BMJ Open  Functional recovery following hospitalisation of patients diagnosed with COVID-19: a protocol for a longitudinal cohort study

Julie C Reid,1 Andrew P Costa,2,3,4,5,6 MyLinh Duong,2 Terence Ho,2 Rebecca Kruisselbrink,2,3 Parminder Raina,4,8 Renata Kirkwood,1 Aaron Jones,3,4 Sophie Corriveau,2 Lauren E Griffith,4 Shariq Haider,2 Maura Marcucci,2,4 Maureen Markle-Reid,6 Hope Morrison,1 Natya Raghavan,2 Connie Schumacher,7 Brenda Vrkljan,1 Mats Junek,2 Leslie Martin,2 Ameen Patel,2 Carla Girolametto,8 Tyler Pitre,2,3 Marla K Beauchamp,1,2,5,6 On behalf of the COREG Investigators

ABSTRACT

Introduction COVID-19 is an international public health crisis with more than 132 million infections worldwide. Beyond acute infection, emerging data indicate patients diagnosed with COVID-19 may experience persistent sequelae similar to survivors of sepsis or acute respiratory syndromes, including mobility limitations and fatigue. However, there is limited evidence on the trajectory of functional recovery in those hospitalised with COVID-19. The primary aim of the Coronavirus Registry Functional Recovery (COREG-FR) study is to understand the trajectory of functional recovery among individuals hospitalised for COVID-19 over the medium (up to 6 months) and longer term (6–12 months) that will guide clinical care and optimal management of serious COVID-19 illness and recovery.

Methods and analysis COREG-FR is a multicentre longitudinal cohort study. We will enrol a minimum of 211 adults age 18 years and older with COVID-19 from five hospitals. Participants will be followed from admission to hospital as an inpatient, to hospital discharge, and at 3-month, 6-month, 9-month and up to 12-month post-hospital discharge. We will conduct telephone interviews at ward admission and discharge, and telephone interviews plus in-person assessments of physical function and lung function at all remaining follow-ups. Our primary outcome is the Activity Measure for Post-Acute Care mobility scale measured at all time points. We will conduct linear mixed effects regression analyses to explore determinants of functional outcomes after COVID-19 illness. Subgroup analyses based on age (≤65 vs >65 years), frailty status (Clinical Frailty Scale score ≤4 vs >5) and variants of concern will be conducted.

Ethics and dissemination COREG-FR has been approved by Research Ethics Boards at participating sites. We will disseminate this work through peer-reviewed manuscripts, presentations at national and international meetings and through the established COREG website (www.coregontario.ca). COREG-FR is designed as a data platform for future studies evaluating COVID-19 recovery.

Trial registration number NCT04602260; Pre-results.

INTRODUCTION

First identified in late 2019, SARS-CoV-2 has caused a global pandemic with over 132 million infections and over 2.8 million deaths worldwide as of 31 March 2021.1 In the Canadian province of Ontario, there have been more than 370 000 infections and 7475 deaths.2 Importantly, the risk for hospitalisation and death due to COVID-19 increases steadily with age, with adults age 40 years and older accounting for 91% of hospitalisations and nearly 100% of deaths.3 Although there has been a rapid and coordinated response to study the effects of COVID-19 in the acute stages, data focused on medium-term and long-term functional recovery is limited.

Survivors of serious illnesses, such as sepsis4–6 and other acute respiratory syndromes,7 8 are known to have a higher risk for long-term sequelae, including persistent mobility limitations. While such sequelae have been attributed to extensive bed rest and/or prolonged stays in the intensive care unit (ICU),9–11 severity of illness and illness...
pathology have also been identified as critical factors affecting functional recovery. Emerging data suggest survivors of COVID-19 also experience persistent, long-term consequences. Indeed, a recent study by Huang et al. followed 1733 patients hospitalised due to COVID-19 for 6 months to characterise patient-reported symptoms, quality of life and physical function. Seventy-six per cent of patients reported at least one symptom at follow-up, with the most common being fatigue (76%), muscle weakness (63%) and sleep difficulties (26%). Other studies evaluating shorter term outcomes (6–12 weeks) demonstrated similar results, including persistent symptoms of fatigue, dyspnoea and myalgia. Chopra et al. followed patients for 60-day post-hospital discharge and reported that 39% of those hospitalised with COVID-19 were unable to return to previous activity levels, with 38% (n=75 of 195) reporting they were either unable to return to paid work due to their health (n=45) or returned at reduced hours or modified duties (n=30).

