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RESEARCH PROPOSAL

Life After covid-19 (LATER-19): a protocol for a prospective, longitudinal, cohort study of symptoms, physical function and psychological outcomes in the context of a pandemic

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Abstract

Introduction (COVID-19) disease can present with respiratory tract infection and influenza-like symptoms. Although increased symptoms during physical exertion and impairments in lung function have been recently reported as some of the negative effects of COVID-19, no study has defined the recovery trajectories during and following the acute phase of the disease from a symptomatic, physical or psychological perspective. The proposed study will aim primarily to provide a multidimensional analysis of the 12-month recovery of symptoms, physical function, health-related quality of life (HRQoL), and psychological function in adults following a diagnosis of COVID-19.

Methods This report describes the method for a prospective, longitudinal, single-area multi-centre cohort study. Possible international extension is envisaged. Eligibility criteria are patients > 18 years old with a confirmed diagnosis of COVID-19, who provide informed consent. Exclusion criteria include those with pre-existing neuromuscular disorders likely to affect the measures of physical function, diagnosed pre-existing mental illness and significant cognitive impairment likely to affect responses to self-report measures. The study assessment protocol is in two parts. Part A will be undertaken by inpatients, who will undergo added clinical and symptom assessments every 48 hours during the admission. At discharge, participants will be eligible for Part B, incorporating assessments at four time points: on discharge and 3, 6, and 12 months from hospital admission. Assessments will include: symptoms (fatigue and shortness of breath), physical function (functional capacity and peripheral muscle force), HRQoL and psychological (feelings of anxiety and depression, and posttraumatic stress) function. Associations of patient and clinical characteristics predictors with longitudinal in-hospital clinical and symptomatic outcomes will be examined using generalised linear mixed models (GLMM) with random subject effects. Corresponding associations of patient characteristic, clinical pathway and rehabilitation pathway predictors with recovery trajectories will also be examined.

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Introduction

Patients infected with SARS-CoV-2 (COVID-19 disease) present with respiratory tract infection and symptoms such as fever, cough, fatigue, sputum production and/or breathlessness.¹ The spectrum of COVID-19 varies from

asymptomatic infection through mild upper respiratory tract illness, to severe and potentially fatal viral pneumonia with respiratory failure. The Chinese Centre for Disease Control and Prevention reported that 70,420 of the 80,928 confirmed cases in China are "cured and discharged from

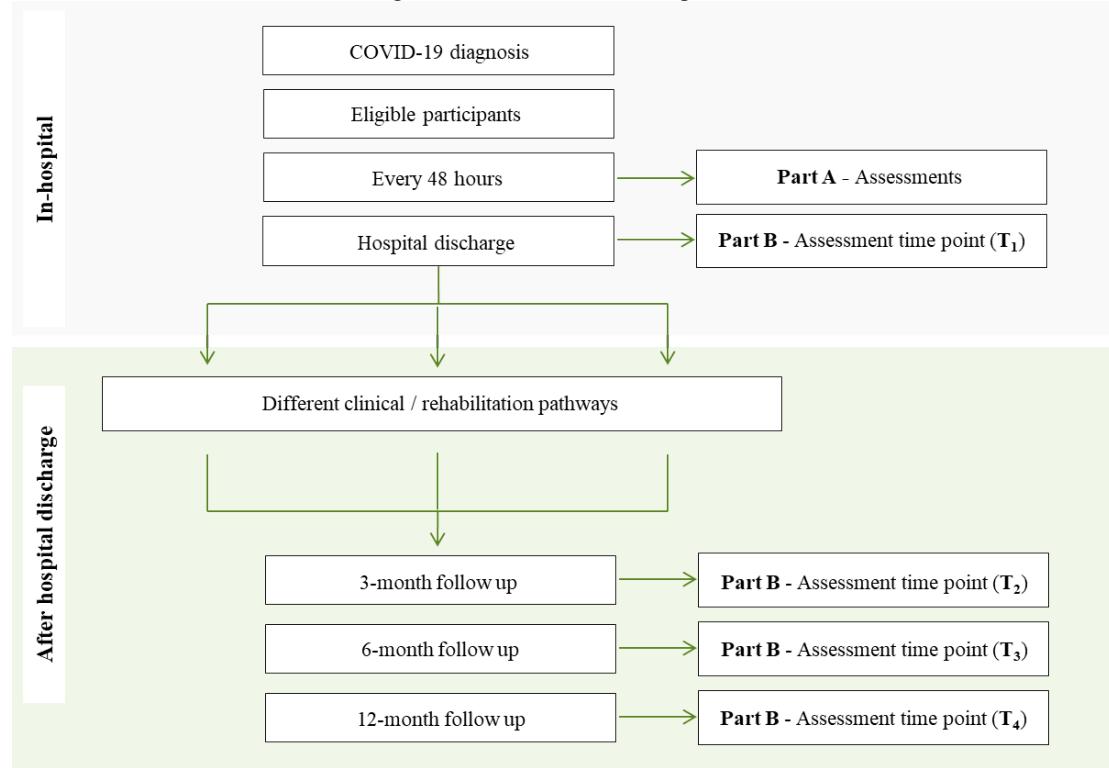
hospital," while 3,245 have died.² However, in the early stage of this pandemic, and due mainly to the lack of understanding of the properties of the virus, inadequate medical protection, high infectivity and absence of effective treatment there was a dramatic increase in the number of patients exceeding medical resources. As a result, the initial patient discharge rate was reported to be relatively low.³ Scientists and health care workers around the world are working to improve treatments in order to reduce mortality, and improved recovery rates are anticipated. Chronic morbidity due to permanent organ damage in some patients is likely, and many patients who have recovered from the acute illness will need ongoing health care and allied health support.

