National Institute for Health and Care Excellence

COVID-19 rapid guideline: managing the long-term effects of COVID-19

[E] Evidence reviews for monitoring and referral

NICE guideline NG188

December 2020

Guideline version (Final)

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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

COVID-19 rapid guideline: managing the long-term effects of COVID-19 (NG188)

Review questions 6 and 7: monitoring and referral

December 2020

Literature search

NICE's information services team identified relevant evidence through focused evidence searches between 22 and 28 October 2020 (see appendix 3). Additional studies were also considered from NICE surveillance up to 28 October 2020. Results from the literature searches and surveillance were screened using their titles and abstracts for relevance against the criteria from the protocol (see appendix 2). Four reviewers screened titles and abstracts. Having identified the evidence, four reviewers assessed the full text references of potentially relevant evidence to determine whether they met the inclusion criteria for this evidence review. All uncertainties were discussed amongst the reviewers and referred to an adviser if needed. See appendix 4 for the study flow chart of included studies.

Healthcare Improvement Scotland knowledge management team also conducted a search to identify qualitative evidence to support the questions in this review. See Managing the long-term effects of COVID-19: the views and experience of patients, their families and carers for more information. This review will be referred to in this document as 'patient lived experience'.

Methods and process

This evidence review was developed using the methods and processes described in the methods chapter.

Review question 6

What monitoring is helpful to assess deterioration or recovery in people with ongoing physical and mental health symptoms and problems carrying out usual activities, including work, education and leisure, following acute COVID-19?

The review protocol is shown in appendix 2.

Review question 7

What symptoms or signs indicate that referral to specialist care is needed for assessment or management of post-COVID-19 syndrome?

The review protocol is shown in appendix 2.

Although the review questions 6 and 7 focused on post-COVID-19 syndrome, the panel concluded that referral and monitoring should not be confined to people who experience symptoms beyond 12 weeks. The evidence, patient experience and the panel's experience pointed to the need for support for those experiencing ongoing symptoms beyond 4 weeks, to help avoid deterioration in people's conditions and enable people to receive early preventative support.

Included studies (for review questions 6 and 7)

In total, 4,104 references were identified through the searches. Of these, 505 were included and ordered for full text assessment. A total of 58 references were included for the whole guideline, 3 of which were included for this review.

For review question 6, 3 references were included: a descriptive cohort study (D'Cruz et al, 2020); a rapid narrative review with practice recommendations (Greenhalgh et al, 2020a); and practice recommendations in the form of a proposed pathway (Salawu et al, 2020). See table 1 for more details on the identified studies.

For review question 7, 1 reference was included: the same rapid narrative review with practice recommendations (Greenhalgh et al, 2020a) as for review question 6. See table 1 for more details on the identified studies.

Due to the paucity of included evidence, additional information based on 3 references providing guidance (Barker-Davies et al, 2020; COVID Trauma Response Working Group, 2020; Spruit et al, 2020) (See appendix 5) was also presented at the expert panel meeting.

Table 1 Included studies for review question 6: Monitoring to assess deterioration or recovery following acute COVID-19; and for review question 7: Referral to specialist post-COVID-19 syndrome services

Study	Country, study design, dates	Population (n)	Monitoring/ referral aspects	Timeframe	Main results
D'Cruz 2020	UK, Descriptive cohort study (prospective) June to July 2020	119 COVID-19 survivors previously hospitalised with PCR-confirmed severe COVID-19 pneumonia (mean age 58.7)	Chest radiography to assess recovery following respiratory symptoms	4 to 6 weeks post-discharge Median (IQR) times between hospital admission and discharge to follow-up assessment were 76 (71 to 83) days and 61 (51 to 67) days, respectively	Persistent symptoms, adverse mental health outcomes and physiological impairment are common, 2 months after severe COVID-19. Follow-up chest radiograph is a poor marker of recovery. (refer to evidence table). Authors recommend: 'Holistic face-to-face (or virtual) assessment' to facilitate early recognition and management of post-COVID sequelae, in this group
Greenhalgh 2020a	UK, Overarching practice recommendations for primary care, based on narrative review and expert opinion	Patients who have a delayed recovery from an episode of COVID-19 managed in community or standard hospital ward	Pulmonary/ Neuro/ Cardiology/ Mental health referral Symptom monitoring in primary care	Post-acute COVID-19 defined as >=3 weeks from onset of first symptoms, and chronic COVID-19 as extending beyond 12 weeks	Authors recommend: Self-management: Daily pulse oximetry and safety netting advice Authors recommend: Safety netting and referral: Patient should seek medical advice if concerned e.g. worsening breathlessness, PaO2<96%, unexplained chest pain, new confusion, focal weakness. Specialist referral based on clinical findings, e.g. to Respiratory, Cardiology, or Neurology