We identified three cohort studies that followed patients for 12 months post-COVID-19 related hospitalisation with sample sizes ranging from 83 to 1276 patients. All studies reported substantial improvements across the recovery trajectory in terms of symptoms, clinical findings (eg, chest CT) and physical function (as measured by 6 min walk distance, Barthel Index or Lawton-Brody Scale), with many domains returning to predicted values by 12 months. However, all studies reported a proportion of patients, up to 57%, with at least one persistent symptom at 1 year. While these studies provide early evidence of the lasting consequences of COVID-19, comprehensive, prospective, long-term (ie, beyond 6 months) data using standardised outcome measures that track functional recovery are still limited. In addition, most studies to date have not included premorbid assessments of functioning. Furthermore, with the emergence of new variants of concern (VOCs), there is an urgent need to understand their impact on recovery and patient outcomes.

Understanding the medium-term (up to 6 months) and longer term (6–12 months) trajectory of functional recovery for adults hospitalised with COVID-19 is critical to inform health and rehabilitation interventions for survivors and improve patient outcomes. The Coronavirus Registry (COREG) Functional Recovery (COREG-FR) study (NCT04602260) is an extension of COREG (NCT04508959), a COVID-19 registry research platform capturing comprehensive data on all patients during hospitalisation with COVID-19 in the Waterloo, Niagara and Hamilton regions (seven hospitals (www.coregontario.ca). The objectives of COREG-FR are to: (1) characterise the functional recovery of hospitalised adults (age 18+ years) diagnosed with COVID-19 at 3-month, 6-month, 9-month and up to 12-month post-hospital discharge in terms of mobility, daily activity, cognition, lower extremity function, pulmonary function and symptoms and (2) examine the determinants of functional outcomes after COVID-19 illness for hospitalised adults, including exploring the impacts of age, frailty status, comorbidities and new VOC.

METHODS AND ANALYSIS

Study design

This is a multicentre longitudinal cohort study that will prospectively collect data on individuals admitted to hospital with COVID-19 since the start of the pandemic. Patients hospitalised prior to study initiation in July 2020 will be recruited retrospectively; their follow-ups will be conducted prospectively starting with the first applicable time point after recruitment. Retrospective recruitment will go as far back as the first documented hospital admission date in the COREG database, which was 9 March 2020. Hospital admission and discharge data will be collected retrospectively. Figure 1 shows the study schema.

Study population

We will include adult patients, age 18 years and older who are either currently hospitalised or recently discharged due to COVID-19 infection in accordance with the International Severe Acute Respiratory and emerging Infection Consortium definition. Participants will be recruited from five hospitals in Hamilton and Kitchener-Waterloo regions. Participants must be able to communicate in English in order to provide informed consent and complete the follow-up assessments. We will exclude those who were previously institutionalised (eg, in long-term care), with premorbid severe mobility limitations (eg, unable to stand without physical assistance), and with cognitive impairment limiting their ability to complete follow-up assessments.

For individuals admitted to hospital prior to study initiation (July 2020), we will identify them through the COREG registry and approach consecutive patients that meet inclusion criteria. Prospectively, site leads will identify potential patients through daily Infection Prevention and Control data, either from confirming a positive case by nasopharyngeal swab or a confirmed case from the day of admission to a medical unit, emergency department or ICU. These patients will be concurrently entered into COREG and approached to participate in this extension study, either while still in hospital or shortly after discharge to home.

Patient and public involvement

The patients in this study were not involved in the development of the research question or design of this study. They will not be involved in recruitment or conduct of the study; however, we will include patient partners in the interpretation of results and dissemination of findings to ensure we represent what is most important to survivors, including how we define and describe long COVID-19.

Study procedures

Included hospital patients will be assessed on admission to a medical unit, at hospital discharge, and at 3-month,
6-month, 9-month and up to 12-month post-hospital discharge. Hospital admission and discharge data will be collected by review of the medical record and by telephone interviews as described further. Post-hospital discharge assessments will consist of telephone questionnaires and home visits to assess physical function and lung function. Two research physiotherapists affiliated with the study will conduct the home assessments. Both the physiotherapists and participants will be screened for symptoms of COVID-19 prior to the home visit and personal protective equipment will be worn by both parties, except during the spirometry tests where the participant will not be able to be masked. Table 1 outlines study measures and time points.