Twenty-three percent of patients with severe acute respiratory syndrome caused by SARS-CoV-1 (SARS) had impaired lung function and a reduced exercise capacity after 1 year compared to normal predicted values.^{4,5} Similarly, there is a strong suggestion of prolonged lung function deficits in some patients with COVID-19. A recently published study⁶ on 50 middle-aged (median [interquartile range] 54 [46 to 62]; 44% female) patients reported that 27 (54%) had impaired lung function 30 days after the onset of symptoms. In another study, 14 of 55 "recovered" COVID-19 patients had lung function abnormalities 3 months after resolution of the acute disease,

and radiological abnormalities were present in 39 patients.⁷ Given the intensive medical management for people with severe loss of respiratory function including prolonged mechanical ventilation, sedation and use of neuromuscular blockade, these patients are likely to be at high risk of intensive care unit acquired weakness (ICU-AW).⁸ This disease has independent long-term effects on symptoms and physical function.⁹ It is therefore desirable to define the clinical trajectory in these patients so as to provide them with appropriate rehabilitative interventions from a symptomatic, physical and psychological perspective.

The primary aim of the proposed study is to therefore provide a multidimensional analysis of recovery over 12 months following diagnosis and hospital admission in adults with COVID-19, with possible extension if recovery trajectories are more prolonged. The specific objectives are to document the duration of symptoms and the time course of physical and psychological recovery during and following the acute (in-hospital or at home) phase of the disease; detect risk factors for patients who deteriorate in spite of treatment; and identify factors and specific elements of pragmatic rehabilitation programs that are associated with recovery of symptoms (fatigue and shortness of breath), physical function (functional capacity and peripheral muscle force), HRQoL, feelings of anxiety and depression, and post-traumatic stress over 12 months.

Figure 1 Flow of assessment protocol



Methods

This will be a prospective, longitudinal, multi-centre cohort study led by Allied Health staff at Fiona Stanley Hospital, in collaboration with Royal Perth Hospital and Sir Charles Gairdner Hospital in Perth, Western Australia (WA). It is designed to complement the Western Australian Health Translation Network (WAHTN) COVID Research Response (CRR). The WAHTN is a state-wide collaborative network of WA's universities, medical research institutes, public and private hospitals, PathWest and the WA Department of Health. International collaboration is also a possibility.

Eligibility Criteria

Adults > 18 years of age and who have tested positive for COVID-19 admitted to the participating hospitals will be eligible to participate. Informed consent will be sought. Exclusion criteria will be pre-existing neuromuscular disorders thought to affect the measures of physical function or known mental illness, or significant communication or cognitive impairment thought to affect responses to self-report measures. Participants will be given a unique study ID, and may withdraw consent at any time, but data accumulated to that point will be retained with assent from the patient.

Outcome assessment Protocol and Timeline

This study assessment protocol has been designed in two parts. The participant flow through this study's assessment protocol is outlined in Figure 1. The outcome assessment protocol is outlined in Table 1.

