMRC COVID-19 Recovery Service,27 was also performed when needed.

**DISCUSSION**

Three months after acute COVID-19 illness, SOB, fatigue, cough and anxiety/mood disturbances were the most commonly reported ongoing symptoms. This study also shows anxiety/mood disturbance and pain are more likely in patients who did not receive laboratory confirmation of their diagnosis. The acute and post-acute symptoms experienced within the military population mirror those detected by other self-reported studies, suggesting potentially similar rehabilitation requirements.23 28 These principal symptoms should be a key consideration for the rehabilitation of individuals with post-COVID-19 syndrome.

Those without laboratory confirmation had a delay in their time-to-VTC compared with those with confirmation. The relationship between time-to-VTC and SOB on moderate activity may indicate that delay exacerbates such symptoms and that early intervention, as recommended by NICE, is favourable. Given the reported difficulty of this group accessing medical support without a confirmed diagnosis, efforts should be made to give access to services based on clinical need, not testing status.21

Cases from early in the pandemic are less likely to receive laboratory confirmation, due to UK testing policy and testing unreliability, especially for those self-isolating at home. This diagnostic uncertainty, allied to a poorly understood disease process, especially in the post-acute phase, is likely to contribute to prevalent mood disturbance and pain, reinforcing the need for education and rehabilitation of patients without a positive test where clinical suspicion is high.
The recently published NICE COVID-19 guidance (NG 188) recommends do not exclude people from referral for multi-disciplinary assessment...based on the absence of a positive SARS-CoV-2 test.\textsuperscript{23} Our findings support this statement and highlight the need to plan rehabilitation services for all patients with symptoms consistent and high clinical suspicion of post-COVID-19 syndrome, irrespective of test results, as there may be the potential for deterioration in symptoms for patients experiencing difficulties accessing rehabilitation.

The location of acute care could be used as a proxy marker for the severity of the acute illness. Existing services cater for this population, on the expectation of severe post-acute and chronic symptoms in those requiring increased acute management. The current study has not shown acute symptoms or location of care to be predictive of post-COVID-19 symptoms. Although both admission and laboratory confirmation were negatively associated with symptoms of anxiety and mood, when combined in a multiple model, only laboratory confirmation remained significant. Therefore, lack of laboratory confirmation may have a contributory effect on mood disturbance. These results highlight the need for rehabilitation services tailored to those with less severe acute illness who have ongoing issues post-COVID-19.

With the use of telemedicine, DMRC Stanford Hall has been able to offer innovative and timely assessment, accessible to patients, with triage and interventions in line with recommendations from professional bodies and other UK rehabilitation centres.\textsuperscript{9 11 23 29 30} Issues encountered at DMRC Stanford Hall during creation and delivery of this tool have been elsewhere, with similar findings described by preliminary use of telemedicine in 196 consultations by Canadian Armed Forces.\textsuperscript{31} Robitaille and MacRae describe the need for reliable technological platforms (preferably VTC over telephone), with standardised patient information and using patient feedback to improve services, and specific equipment, training and location requirements.\textsuperscript{31}

Given the likely demand of post-COVID-19 care, with estimate of 10% of individuals suffering prolonged symptoms,\textsuperscript{8} it is likely that some of this will be provided by non-rehabilitation specialists, as part of their parent specialty (such as respiratory medicine), or in the new models of care recently commissioned by NHS England.\textsuperscript{32} The findings from this study have relevance for the commissioning and development of these much-needed clinical services, and any individual training required to meet this demand.

The approach of instigating early rehabilitation prescription is thought to be safe and effective and is the focus of ongoing UK Defence medical research, with the longitudinal study, Military COVID-19 Observational outcomes and Complications in Viral Infectious Disease (M-COVID, Study No. 1061/MODREC/20), following up patients for a year to understand the longer term complications of COVID-19.

**Table 4** Multiple hierarchical binary logistic model predicting anxiety/mood disturbance with laboratory confirmation/no laboratory confirmation (LC/NLC) and admission to hospital as covariates

| Variable                | b (SE) | 95% CI for OR | Lower | Odds | Upper |
|-------------------------|--------|---------------|-------|------|-------|
| (A) Coefficients of the model predicting anxiety/mood disturbance: model 1 |        |               |       |      |       |
| Constant                | -0.021 | (0.205)       | 0.980 | 1.00 | 1.02  |
| LC/NLC                  | -1.169 | (0.368)       | 0.257 | 0.15 | 0.31  |
| (B) Coefficients of the model predicting anxiety/mood disturbance: model 2 |        |               |       |      |       |
| Constant                | 0.033  | (0.213)       | 0.100 | 1.05 | 1.87  |
| LC/NLC                  | -1.041 | (0.388)       | 0.354 | 0.16 | 0.75  |
| Admitted                | -0.430 | (0.444)       | 0.650 | 0.27 | 1.55  |