Patients admitted to hospital due to COVID-19 prior to study initiation in July 2020 will similarly be prospectively assessed at 3, 6, 9 and up to 12 months after hospital discharge, starting with the closest time point after recruitment. Hospital admission and discharge data will be collected retrospectively. After consent (or coinciding with the consent phone call per the patient’s preference), patients will receive one phone call to complete premorbid, hospital admission and hospital discharge questionnaires.

In the case of future surges in COVID-19 infections and the possibility for reinstitution of strict lockdown measures, home visits may be paused. In that event, or in the event that a patient declines home visits, follow-ups will be conducted by phone only and will include the standardised patient-reported questionnaires typically administered during the home visit (see Table 1). Spirometry and physical function measures will not be completed remotely at this time.

Data and measures
At baseline, we will collect demographic and health information from COREG, including age, sex at birth, ethnicity, comorbidities, onset date of first or earliest COVID-19 symptoms, as well as data related to VOC (from the medical record as available) and vaccination status. We will extract COVID-19 illness symptoms from hospital admission (eg, fever, cough, myalgia, nausea or vomiting, etc), vital signs (eg, temperature, heart rate, blood pressure, etc) and data on patients’ COVID-19 hospitalisation, including length of stay, ICU admission (including the need for oxygen therapy and mechanical ventilation), medications (eg, dose and duration of steroids), complications and any other documented treatments (eg, prone positioning).

At the first phone call, we will collect premorbid medical information, including alcohol use, smoking status and history, and medication use. We will also collect premorbid data on physical function (eg, falls history, gait aid use and basic mobility status), socioeconomic status (eg, household income, level of education and employment situation), living situation (eg, type of dwelling and living alone), cognitive status and frailty status (for those age 60+ years only).

At all subsequent follow-ups, we will collect data on any changes in the baseline information outlined previously, and any persistent or new symptoms. We will also collect data on functional outcomes as described further. Outcome measures were chosen in consultation with frontline clinicians and based on international consensus recommendations. Physical function measures were selected based on the following criteria: (1) administration time <5 min, (2) easily conducted by clinicians and
nurses if needed, (3) commonly used by clinicians in respiratory rehabilitation or in hospitalised settings and (4) evidence for their psychometric properties in adults.

**Primary outcome**

The Activity Measure for Post-Acute Care (AM-PAC), specifically its basic mobility domain, is our primary outcome. The AM-PAC is a patient-reported activity limitation instrument based on the International Classification of Functioning, Disability, and Health that assesses three domains: basic mobility, daily activities and applied cognition. Each item is scored from 1 (unable to perform) to 4 (none or no difficulty) with lower scores indicating lower levels of function (ie, patients have much difficulty or are unable to perform certain tasks). The AM-PAC can be clinician administered or patient-reported and has been validated for patients receiving postacute care services. It has shown to be more responsive to change than the commonly used Functional Independence Measure (FIM). There is both an inpatient and outpatient version of the AM-PAC, with the inpatient version shortened to 6-items (AM-PAC 6 Clicks). The AM-PAC Mobility and Cognition subscales will be administered in reference to premorbid functioning. We will use these premorbid scores to define functional recovery. The 6 Clicks questionnaire will be administered at hospital admission and discharge to measure current functional status, and the full AM-PAC will be administered at all follow-up time points. Individual domain scores are converted to a standardised score, which allows comparison across the different forms (eg, daily activities inpatient scores can be compared with daily activities outpatient scores). Furthermore, by allowing comparison of domain scores across forms, the transformed scores can be used to assess change over time.

**Secondary outcomes**

We will assess a number of secondary outcomes to characterise the functional recovery trajectory of patients with COVID-19.

**Supports and activity**

We will record information not captured in COREG, including health-related or emotional supports.