	Part A: in-hospital ISARIC schedule	Part B: Hospital discharge-12 months	
	Every 48 h	T1	T2-T4
Fatigue at rest	✓	✓	
Dyspnoea at rest	✓	✓	
Fatigue with activity		✓	✓*
Dyspnoea on exercise		✓	✓*
Functional capacity	✓	✓	✓ ^α
Limb power	✓	✓	✓ ^α
Quality of life		✓	✓
Anxiety/depression		✓	✓
Post-traumatic stress	✓	✓	

Table 1. Study outcome assessment protocol. *Collected in patients with ≥ 7 days of length of hospital stay; ^α Sit-to-stand and peripheral muscle power collected where feasible in person or using video conference. ISARIC = International Severe Acute Respiratory and emerging Infection Consortium (<https://isaric.tghn.org/>); T₁, at discharge; T₂, T₃, and T₄; at 3, 6 and 12 m after initial presentation.

Outcomes and Measures

A detailed description of the tests and tools used to assess each outcome measure in Parts A and B is included in the Supplementary Information (after references).

Part A: Acute Hospital Period

Part A will be undertaken by participants during their hospital stay. They will receive standard treatment but will have additional clinical and symptom assessments every 48 hours. The assessments will be performed via phone communication with the participant (who will be in isolation); with the assistance of the attending nurse and/or from distant observation of participant's performance (in the tests related to physical function) via a glass window. This will be on a case-by-case basis. In the case of patient admission to the intensive care unit (ICU) and the need for mechanical ventilation, the assessments will not be attempted while intubated but will resume following extubation from mechanical ventilation in ICU. Routine collection of symptoms and an abridged physical assessment will provide valuable insight into the acute course of the disease to the development of adaptive algorithms to predict those who deteriorate. The first assessment will occur on recruitment and will be completed every 48 hours during the hospital stay.

Symptoms of fatigue and shortness of breath will be assessed using The Edmonton Symptom Assessment Scale (ESAS).^{10,11} The physical assessments will comprise measures of functional capacity, using the 1-minute sit-to-stand test (1STS),¹² and peripheral muscle power (handgrip power) measured using a hydraulic hand dynamometer (Jamar; JA Preston Corporation; MI, USA).¹³ In view of the safety challenges and physical distancing requirements for COVID-19 positive patients, the physical testing has been abridged to clinical tests which can be completed by researchers and treating clinicians (physiotherapists or nurses).

Part B: Discharge to 12 months

Participants will undergo assessments (Table 1) at four time points T₁ – T₄: T₁, at hospital discharge; T₂, T₃ and T₄, at 3, 6 12 months dated from the date of admission. Part B assessments T₂ to T₄ will be performed either in person, or via the use of electronic data capture including telehealth systems, REDCap electronic data capture tool and/or the South Metropolitan Health Service Virtual Clinic System (VCS) (data capture via smartphone).

From T1 to T4 measures to be collected are: (i) functional capacity by the 1STS (face-to-face if the participant remains in contact with clinical services, or remotely by video link); (ii) fatigue related to activities by the Fatigue Severity Scale (FSS);¹⁴ (iii) shortness of breath during activities by the Modified Medical Research Council Dyspnoea Scale (MMRC);¹⁵ (iv) health-related quality of life by the EuroQol 5 dimensions – five response level (EQ-5D-5L);¹⁶ (v) feelings of anxiety and depression: Hospital Anxiety and Depression Scale (HADS);¹⁷ and (vi) posttraumatic stress: Impact of Events Scale–6 (IES-6).^{18,19}

Clinical data and other information

Clinical data will be available in the form of Tier 0 clinical data as per the ISARIC / WHO RAPID minimum dataset (<https://isaric.tghn.org/COVID-19-CRF/>) captured during the WAHTN COVID-19 Research Response program. The data will consist of patient demographics (age, gender, body-mass index at admission), pre-existing comorbidities, short term outcomes such as number of days in intensive care unit, duration of mechanical ventilation, length of hospital stay, recorded mobility status (average distance walked per day), and average daily distance during hospital stay. These data will assist predictive modelling and to identify factors affecting clinical variability after hospital discharge. At T2, patients will be asked to provide a total number of days in isolation as well as information on use of so-called “wellbeing apps” (exercise, mindfulness, meditation, etc.).

Data management

Study data will be recorded and held electronically in the REDCap electronic data capture tool hosted at the Department of Health Western Australia.^{20,21} REDCap is a secure, web-based software platform designed to support data capture for research projects. This data will only be accessible to the recruiters and senior coinvestigators who have established and, or been granted permission to access the database.