(A) $R^2=0.092$ (Nagelkerke). Model (1) $\chi^2=10.916$, $p=0.001$, $^*p=0.001$.  
(B) $R^2=0.100$ (Nagelkerke). Model (2) $\chi^2=11.872$, $p=0.003$, $^*p=0.007$, $^++p=0.332$.  
Block (2) $\chi^2=0.956$, $p=0.328$. Model 1 retained as final model.  
N=3 standardised residuals $>2$, no Cook’s distances $>$1, n=10 leverage $>$300% of average, no DFBeta $>$1.
error is a risk in observational studies, particularly in a novel condition where time and data to form more nuanced hypotheses are limited.

During the coding process, if a tick box pertaining to an individual symptom was not checked, the inference was taken that the symptom was not present. The effect of this on the current study would be an underestimate of symptom prevalence. In addition, three assessment tools had incomplete outcomes recorded.

With the exception of occasional VTC platform failures, at which point, a telephone call was performed, there were no reported adverse effects with the delivery of the tool. Further detail on comorbidities, ethnic background, medication history and other risk factors for more severe COVID-19 infection would have been helpful to explore links between post-COVID-19 pathology and initial disease process. Due to the clinical focus of the rehabilitation tool, this was beyond the scope of the current study and further studies are ongoing within DMRC.

Conclusions
Post-COVID-19 symptoms should be considered in all patients, regardless of the acute illness severity and whether they have had laboratory confirmation. A significant proportion of patients require assessment and management, with symptoms such as SOB, fatigue and mood disorders impacting on ADLs and return to work, amenable to bespoke rehabilitation programmes. The creation and development of the DMRC Stanford Hall remote COVID-19 rehabilitation assessment tool early in the pandemic have allowed timely MDT rehabilitation and support. This tool offers a structure to remote assessment appropriate for any experienced or inexperienced rehabilitation providers.

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Contributors
MC, OOS and RB-D conceived the idea of the study. MC, MM, SL, AS and GW made up the working group for the tool design. MC, MG, SB and RP performed the assessments. OOS drafted and edited the manuscript. KT reviewed and coded all consultations. RB-D edited the manuscript and performed statistical analysis. All authors approved the final version.

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None declared.

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Data availability statement
Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplemental information. Relevant, anonymised data are uploaded as supplemental files. Further requests for data will need to be done through the Ministry of Defence.

Supplemental material
Requests for data will need to be done through the Ministry of Defence. Relevant, anonymised data are uploaded as supplemental files. Further information. Relevant, anonymised data are uploaded as supplemental files. Further statement for post-COVID-19 rehabilitation.

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| Medical Screening | Enter Y / N to all that apply | Details |
|-------------------|-----------------------------|---------|
| Covid             |                             |         |
|                   | Confirmed positive Covid test? |         |
| Covid symptom checker in acute illness | | Date of start of symptoms: Date of discharge / end of acute symptoms: |
| Fever             | Muscle aches                |         |
| Cough             | Joint pain                  |         |
| Sore throat       | Fatigue                     |         |
| Runny Nose        | Shortness of Breath         |         |
| Loss of smell / taste | Other                  |         |
| Bedding down facility | Oxygen therapy      |         |
| Hospital ward     | NIV                         |         |
| Hospital ITU      | Intubation & ventilation    |         |
|                   | ECMO                        |         |
|                   | Any rehab info given from hospital to the patient | |
|                   | Discharge summary available at time of TTC | |
|                   |                             |         |
| Medical           | At any time during hospitalisation did the patient experience any of the following: | |
|                   | Pneumonia                   | Cardiac arrhythmia | Seizure | Acute renal injury |
|                   | Bronchiolitis               | Cardiac arrest    | Meningitis / Encephalitis | Pancreatitis |
|                   | Acute Respiratory Distress Syndrome | Cardiomyopathy | Entrapment neuropathies | Liver dysfunction |
|                   | Bacteraemia / Secondary infection | Endocarditis | Bleeding | Skin pressure sore |
|                   | Myocarditis / Pericarditis | Cardiac arrhythmia | Anaemia | Acute renal injury |
|                   |                             |         |
| NB imaging, blood, ECG, pulmonary function results | | |
| Existing Conditions | Any other current medical conditions | Details, management and medications |
|                   | Any previous cognitive or mental health conditions | |
|                   | Any previous ACE inhibitor or ARB | |
| Functional status | Enter Y/N to all that apply | Details |
|-------------------|----------------------------|---------|
| **Respiratory & Exercise** | | Current physical activity level / exercise tolerance |
| | | (Walking, running, cycling - duration / distance) |
| | | (Number of flights of stairs) |
| | | Current Smoker |
| | | Ex-smoker (When quit? pack year history) |
| | | Non-Smoker |
| | | Shortness of breath (SOB) |
| | | SOB at rest |
| | | SOB on minimal activity |
| | | SOB moderate activity / light physical exercise |
| | | No SOB on normal physical exercise |
| **Neurology & Locomotor** | | |
| | | Headache |
| | | Dizziness |
| | | Localised motor weakness |
| | | Localised numbness/ hypersensitivity |
| | | Generalised weakness |
| | | Fatigue |
| **Pain** | | |
| | | Local |
| | | Widespread |
| **Limitations in Activities of Daily Living** | | |
| | | Washing and Dressing |
| | | Toileting and continence |
| | | Transfers (Car/bed, on/off/floor, sit to stand) |
| | | Domestic Tasks (Cooking, cleaning, shopping) |
| | | Any aids being used? |
| **Nutrition** | | |
| | | Eating/Drinking (swallowing & appetite) |
| | | Diarrhoea |
| | | Illness related weight loss |
| **Sleep** | | |
| | | Getting to sleep |
| | | Staying asleep i.e. unplanned waking |
| | | Nightmares |
| **Mood** | | |
| | | Low mood / Depression (NB thoughts DSH) |
| | | Worries / anxiety |
| | | Other |
### Cognitive
- Memory
- Concentration
- Attention
- Confusion
- Speech