### Table 1 Schedule of events for this longitudinal cohort study

| Instrument                                    | Premorbid* | Admission (to ward)* | Hospital discharge* | 3 months | 6 months | 9 months | 12 months |
|-----------------------------------------------|------------|----------------------|---------------------|----------|----------|----------|----------|
| COREG demographics                            | ✔          |                      |                     |          |          |          |          |
| COREG symptoms and hospital stay info         | ✔          |                      |                     | ✔        | ✔        | ✔        |          |
| Demographics and medical info                 | ✔          |                      |                     |          |          |          |          |
| Symptoms                                      | ✔          | ✔                    |                     | ✔        | ✔        | ✔        | ✔        |
| Follow-up interview                           |            |                      | ✔                   | ✔        | ✔        | ✔        | ✔        |
| Clinical Frailty Scale (only for 60+ years)   | ✔          |                      |                     | ✔        | ✔        | ✔        | ✔        |
| AM-PAC Inpatient (6 Clicks)                    | ✔          |                      |                     | ✔        | ✔        | ✔        | ✔        |
| AM-PAC Outpatient                             | ✔†         |                      |                     | ✔        | ✔        | ✔        | ✔        |
| Post-COVID-19 Functional Status Scale         |            |                      |                     | ✔        | ✔        | ✔        | ✔        |
| Functional Independence Measure               |            |                      |                     | ✔        | ✔        | ✔        | ✔        |
| MRC Breathlessness Scale                      |            |                      |                     | ✔        | ✔        | ✔        | ✔        |

*Data will be collected at the first phone interview.
†Only mobility and cognition subscales are collected premorbid.
‡These outcome measures can be administered by telephone in the event that home visits are paused.
AM-PAC, Activity Measure for Post-Acute Care; EQ-5D-5L, EuroQoL-5D-5L; MRC, Medical Research Council.
individuals are receiving or wish they were receiving, any follow-up care they are receiving or have received since discharge from hospital (eg, pulmonary or physical rehabilitation) and mobility status (including risk for falling, level of physical activity and others).

Clinical Frailty Scale (CFS)
We will administer the CFS for patients aged 60 years and older to determine frailty status.29 This interview-based scale asks patients about their independence and physical abilities to determine their frailty status from 1 (very fit) to 9 (terminally ill).30 The CFS is a valid tool to identify frail and ill older adults. While the CFS has not been validated in patients ≤65 years, evidence suggests that frailty reflects biological age, rather than chronological age and therefore warrants evaluation in those younger than 65 years.31 Specific to COVID-19, evidence shows that disease outcomes in hospitalised patients 18 years and older were better predicted by frailty than by age or comorbidity.32

Post-COVID-19 Functional Status Scale (PCFSS)
Developed in early 2020, this five-point scale assesses how individuals have been affected in their everyday life by COVID-19 illness and recovery.33 Lower grades indicate better functioning, with grade 0 representing the absence of symptoms or functional limitations and grade four reflecting severe limitations and symptom burden.33 The PCFSS can be patient-reported following a flow diagram series of questions to result in a grade, or it can be administered via structured interview, which is more comprehensive. We will conduct the structured interview over the phone and the patient-reported flow chart during the home visits.

Functional Independence Measure
The FIM assesses patients’ functional status based on the level of assistance they require, with grading categories ranging from ‘total assistance with helper’ to ‘complete independence with no helper’.34 35 Evaluated tasks include bowel and bladder control, transfers, locomotion, communication and social cognition. The FIM has good inter-rater reliability, construct validity and responsiveness to change in adults 45 years and older.36 We included the FIM at 3-month and 6-month post-hospital discharge, as an established measure by which to compare the responsiveness of the AM-PAC and PCFSS. This measure will be administered by telephone interview, which has been shown to be a valid alternative to the traditional multidisciplinary observational method of administration with total score agreements (intraclass correlation coefficients) ranging from 0.65 to 0.92.37–39

Impact of Event Scale-Revised
This self-report measure includes 22 items that capture subjective distress caused by traumatic events. Each item is rated on a five-point scale from 0 (‘not at all’) to 4 (‘extremely’) with total scores from 0 to 88; lower scores indicate less distress. The three subscales are intrusion, avoidance, and hyperarousal; subscale scores can be calculated separately.40 41

Hospital Anxiety and Depression Scale (HADS)
The HADS is a 14-item two-dimension scale that identifies depression and anxiety among physically ill patients. Scores range from 0 to 21, with higher scores indicating higher levels of anxiety. In the general ill population, a cut-off of ≥28 indicates depression.42

EuroQol-5D-5L (EQ-5D-5L)
The EQ-5D-5L is a six-item questionnaire measuring health-related quality of life.43 It assesses five domains (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each containing five responses from no problems to extreme problems or ‘unable to’ in a domain.44 There is also an overall question of health state using a visual analogue scale from 0 (poor state of health) to 100 (good state of health). The EQ-5D-5L will be used to evaluate change in health-related quality of life over the course of recovery, and scores will be compared as such.