Sample size and statistical analysis plan

In this observational trial all suspected and proven COVID-19 positive inpatients in each facility will be given the opportunity to join the study. A 50% recruitment rate is envisaged, owing to the complexity of engaging patients in isolation and availability of recruitment staff resources.

Descriptive summaries will include mean \pm SD or median [interquartile range] for continuous data, and frequency distributions for categorical data [counts or

percentage]. Comparisons of patient baseline characteristics (gender, age, comorbidities) and clinical characteristic data by disease severity (mild or severe/critical) will be undertaken using parametric independent t-tests or oneway ANOVA for normally distributed continuous data and non-parametric Mann-Whitney U or Kruskall-Wallis H tests for continuous data not confirmed to display a normal distribution. Chi-squared or Fisher’s Exact tests, as appropriate, will be applied for categorical data.

Associations of patient and clinical characteristic predictors with longitudinal in-hospital symptomatic and physical functioning outcomes (including ESAS, 1STS, handgrip force) will be examined using generalised linear mixed models (GLMM) with random subject effects, adjusting for disease severity, length of stay in ICU and in hospital, and selected baseline (admission) characteristics. Associations of patient characteristic, clinical pathway and rehabilitation pathway predictors with post-discharge recovery trajectories (including 1STS, FSS, MMRC, EQ-5D-5L, HADS, IES-6 and clinical sequelae) will be examined using GLMM with random subject effects, adjusting for disease severity and selected baseline (discharge) characteristics. All models will be implemented as univariable and predictive multivariable models, with all covariates univariately significant at alpha=0.15 considered as candidate predictors in the multivariable models. Potential confounding variables informed by the literature will also be included in the multivariable models. Results will be summarised using estimated marginal means and 95% CI for continuous outcomes or odds ratios (OR) and 95% CI for categorical outcomes. Model fit will be assessed using residuals checking and cross-validation of models will be undertaken by splitting the dataset to form training and test sets if the sample is large. Missing data points in longitudinal data will be accounted for by the use of maximum likelihood estimation (MLE) methods in the models. Temporal outcomes including time to death and time to discharge in the in-hospital analysis and time to reach recovery milestones, defined according to EQ5D age and gender appropriate norms, in post-discharge analysis will be assessed using Kaplan-Meier survival probabilities and compared between relevant patient characteristic, clinical pathway and rehabilitation pathway predictors using Log rank tests. Effects of these predictors on temporal outcomes will be examined using Cox proportional hazards regression models, censoring at 12 months post-admission and adjusting for relevant baseline patient and clinical characteristics. Results will be summarised using

hazard ratios (HR) and 95% CI. Sensitivity analyses will be performed on patients who are engaged in any other forms of exercise/wellbeing apps/activities and those who are not. Stata MP version 16.0 (StataCorp LP, College Station, TX) will be used for data analysis. All hypotheses will be two-sided and significance will be set at alpha = 0.05. All analyses will be conducted by senior biostatisticians (coinvestigators AJ and HJC).

Provenance: Externally reviewed

Ethics & Dissemination: The protocol has been granted Ethical approval by the South Metropolitan Health Service Human Research Ethics Committee (HREC) (REG 0000004040), with reciprocal approval at the other sites. Results will be published after peer review and disseminated in the community by the consumer group representatives in the LATER-19 advisory group.

Conflicts or declarations of interest: None declared

Funding interests: Supported by the WA Department of Health and the WA Health Translation Network (COVID-19 Research Grants Program). EuroQOL has licensed use of the EQ-5D-5L.

Author Contribution: DWE, LN, AM, LVLD and VC contributed to study conception and design. PG obtained Ethical approval and wrote the initial manuscript. AJ prepared the statistical analysis. The LATER-19 Coinvestigator Group has advised regarding study design and development.