### Social and occupational
- Current job role
- Housing, who is patient living with family, children etc
- Any issues at home for example family relationships, safeguarding, childcare

### Rehabilitation issues and planning
#### Key issues / problem list
NB Patient must have had at least 2 weeks rest from end of acute symptoms before commencing exercise.

#### Key Management Plan
- Pain management advice
- Exercise advice and progression plan
- Breathing technique advice
- Cognitive advice
- Mental health / normalisation advice
- Fatigue management advice
- Sleep strategies & advice
- Pacing strategies & advice
- ADL strategies & advice
- Dietary advice
- Welfare advice and sources of support
- Lancashire post hospital rehab website

#### Telephone Triage Outcome
- Admission to DMRC for Covid Rehab Course
- Remote interventions
- Telephone follow up
- Open appointment
- Discharge from DMRC Covid Rehab
- Referral to primary care
- Referral to secondary care specialist
- DCRS investigation battery
Supplementary data file to; Rehabilitation post COVID-19 – Cross-sectional observations using the Stanford Hall remote assessment tool.

Exploratory univariate binary logistic regressions for post-acute symptoms with a prevalence of greater than 30%:

Cross tabulations were checked for each independent categorical variable ensuring each cell contained greater than 1 case and the no more than 20% of independent variables for consideration in the multivariate model contained less than 5 cases (Field 2014 4th Ed p.770).

1. Dependent variable: Post-acute Fatigue

| Independent variable | Direction of effect | Odds ratio   | 95% CI     | Sig. |
|----------------------|---------------------|--------------|------------|------|
| Age                  | Less likely with increased age | 0.980 | 0.945-1.016 | 0.276 |
| Time to VTC          | Less likely with increased time to VTC | 0.971 | 0.936-1.007 | 0.113 |
| LC/NLC               | Less likely with LC | 0.663 | 0.329-1.336 | 0.250 |
| Admitted             | Less likely if admitted | 0.680 | 0.315-1.470 | 0.327 |
| Acute SOB            | More likely with acute SOB | 1.397 | 0.649-3.008 | 0.393 |
| Acute Fever          | Less likely with acute fever | 0.585 | 0.253-1.352 | 0.210 |
| Acute Fatigue        | More likely with acute fatigue | 1.617 | 0.776-3.369 | 0.199 |
| Acute Cough          | Less likely with acute cough | 0.726 | 0.347-1.518 | 0.394 |

No significant univariate relationships identified predictive of post-acute fatigue. Multivariate model not pursued.