Fatigue Visual Analogue Scale
This visual scale allows individuals to rate their global fatigue from 0 (worst fatigue) to 10 (normal).51 45

Medical Research Council breathlessness scale
This brief questionnaire contains five statements describing a range of breathlessness from only becoming breathless with strenuous exercise (grade 1) to being too breathless to leave the house (grade 5). Higher grades indicate more functional limitations due to breathlessness.46

Pulmonary function tests
We will collect physiological measures, such as the need for ongoing supplemental oxygen, along with prebronchodilator spirometry measurements, including forced expiratory volume in 1-second (FEV₁), forced vital capacity (FVC), and FEV₁/FVC ratio following American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines.47 Both research physiotherapists completed training with a pulmonologist on conducting these spirometry tests. Spirometry will be conducted with the participant sitting and wearing a nose clip. Up to a maximum of eight forced expiratory manoeuvres will be permitted to obtain three acceptable efforts, which will be recorded and graded at a later date. All recorded tests, including the spirographs, will be independently graded for acceptability and reproducibility by two pulmonologists following ATS/ERS criteria.48

Short Performance Physical Battery (SPPB)
The SPPB combines the results of three tests of physical function (gait speed over 4 m, five-repetition chair stand, progressive balance test) to assess lower extremity function. Tests are scored on a five-point scale from 0 (patient unable to perform) to four based on the time the patient takes to complete the walk, chair stands and balance tests.
with a sum score from 0 (worst performance) to 12 (best performance).49 50 The SPPB has good to excellent test–retest reliability in older adults (intraclass correlation coefficient 0.81 to 0.91).51–53 Cut-off scores of ≤10 indicate increased odds of mobility disability54 and scores of ≤7 indicate increased odds ofrehospitalisation or death.55

Oxygen saturation (SpO₂)
SpO₂ will be measured using a fingertip pulse oximeter to detect hypoxia and to evaluate any persistent hypoxia post-COVID-19 illness. We will measure SpO₂ before and after the spirometry and physical function assessments based on the findings of a recent systematic review highlighting the importance of assessing exertional desaturation in patients with COVID-19.56 Based on existing evidence, authors recommend that a drop of 3% in SpO₂ measurements from rest to exertion should be cause for further assessment.56

Sample size
We will enrol consecutive patients until a minimum sample of 211 is recruited or until the end of our operational funding window. We calculated sample size based on detecting a minimal clinically important change of 3.3 points (SD 7.3) from premorbid scores in the AM-PAC mobility score over 12 months,57 which corresponds to an effect size of 0.23, assumes a power of 80% with alpha set to 0.05 and accounts for 30% loss to follow-up.58 To date, 130 patients have been enrolled and recruitment is ongoing.

Proposed statistical methods
Descriptive analyses for continuous variables using measures of central tendency and dispersion will be conducted. McNemar’s test will be used to evaluate within-subject change in categorical variables across follow-up, and paired t-tests will be used to examine changes in continuous variables. If paired differences in continuous variables are not normally distributed, then the Wilcoxon signed-rank test will be used. We will conduct linear mixed effect regression analyses to determine how sociodemographic and clinical factors are associated with long-term functional recovery. Significance will be set at p<0.05. We will conduct a priori subgroup analyses based on age (≤65 vs >65) and frailty status (CFS ≤4 vs CFS >5) and VOC as permitted by sample size. If missing data is minimal (≤5%) we will conduct a complete case analysis, otherwise we will use multiple imputation.

We will perform interim analyses as data become available to provide as real-time information as possible to inform pandemic care. While this data platform is being developed to answer the core questions outlined previously, the data will be made available to researchers who wish to conduct additional analyses related to COVID-19 recovery.

Data management and confidentiality
We will keep all collected data confidential with only the research team having access to completed questionnaires. At the beginning of the study, each participant will be assigned a unique identifier, and all data sources will be deidentified and coded. Records will only be electronic and will be stored on REDCap through the McMaster University network servers. REDCap is a secure web application that is protected by usernames and passwords that are assigned to individuals responsible for collecting data. Per Hamilton Integrated Research Ethics Board (HiREB) requirements, we will store all data for 5 years after data collection is completed.