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References

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020; 382: 1708-1720.
2. Data from China shows the majority of people with Covid-19 only suffer mild symptoms, then recover. 2020; <https://edition.cnn.com/2020/03/20/health/covid-19-recovery-rates-intl/index.html>. Accessed 20 March, 2020.
3. Li L-Q, Huang T, Wang Y-Q, Wang Z-P, Liang Y et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol* 2020; 92: 577-583. doi: 10.1002/jmv.25757.
4. Hui DS, Joynt GM, Wong KT, Gomersall CD, Li TS et al. Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. *Thorax.* 2005; 60: 401-409.
5. Hui DS, Wong KT, Ko FW, Tam LS, Chan DP et al. The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. *Chest.* 2005; 128: 2247-2261.
6. Frija-Masson J, Debray M-P, Gilbert M, Lescure F-X, Travert F et al. Functional characteristics of patients with SARS-CoV-2 pneumonia at 30 days post infection. *Eur Resp J.* 2020 56: 2001754. DOI 10.1183/13993003.01754-2020.
7. Zhao Y-m, Shang Y-m, Song W-b, Li Q-q, Xie H et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinicalMedicine* <https://doi.org/10.1016/j.eclinm.2020.100463> (Accessed 22/9/20).
8. Kress JP, Hall JB. ICU-acquired weakness and recovery from critical illness. *N Engl J Med.* 2014; 370: 1626-1635.
9. Herridge MS, Tansey CM, Matté A, Tomlinson G, Diaz-Granados N et al. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med.* 2011; 364: 1293-304.
10. Chang VT, Hwang SS, Feuerman M. Validation of the Edmonton Symptom Assessment Scale. *Cancer.* 2000; 88: 2164-2171.
11. Dudgeon DJ, Harlos M, Clinch JJ. The Edmonton Symptom Assessment Scale (ESAS) as an audit tool. *J Palliat Care.* 1999; 15: 14-19.
12. Bohannon RW, Crouch R. 1-Minute Sit-to-Stand Test: Systematic review of procedures, performance, and clinimetric properties. *J Cardiopulm Rehabil Prev.* 2019; 39: 2-8.
13. Spruit MA, Sillen MJ, Groenen MT, Wouters EF, Franssen FM. New normative values for handgrip strength: results from the UK Biobank. *J Am Med Dir Assoc.* 2013; 14: 775 e775-711.
14. Hjollund NH, Andersen JH, Bech P. Assessment of fatigue in chronic disease: a bibliographic study of fatigue measurement scales. *Health Qual Life Outcomes.* 2007; 5: 12.
15. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax.* 1999; 54:581-586.
16. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res.* 2011; 20: 1727-36.
17. Snaith RP. The Hospital Anxiety And Depression Scale. *Health Qual Life Outcomes.* 2003; 1: 29.
18. Thoresen S, Tambs K, Hussain A, Heir T, Johansen VA, Bisson JI. Brief measure of posttraumatic stress reactions: impact of Event Scale-6. *Soc Psychiatry Psychiatr Epidemiol.* 2010; 45: 405-412.
19. Hosey MM, Leoutsakos JS, Li X, Dinglas VD, Bienvenu OJ et al. Screening for posttraumatic stress disorder in ARDS survivors: validation of the Impact of Event Scale-6 (IES-6). *Crit Care.* 2019; 23: 276.
20. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Informatics.* 2019; 95: 103208.
21. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009; 42: 377-381.

Supplementary information

Study details

Life AFTER covid-19 (LATER-19): a protocol prepared for a prospective, longitudinal, cohort study of symptoms, physical function and psychological outcomes in the context of a pandemic

Outcomes and Measures

Part A: Acute Hospital Period

During the inpatient stay, routine collection of symptoms and an abridged physical assessment will provide valuable insight into the acute course of the disease to the development of adaptive algorithms to predict those who deteriorate. The first assessment will occur on recruitment and will be completed every 48 hours during the hospital stay.

Symptoms: Fatigue and shortness of breath. The Edmonton Symptom Assessment Scale (ESAS). The ESAS was designed to assist in the assessment of symptoms. The severity of symptoms (in this case fatigue and shortness of breath) at the time of assessment is rated between 0 (symptom absent) and 10 (worst possible severity) on a numerical scale.^{1,2}

Functional capacity: 1-minute sit-to-stand test (1STS). Functional fitness capacity will be measured via the 1STS. A chair with a height between 45 and 52cm will be used. Participants will be instructed to fold their arms across their chest and perform the stand up and sit-down movements as quickly as possible for 1 minute. The total number of sit-to-stand repetitions will be recorded as the test result in addition to the patient's nadir peripheral oxygen saturation (SpO₂) during the test. Oxygen desaturation will be defined as a ≥4% fall in SpO₂ to <90%.³

Peripheral muscle power: handgrip force. Handgrip force will be measured using a hydraulic hand dynamometer (Jamar; JA Preston Corporation; MI, USA). Participants will undertake three trials of handgrip force on the first day (to account for learning effects) and one trial on the subsequent assessment days. Peak handgrip force will be assessed bilaterally, on position 2 of the dynamometer, with the elbow at 90° of flexion and the forearm and wrist in a neutral position. Measures will be expressed in absolute values and as a percentage of the predicted value in a healthy population.⁴ Where the patient is unable, or declines to complete the repeated measures protocol, a single grip strength measure assessed for their dominant hand will be recorded.