2. Dependent variable: Post-acute cough

| Independent variable | Direction of effect | Odds ratio   | 95% CI     | Sig. |
|----------------------|---------------------|--------------|------------|------|
| Age                  | Less likely         | 0.977 | 0.944-1.010 | 0.171 |
| Independent variable | Direction of effect                     | Odds ratio | 95% CI         | Sig.  |
|----------------------|-----------------------------------------|------------|----------------|-------|
| Age                  | More likely with increased age           | 1.008      | 0.975-1.043    | 0.630 |
| Time to VTC          | Less likely with increased time to VTC  | 0.957      | 0.922-0.994    | 0.022*|

One univariate relationship identified predictive of post-acute fatigue. Final univariate model for prediction of post-acute cough below:

Coefficients of the model predicting post-acute cough

| b (SE) | 95% CI for Odds ratio |
|--------|-----------------------|
|        | Lower | Odds | Upper |
| Constant | -0.405 (0.323) | 1.247 | 2.607 |
| Acute SOB | 0.958* (0.376) | 5.452 |

R²=0.056 (Nagelkerke). Model (1) \( \chi^2 = 6.646, p=0.010, *p=0.011 \)

SE = Standard error, CI=Confidence Interval. No standardised residuals > 2, no Cook’s distances >1, no leverage > 300% of average, No Dβeta > 1.
One univariate relationship identified predictive of SOB on mild activity. Final univariate model for prediction of SOB on mild activity:

| Independent variable | Direction of effect | b (SE) | 95% CI for Odds ratio | Sig. |
|----------------------|---------------------|--------|-----------------------|------|
| Constant             |                     | 0.237(0.319) | Lower 0.922, Upper 0.994 | 0.157 |
| Time to VTC          | More likely if admitted | -0.044*(0.019) | Lower 0.957, Upper 0.994 | 0.018 |

R² = .048 (Nagelkerke). Model (1) χ² = 5.561, p = 0.018, *p = 0.022

SE = Standard error, CI = Confidence Interval. No standardised residuals > 2, no Cook’s distances >1, no leverage > 300% of average, No DFbeta > 1.

Note the reciprocal (positive) relationship between time to VTC and SOB on moderate activity below (point 5) as SOB on mild or moderate activity were mutually exclusive the more biologically plausible relationship at point 5 was retained in favour. In summary patients with increased time to VTC were less likely to have SOB on mild activity because they had SOB on moderate activity.

4. Dependent variable: anxiety/mood disturbance

| Independent variable | Direction of effect | Odds ratio | 95% CI | Sig. |
|----------------------|---------------------|------------|--------|------|
| Age                  | Less likely with increased age | 0.976 | 0.943-1.010 | 0.157 |
| Time to VTC          | More likely with increased time to VTC | 1.029 | 0.993-1.065 | 0.113 |
### Table: Coefficients of the model predicting anxiety/mood disturbance

| Independent variable | Direction of effect      | Odds ratio | 95% CI | Sig.  |
|----------------------|--------------------------|------------|--------|-------|
| Age                  | Less likely with increased age | 0.982      | 0.947-1.018 | 0.312 |
| Time to VTC          | More likely              | 1.039      | 1.001-1.078 | 0.044*|

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**Two univariate relationships identified predictive of anxiety/mood disturbance. Final univariate model for prediction of anxiety/mood disturbance below:**

Coeficients of the model predicting anxiety/mood disturbance: Model 1

|                | b (SE)       | Lower CI | 95% CI for Odds ratio | Sig.  |
|----------------|--------------|----------|-----------------------|-------|
| Constant       | -0.021 (0.205) |          |                       |       |
| LC/NLC         | -1.169*(0.368) | 0.151    | 0.311                 | 0.639 |

R² = 0.092 (Nagelkerke). Model (1) \( \chi^2 = 10.916, p = 0.001, ^*p = 0.001. 

Coeficients of the model predicting anxiety/mood disturbance: Model 2

|                | b (SE)       | Lower CI | 95% CI for Odds ratio | Sig.  |
|----------------|--------------|----------|-----------------------|-------|
| Constant       | 0.033(0.213)  |          |                       |       |
| LC/NLC         | -1.041*(0.388) | 0.165    | 0.353                 | 0.756 |
| Admitted       | -0.430*(0.444) | 0.272    | 0.650                 | 1.552 |

R² = 0.100 (Nagelkerke). Model (2) \( \chi^2 = 11.872, p = 0.003, ^*p = 0.007, ^+p = 0.332. \) Block (2) \( \chi^2 = 0.956, p = 0.328. \) **Model 1 retained as final model.**

SE = Standard error, CI=Confidence Interval. N=3 standardised residuals > 2, no Cook’s distances >1, n=10 leverage > 300% of average, No DFbeta > 1.