ETHICS AND DISSEMINATION
Ethics and informed consent
This study has been approved by the HiREB for all Hamilton study sites, and by the Tri-Hospital Research Ethics Board for Kitchener-Waterloo sites. Participation in this study is voluntary, and participants provide informed consent.

Dissemination
We will report this study in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology Statement.58 We will disseminate results at national and international academic conferences, through peer-reviewed publications, through communications with key stakeholders and hospital leadership and through the COREG website (www.coregontario.ca). This study will contribute important data to advance our understanding of the recovery of physical function and rehabilitative care needs of survivors of serious COVID-19 illness.

Author affiliations
1School of Rehabilitation Science, McMaster University, Hamilton, Ontario, Canada
2Department of Medicine, McMaster University, Hamilton, Ontario, Canada
3Michael G. DeGroote School of Medicine, Waterloo Regional Campus, McMaster University, Kitchener, Ontario, Canada
4Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada
5The Research Institute of St. Joe’s Hamilton, St. Joseph’s Healthcare Hamilton, Hamilton, Ontario, Canada
6McMaster Institute for Research on Aging, McMaster University, Hamilton, Ontario, Canada
7Department of Nursing, Brock University, St. Catharines, Ontario, Canada
8Department of Research, Innovation, and Clinical Trials, Grand River Hospital, Kitchener, Ontario, Canada

Twitter Julie C Reid @PT_julie_r and Lauren E Griffith @LaurenGriff1

Acknowledgements The authors are grateful to Zachary Hollingham, Tara Noble, Catherine Young, Kristin Drury, Lisa Wolfe, Darly Dash and Megan Donaghy-Hughes for their assistance with study coordination and data collection.

Contributors MB, APC, MD, TH and RKr conceived the study. MB, JCR, APC, MD, TH, RKr, PR, RKi, AJ, SC, NR, MM, LEG, CS, BV, MM-R, SH, LM, AP and CG assisted in designing the study. JCR, RKi, HM, SC, MJ, CG and TP are assisting with data collection. JCR led the writing of the manuscript in consultation with MB. All authors read, provided feedback and approved the manuscript for submission.

Funding MB, PR and MM-R are each funded by a Canada Research Chair. The COREG Registry and COREG-FR are funded by a Canadian Institutes of Health Research grant (172754). The COREG Registry is also funded by a Hamilton Academic Health Sciences Organisation grant (HAH-21-04).

Disclaimer The funders have no role in study design, data collection and analysis, decision to publish, or preparation of this manuscript.
Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, of the research. Further details are available in the Methods section.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commerciALLY, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs
Andrew P Costa http://orcid.org/0000-0001-9212-5641
Aaron Jones http://orcid.org/0000-0002-0282-3614
Lauren E Griffith http://orcid.org/0000-0002-2794-9692
Tyler Pitre http://orcid.org/0000-0003-3015-0723
Marla K Beauchamp http://orcid.org/0000-0003-2843-388X