In view of the safety challenges and physical distancing requirements for COVID-19 positive patients, the physical testing has been abridged to clinical tests which can be completed by researchers and treating clinicians (physiotherapists or nurses). It is recommended that the validity and reliability be optimised by adhering to the standardised methodology herein, developed with co-investigator consensus, and then, where feasible instruction of local research outcome collectors by the Site Coordinator. Where queries arise, please contact CPI Edgar (dale.edgar@health.wa.gov.au).

Part B: From Hospital Discharge to 12 months

Functional capacity: 1-minute sit-to-stand test (1STS). This measure will continue to be collected face-to-face if the participant remains in contact with clinical services, or will be completed remotely during a video conference consultation if face to face appointments are no longer occurring.

Fatigue related to activities: the Fatigue Severity Scale (FSS). The FSS is a 9-item questionnaire with questions related to how fatigue interferes with certain activities. The items are scored on a 7-point scale ranging between strongly disagree (1 point) and strongly agree (7 points). The minimum score is 9 and maximum is 63. The higher the score the greater is the severity of fatigue.⁵ The FSS is the most commonly used fatigue specific questionnaire.⁶

Shortness of breath during activities: Modified medical research council dyspnoea scale (MMRC). Functional limitation resulting from dyspnoea will be assessed using the MMRC dyspnoea scale. This simple but validated⁷ scale comprises five statements. The participant selects the statement which best reflects their level of limitation in activities of daily life due to breathlessness. The score ranges between 0 and 4, with greater scores indicating worse dyspnoea during activities.

Health-related quality of life: the EuroQol 5 dimensions – five response level (EQ-5D-5L).

The EQ-5D-5L is the most widely applied generic multi-attribute utility instrument. Each dimension in the EQ-5D-5L has five response levels ranging between no problems (Level 1) and extreme problems (Level 5). There are 3,125 possible health states defined by combining one level from each dimension, ranging from 11111 (full health) to 55555 (worst health).⁸ EQ-5D-5L health states are converted into a single index ‘utility’ score using a scoring algorithm based on public preferences. In this study, the UK value set and scoring algorithm will be used to calculate utility scores as an Australian scoring algorithm is not yet available. The instrument also includes a visual analogue scale (EQ-VAS) which provides a single global rating of self-perceived health and is scored on a 0 to 100 mm scale representing “the worst...” and “the best health you can imagine”, respectively.

Feelings of anxiety and depression: Hospital Anxiety and Depression Scale (HADS).

Feelings of anxiety and depression will be measured using the HADS.⁹ It comprises 14 statements describing symptoms of depression (7 items) and anxiety (7 items). Response options for each question range from 0 to 3, with a total range score between 0 and 21 for the depression and anxiety subscales. Higher scores represent greater feelings of depression and/or anxiety. Scores ≤ 7 are considered normal, scores > 7 and < 11 are considered borderline abnormal and values ≥ 11 are suggestive of a likely clinical diagnosis of depression or anxiety.⁹

Post-traumatic stress: Impact of Events Scale–6 (IES-6).

Symptoms of posttraumatic stress will be measured using the IES-6.¹⁰ The IES-6 has shown to be a robust measure of posttraumatic stress reactions, and has been shown to be a reliable and valid screening tool in survivors of acute respiratory distress syndrome.¹¹ The measure contains six items relating to symptoms of hyperarousal, intrusion and avoidance. Response options range from 0 (“not at all”) to 4 (“extremely”). The scale produces a total score, calculated as the mean of the six items, with higher scores indicating higher levels of distress.