5. Dependent variable: SOB on moderate activity
| Condition          | Association with increased time to VTC | Lower 95% CI | Upper 95% CI | p-value |
|-------------------|----------------------------------------|--------------|--------------|---------|
| LC/NLC Less likely with LC | 0.975 | 0.482-1.972 | 0.945 |
| Admitted Less likely if admitted | 0.616 | 0.266-1.426 | 0.258 |
| Acute SOB More likely with acute SOB | 1.423 | 0.630-3.217 | 0.397 |
| Acute Fever More likely with acute fever | 2.145 | 0.904-5.089 | 0.083 |
| Acute Fatigue More likely with acute fatigue | 1.151 | 0.539-2.458 | 0.717 |
| Acute Cough More likely with acute cough | 1.664 | 0.788-3.513 | 0.181 |

One univariate relationship identified predictive of post-acute SOB on moderate activity. Final univariate model for prediction of post-acute SOB on moderate activity below:

Coefficients of the model predicting SOB on moderate activity

| b (SE) | Lower 95% CI for Odds | Odds | Upper 95% CI for Odds |
|--------|----------------------|------|-----------------------|
| Constant | -1.428(0.354) | 1.001 | 1.039 | 1.078 |
| Time to VTC | 0.038*(0.019) | 1.039 | 1.078 |

R²=0.037 (Nagelkerke). Model (1) \( \chi^2=4.087, p=0.043, *p=0.044 \)

SE = Standard error, CI=Confidence Interval. No standardised residuals > 2, no Cook’s distances >1, n=2 leverage > 300% of average, No DFbeta > 1.
STROBE Statement—checklist of items that should be included in reports of observational studies

| Item No. | Recommendation | Page No. | Relevant text from manuscript |
|----------|----------------|----------|-------------------------------|
| **Title and abstract** | | | |
| 1 | *(a)* Indicate the study’s design with a commonly used term in the title or the abstract | 1 | Title |
| | *(b)* Provide in the abstract an informative and balanced summary of what was done and what was found | 1/2 | Abstract |
| **Introduction** | | | |
| 2 | Explain the scientific background and rationale for the investigation being reported | 3/4 | Introduction |
| **Objectives** | | | |
| 3 | State specific objectives, including any prespecified hypotheses | 4 | Introduction |
| **Methods** | | | |
| 4 | Present key elements of study design early in the paper | 1, 5/6 | Abstract / Method |
| 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 5/6 | Method |
| **Participants** | | | |
| 6 | *(a)* Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | N/A | |
| | Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls | | |
| | Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants | | |
| | *(b)* Cohort study—For matched studies, give matching criteria and number of exposed and unexposed | | |
| | Case-control study—For matched studies, give matching criteria and the number of controls per case | 5 | Method |
| 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 5/6 | Method, supplementary data file, table 4 |
| **Data sources/measurement** | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 5/6 | Method, supplementary data file, table 1-4 |
| **Bias** | 9 | Describe any efforts to address potential sources of bias | 8 | Strengths and limitation |
| **Study size** | 10 | Explain how the study size was arrived at | 5/6 | Method |

Continued on next page
### Quantitative variables

Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. 5/6 Method

### Statistical methods

(a) Describe all statistical methods, including those used to control for confounding 5/6 Method

(b) Describe any methods used to examine subgroups and interactions 5/6 Method

(c) Explain how missing data were addressed 8 Strength and limitations

(d) **Cohort study**—If applicable, explain how loss to follow-up was addressed

**Case-control study**—If applicable, explain how matching of cases and controls was addressed

**Cross-sectional study**—If applicable, describe analytical methods taking account of sampling strategy 5/6 Methods

(e) Describe any sensitivity analyses N/A

### Results

#### Participants

(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed 6 Results

(b) Give reasons for non-participation at each stage N/A

(c) Consider use of a flow diagram N/A

#### Descriptive data

(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders 6 Results, table 1-2

(b) Indicate number of participants with missing data for each variable of interest 8 Strength and limitations, supplementary data file

(c) **Cohort study**—Summarise follow-up time (eg, average and total amount) N/A

#### Outcome data

**Cohort study**—Report numbers of outcome events or summary measures over time N/A

**Case-control study**—Report numbers in each exposure category, or summary measures of exposure N/A

**Cross-sectional study**—Report numbers of outcome events or summary measures 8/9 Tables 1-4

#### Main results

(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included 6/7 Results, table 2-3

(b) Report category boundaries when continuous variables were categorized N/A

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A

Continued on next page
Other analyses 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses 3/4 Introduction, method, table 2-3

**Discussion**

| Key results | 18 Summarise key results with reference to study objectives | 8/9 Discussion |
| Limitations | 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 7/8 Strengths and limitations |
| Interpretation | 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 10 Discussion |
| Generalisability | 21 Discuss the generalisability (external validity) of the study results | 10/11 Discussion |

**Other information**

| Funding | 22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | N/A |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.