REFERENCES
1 Organization WH. WHO Coronavirus Disease (COVID-19) Dashboard. Secondy WHO Coronavirus Disease (COVID-19) Dashboard. 2021. Available: https://covid19.who.int
2 Ontario Go. COVID-19 (coronavirus) in Ontario. Available: https://covid-19.ontario.ca/data
3 Ontario PH. Ontario COVID-19 data tool. Secondary COVID-19 Open access accessible.
4 Iwashyna TJ, Ely EW, Smith DM, et al. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med 2011;364:1293–304.
5 Prescott HC, Angus DC. Enhancing recovery from sepsis: a review. JAMA 2018;319:62–75.
6 Needham DM, Davidson J, Cohen H, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders’ conference. Curr Care Med 2012;40:502–9.
7 Herridge MS, Tansey CM, Matte A, et al. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med 2011;364:1293–304.
8 Ahmed H, Patel K, Greenwood DC, et al. Long-term clinical outcomes in survivors of severe acute respiratory syndrome and middle East respiratory syndrome coronavirus outbreaks after hospitalisation: a systematic review and meta-analysis. J Rehabil Med 2020;52:jrm0063.
9 Brown CJ, Friedkin RJ, Inouye SK. Prevalence and outcomes of low mobility in hospitalized older patients. J Am Geriatr Soc 2004;52:1263–70.
10 Brown CJ, Redden DT, Flood KL, et al. The unrecognized epidemic of low mobility during hospitalization of older adults. J Am Geriatr Soc 2009;57:1660–5.
11 Gill TM, Areore HG, Gafahrer EA, et al. Change in disability after hospitalization or restricted activity in older persons. JAMA 2010;304:1919–28.
12 Huang C, Huang L, Wang Y, et al. 6-Month consequences of COVID-19 in patients discharged from Hospital: a cohort study. Lancet 2021;397:220–6.
13 Sudre C, Murray B, Verasvskys T. Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid symptoms study APP medRxiv 2020.
14 Mandal S, Barnett J, Brill SE, et al. ‘Long-COVID’: a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. Thorax 2021;76:396–398.
15 Carfi A, Bernabei R, Landi F, et al. Persistent symptoms in patients after acute COVID-19. JAMA 2020;324:603–5.
16 Chopra V, Flanders SA, O’Malley M, et al. Sixty-day outcomes among patients hospitalized with COVID-19. Ann Intern Med 2021;174:576–8.
17 Huang L, Yao Q, Gu X, et al. 1-Year outcomes in hospital survivors with COVID-19: a longitudinal cohort study. Lancet 2021;398:747–58.
18 Wu X, Liu X, Zhou Y, et al. 3-Month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study. Lancet Respir Med 2021;9:477–54.
19 Maestre-Muriz MM, Arias Ángel, Mata-Vázquez E, et al. Long-Term outcomes of patients with coronavirus disease 2019 at one year after hospital discharge. J Clin Med 2021;10. doi:10.3390/jcm10132945. [Epub ahead of print: 30 Jun 2021].
20 Sprui MA, Holland AE, Singh SJ, et al. COVID-19: interim guidance on rehabilitation in the hospital and Post-Hospital phase from a European respiratory Society and American thoracic Society-coordinated international Task force. Eur Respir J 2020. doi:10.1183/13993003.02197-2020. [Epub ahead of print: 13 Aug 2020].
21 Singh S, Bolton C. Delivering rehabilitation to patients surviving COVID-19 using an adapted pulmonary rehabilitation approach - BTS guidance. Secondary Delivering rehabilitation to patients surviving COVID-19 using an adapted pulmonary rehabilitation approach - BTS guidance, 2020. Available: https://www.brit-thoracic. org.uk/document-library/quality-improvement/covid-19-pulmonary-rehabilitation-for-covid-19-patients/
22 Haley SM, Coster WJ, Andres PL, et al. Activity outcome measurement for postacute care. Med Care 2004;42:149–61.
23 World Health Organization. World Health organization International classification of functioning, disability and health. Geneva: World Health Organization, 2001.
24 Coster WJ, Haley SM, Jette AM. Measuring patient-reported outcomes after discharge from inpatient rehabilitation settings. J Rehabil Med 2006;38:237–42.
25 Jette DU, Stilphen M, Ranganathan VK, et al. AM-PAC “6-Clicks” functional assessment scores predict acute care hospital discharge destination. Phys Ther 2014;94:1252–61.
26 Haley SM, Coster WJ, Andres PL, et al. Score comparibility of short forms and computerized adaptive testing: simulation study with the activity measure for post-acute care. Arch Phys Med Rehabil 2004;85:661–6.
27 Jette DU, Stilphen M, Ranganathan VK, et al. Validity of the AM-PAC “6-Clicks” inpatient daily activity and basic mobility short forms. Phys Ther 2014;94:379–91.
28 Jette DU, Stilphen M, Ranganathan VK, et al. Inter-rater Reliability of AM-PAC “6-Clicks” Basic Mobility and Daily Activity Short Forms. Phys Ther 2015;95:756–66.
29 Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–95.
30 Pulok MH, Theou O, van der Vaal AM, et al. The role of illness acuity on the association between frailty and mortality in emergency department patients referred to internal medicine. Age Ageing 2020;49:1071–9.
31 Hanlon P, Nicholl BJ, Jani BD, et al. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. Lancet Public Health 2018;3:e323–32.
32 Hewitt J, Carter B, Vilches-Moraga A, et al. The effect of frailty on survival in patients with COVID-19 (cope): a multicentre, European, observational cohort study. Lancet Public Health 2020;5:e444–51.
33 Aitk SA, Boon GJAM, Barco S, et al. The Post-COVID-19 functional status scale: a tool to measure functional status over time after COVID-19. Eur Respir J 2020;56. doi:10.1183/13993003.01494-2020. [Epub ahead of print: 02 Jul 2020].
34 Linacre JM, Heinemann AW, Wright BD, et al. The structure and stability of the functional independence measure. Arch Phys Med Rehabil 1994;75:127–32.
35 Heinemann AW, Linacre JM, Wright BD, et al. Prediction of rehabilitation outcomes with disabilities. Arch Phys Med Rehabil 1994;75:133–43.
36 Doida TA, Martin DP, Novov WC, et al. A validation of the functional independence measurement and its performance among rehabilitation inpatients. Arch Phys Med Rehabil 1993;74:531–6.
37 Young Y, Fan M-Y, Hebel JR, et al. Concurrent validity of administering the functional independence measure (FIM) instrument by interview. Am J Phys Med Rehabil 2009;88:766–70.
38 Davies A, Andrén E, Nordholm L, et al. Reliability of an interview approach to the functional independence measure. Clin Rehabil 2001;15:301–10.
39 Vadassery SJ, Kong KH, Ho WML, et al. Interview functional independence measure score: self-reporting as a simpler alternative to multidisciplinary functional assessment. Singapore Med J 2019;60:199–201.
40 Weiss D, Marcar C. The Impact of Event Scale- Revised. In: Wilson J, Keane T, eds. Assessing psychological trauma and PTSD: a Handbook for practitioners. New York: Guilford Press, 1997;399–411.
41 Creamer M, Bell R, Failla S. Psychometric properties of the Impact of Event Scale - Revised. Behav Res Ther 2003;41:1489–96.