References

1. Chang VT, Hwang SS, Feuerstein M. Validation of the Edmonton Symptom Assessment Scale. *Cancer*. 2000; 88: 2164-71.
2. Dudgeon DJ, Harlos M, Clinch JJ. The Edmonton Symptom Assessment Scale (ESAS) as an audit tool. *J Palliat Care*. 1999; 15: 14-19.
3. Morita AA, Bisca GW, Machado FVC, Hernandes NA, Pitta F, Probst VS. Best Protocol for the Sit-to-Stand Test in Subjects With COPD. *Resp Care*. 2018; 63: 1040-49.
4. Spruit MA, Sillen MJ, Groenen MT, Wouters EF, Franssen FM. New normative values for handgrip strength: results from the UK Biobank. *J Am Med Dir Assoc*. 2013; 14: 775 e775-711.
5. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol*. 1989; 46:1121-23.
6. Hjollund NH, Andersen JH, Bech P. Assessment of fatigue in chronic disease: a bibliographic study of fatigue measurement scales. *Health Qual Life Outcomes*. 2007; 5: 12.
7. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*. 1999; 54: 581-586.
8. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P *et al*. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011; 20: 1727-36.
9. Snaith RP. The Hospital Anxiety And Depression Scale. *Health Qual Life Outcomes*. 2003; 1: 29.
10. Thoresen S, Tambs K, Hussain A, Heir T, Johansen VA, Bisson JI. Brief measure of posttraumatic stress reactions: impact of Event Scale-6. *Soc Psychiatry Psychiatr Epidemiol*. 2010; 45: 405-412.
11. Hosey MM, Leoutsakos JS, Li X, Dinglas VD, Bienvenu OJ *et al*. Screening for posttraumatic stress disorder in ARDS survivors: validation of the Impact of Event Scale-6 (IES-6). *Crit Care*. 2019; 23: 276.

Physical Testing Protocols

1 MINUTE SIT TO STAND PROTOCOL

This is a protocol for the 1 Minute Sit to Stand (STS) test. The testing procedures have been informed by recommendations from a systematic review of the literature,¹ with adaptations for the clinical environment, research protocol and hospitalised patient acuity. The test should be completed as an activity ‘bundled’ with other care requirements to minimise risk and PPE use – please check with nursing and other team members if there is any in-room tasks or patient needs that can be attended to in conjunction with completing this test. The recorded details below have the potential to reflect the severity of impact of the disease state and allows those who cannot complete one STS independently to record an outcome on the test. The appropriateness of these categorisations of an effort of up to one STS are yet to be finalised. The weighting of the physical assistance necessary from others to complete the one stand during the time of the test, and the amount of supplemental oxygen required, are yet to be validated.

Equipment:

1x Chair with seat height 45 – 52cm (preferably without arm rests)

1x stop watch / timer

1x pulse oximeter

BORG and Fatigue (/10) scales – printed & to be left in room

PPE as required for self +/- patient, including gown, gloves and appropriate face mask for completing an aerosolising procedure.

Procedure:

This test should be administered face to face in the first instance. Patients within one week of initial symptoms of COVID-19 should have face to face testing. After this time the clinician may determine whether it can be safely administered from the patient window using the IPAD or phone, therefore minimising clinician risk and minimising use of PPE.

1. Initial Screening

- a. Medical approval to conduct the test should be sought for patients who are in the acute phase of their condition. This should be recorded on the data sheet.
- b. Absolute contraindications to this test include:
 - i. Raised troponin
 - ii. Resting heart rate >120 bpm
 - iii. Abnormal / unstable baseline heart rhythms
 - iv. Oxygen requirement >4L / min (ie. not on nasal prongs)
- c. If there are any other concerns about the patient condition – please discuss performing this test with the medical team or a senior clinician.

2. Initial Data Recording

- a. Current clinical observations – Heart rate, Respiratory rate, Blood pressure, Oxygen saturations (SpO_2), Oxygen administered, Resting BORG and leg fatigue.

3. Preparation

- a. If a patient is COVID-19 POSITIVE and a staff member is present in the room at the time of this test:
 - i. The staff member should wear PPE as per the current policy for the location in which the test takes place
 - ii. The patient should wear a surgical mask as this is classed as an aerosolising procedure
- b. If a patient is COVID-19 NEGATIVE and a staff member is present during the test
 - i. PPE should be worn as required for that individual
- c. Record the date of assessment on the data sheet.
- d. Ask the patient to sit in the bedside chair which is positioned against a wall or bed (so that chair is stable and not likely to move) and without wheels.
- e. Ask the patient to position themselves so that their feet are flat on the ground and the calf is forward of the seating surface. Arms are crossed over their chest.
- f. Ensure that tubes or lines attached to the patient are safely positioned.
- g. Demonstrate a sit to stand where possible.

4. Instruct the patient:

“When I say go, I want you to repeatedly stand all the way up and sit down as many times as you can for 1 minute. You are aiming to do as many as you can in that minute.

If you need to rest at any time, you are free to do so, however, you should resume as soon as you can.

If you get chest pain or dizziness, please sit down and inform me.

If I need you to stop for any other reason, I will ask you to stop...

... (If patient is monitoring their own SpO_2 – insert here that the patient “should rest if it reaches <88% and recommence when it goes over 88%”)...

You are aiming to do as many sit-to-stand cycles as you can in 1 minute.”

5. Perform the test

- a. Patient should remain on prescribed resting, or, prescribed exertional FiO_2 during the test
- b. Give the patient a “GO” command and start the timer

- c. Do not provide encouragement but remind to stand up with full hip and knee extension as needed.
 - d. Inform the patient when 30 seconds & 10 seconds remain in the test.
 - e. Stop the test after 60 seconds.
6. Stopping Criteria
- a. The patient should be instructed to rest when:
 - i. SpO₂ falls to less than 88% during the test. Patients can re-commence within the minute test when SpO₂ is equal to or greater than 88%.
 - ii. HR response is of concern. Ie. \geq HR max (220-age) or beta-blocker resting HR +40
 - iii. they report new chest pain or dizziness during the test
7. Recording
- a. Record Oxygen requirements
 - b. Count each repetition and mark on the score sheet.
 - i. Full knee extension is recorded must be achieved for a repetition to be counted. Count each stand upon full knee extension.
 - c. Record the number of repetitions following the “Original” unassisted protocol AND the number of “deviations” to the original protocol on the datasheet
 - d. Record what deviations were taken (eg. Use of arms for balance, not full knee extension, or any other deviation)
 - e. Record the number of rests required, duration of rests and reason for resting.
 - f. If the patient requires physical assistance during the test – they score 0.
 - g. Record the following for the patient rating of the test
 - i. Lowest SpO₂
 - ii. Highest heart rate
 - iii. BORG (Dyspnoea & Leg Fatigue)
 - iv. Limiting factor for completing sit to stands
 - v. Leg fatigue
 - h. Please record any deviations to the protocol in the data sheet
8. Post-test
- a. Recovery: Continuously monitor SpO₂ until return to baseline and record time taken to achieve baseline
 - b. Any equipment that are to be removed from the room
 - i. Should be double wiped with appropriate surface cleaner, if patient is COVID-19 POSITIVE.
 - ii. Should be cleaned with appropriate surface cleaner, if patient is COVID-19 NEGATIVE
 - c. Enter data into the electronic data management system
 - d. Please document any perceived issues, concerns or suggestions about the protocol – these will be collated and discussed regularly with the clinical teams whilst testing occurs.
 - e. Please document this test in the medical record, including the following features.
 - i. Number of sit to stands completed, plus assistance needed if any.
 - ii. FiO₂ used
 - iii. Lowest SpO₂ during test
 - iv. Time to return to baseline SpO₂ after the test
 - v. Other observations recorded
 - vi. Any adverse events during the test
 - vii. Reasons for ceasing the test
 - viii. Any other details determined pertinent for the individual patient

Reference

1. Bohannon RW, Crouch R. 1-Minute Sit-to-Stand Test: SYSTEMATIC REVIEW OF PROCEDURES, PERFORMANCE, AND CLINIMETRIC PROPERTIES. J Cardiopulm Rehabil Prev. 2019; 39: 2-8.

JAMAR GRIP STRENGTH DYNAMOMETRY PROTOCOL

Equipment:
<ul style="list-style-type: none">• Chair• Jamar grip strength dynamometer (GSD)
Preparation:
<ul style="list-style-type: none">• Patient seated in a chair with feet flat on floor
Procedure:
<ul style="list-style-type: none">• Posture: seated with their shoulder adducted and neutrally rotated, elbow at 90 degrees flexion, forearm neutral position and wrist between 0 and 30 degrees flexion and between 0 and 15 degrees ulnar deviation.• Patient holds GSD• GSD is set at the second setting (grip span 4.8cm)• Three alternating left and right, 2 second sustained contractions of maximal efforts performed.
Standardised Instructions:
Instructions to the patient
<ul style="list-style-type: none">• “This device measures the strength of your hands. Please squeeze it as hard as you can with one hand, alternating between left and right.”• “If at any stage you feel dizzy, nauseous or high levels of pain, stop”
Verbal encouragement during each trial:
<ul style="list-style-type: none">• “Squeeze as hard as you can. Harder! Harder! Relax” (instructions to last 2 seconds).
Post-Trial
<ul style="list-style-type: none">• Record the highest peak force reading for left and right sides

LATER-19 Co-investigator Group

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