Reid JC, et al. BMJ Open 2021;11:e053021. doi:10.1136/bmjopen-2021-053021. 7
42 Brennan C, Worrall-Davies A, McMillan D, et al. The hospital anxiety and depression scale: a diagnostic meta-analysis of case-finding ability. J Psychosom Res 2010;69:371–8.

43 Herdman M, Gudex C, Lloyd A, 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.

44 Devlin N, Parkin D, Janssen B. An introduction to EQ-5D instruments and their applications. Methods for analysing and reporting EQ-5D data. Cham: Springer International Publishing, 2020; 1–22.

45 Krupp LB, LaRocca NG, Mun-Nash J, et al. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121–3.

46 Fletcher C. Standardised questionnaire on respiratory symptoms: a statement prepared and Approved by the MRC Committee on the aetiology of chronic bronchitis (MRC breathlessness score). BMJ 1960;2:1665.

47 Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur Respir J 2005;26:319–38.

48 Graham BL, Steenbruggen I, Miller MR, et al. Standardization of spirometry 2019 update. An official American Thoracic Society and European respiratory Society technical statement. Am J Respir Crit Care Med 2019;200:e70–88.

49 Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85–94.

50 Puthoff ML. Outcome measures in cardiopulmonary physical therapy: short physical performance battery. Cardiopulm Phys Ther J 2008;19:17–22.

51 Olsen CF, Bergland A. “Reliability of the Norwegian version of the short physical performance battery in older people with and without dementia”. BMC Geriatr 2017;17:124.

52 Freire AN, Guerra RO, Alvarado B, et al. Validity and reliability of the short physical performance battery in two diverse older adult populations in Quebec and Brazil. J Aging Health 2012;24:863–78.

53 Mangione KK, Craik RL, McCormick AA, et al. Detectable changes in physical performance measures in elderly African Americans. Phys Ther 2010;90:921–7.

54 Vasunilashorn S, Coppin AK, Patel KV, et al. Use of the short physical performance battery score to predict loss of ability to walk 400 meters: analysis from the InCHIANTI study. J Gerontol A Biol Sci Med Sci 2009;64:223–9.

55 Volpato S, Cavalieri M, Sioulis F, et al. Predictive value of the short physical performance battery following hospitalization in older patients. J Gerontol A Biol Sci Med Sci 2011;66:89–96.

56 Kalin A, Javid B, Knight M, et al. Direct and indirect evidence of efficacy and safety of rapid exercise tests for exertional desaturation in Covid-19: a rapid systematic review. Syst Rev 2021;10:1–13.

57 Herridge MS, Cheung AM, Tansey CM, et al. One-Year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med 2003;348:683–93.

58 von Elm E, Altman DG, Egger M, et al. The strengthening of reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg 2014;12:1495–9.