Study	Country, study design, dates	Population (n)	Monitoring/ referral aspects	Timeframe	Main results
					For patients who have had a significant respiratory illness: community follow-up with a chest X-ray at 12 weeks and referral for new, persistent, or progressive symptoms. For those with evidence of lung damage (such as persistent abnormal chest X-ray and oximeter readings), referral to a respiratory service. Authors suggest that subsequent early referral to pulmonary rehabilitation probably aids recovery.
Salawu (2020)	UK, Narrative review and proposed pathway based on authors' clinical experience	Patients previously hospitalised with COVID-19 (both ICU and non-ICU patients)	Use of remote monitoring to assess rehabilitation needs. Assessment to include nurse-led assessment, including review of repeat chest X-ray	4 to 6 weeks and 12 weeks post discharge	Authors recommend: Onward referral to MDT rehabilitation if a need for specialist rehabilitation is identified, or discharge to primary care

Key results

A descriptive cohort study, D'Cruz et al (2020), found that, in patients hospitalised with severe COVID-19 pneumonia, persistent symptoms, adverse mental health outcomes and physiological impairment are common 2 months following COVID-19, with chest radiograph being a poor marker of recovery (see evidence table for further details). Consequently, the authors recommended holistic face-to-face assessment to facilitate early recognition and management of post-COVID sequelae.

Salawu et al (2020) proposed a telerehabilitation pathway based on narrative review and local consensus. Salawu et al proposed assessment at 4- to 6-weeks post-

discharge from hospital, identifying suitable patients who may benefit from a tele-rehabilitation programme; and providing them with the opportunity to enrol. At 12-weeks post-discharge, they proposed nurse-led assessment, including review of repeat chest X-ray (CXR). If a need for specialist rehabilitation was identified, they proposed referral to a multidisciplinary team (MDT) or alternatively discharge to primary care.

Greenhalgh et al (2020) provided practice recommendations based on a rapid narrative evidence review, combined with expert opinion. These were relevant for both monitoring and referral. The authors recommended approaches covering, depending on patient need and clinical findings, self-management including safety netting advice, and specialist referral to various services as appropriate. See results table 1 for further details.

Subgroups

No subgroup data were identified, although it should be noted that D'Cruz et al (2020) used direct data from patients hospitalised with severe COVID-19 only.

Strengths and limitations

The risk of bias (RoB) for studies included in this review was assessed as high using the CASP critical appraisal checklist for cohort studies. See 'quality' for each study in appendix 6, Evidence tables.

No RoB could be undertaken for Salawu et al (2020) or Greenhalgh et al (2020a) due to their not providing any direct evidence, and these publications may be considered at high risk of bias for the purposes of these review questions.

Expert panel discussion - for both monitoring and referral

This section describes how the expert panel considered the evidence in relation to the recommendations within the guidance.

Relative value of different outcomes

The relevant outcomes in the review protocol for monitoring were: Symptom improvement (or worsening); mortality; return to usual activities including

work, education or leisure; quality of life and/or wellbeing; healthcare utilisation, for example number of visits to A&E; adverse events, e.g. side effects or unintended consequences. For referral, these outcomes were: number of referrals to specialist care and association between symptoms and signs and referrals to specialist care.

Outcomes of relevance were reported in D'Cruz (2020), but not in Greenhalgh (2020) or Salawu et al (2020). Neither the included quantitative study or practice proposals were able to provide direct evidence on the specified PICO outcomes, for monitoring or referral.

The panel considered it was important to be able to effectively assess whether a patient had recovered or not, as part of monitoring/follow-up. Recovery would be considered as both symptom improvement - which might include links with quality of life and/or wellbeing - and an ability to return to usual activities, including work, education or leisure, or caring duties.

Quality of the evidence

The study populations in 2 of the 3 publications (D'Cruz et al, 2020; Salawu et al, 2020) focused on hospitalised patients, whereas the guideline is intended to cover both hospitalised and non-hospitalised people. Therefore, not all of the evidence included was generalisable to the wider population the panel wished to provide guidance for. It was acknowledged that the evidence was lacking for this review, with only a narrative review with practice recommendations, a single descriptive cohort study, and a practice model proposal included. Risk of bias was deemed to be high for the applicable study (D'Cruz et al, 2020) and, as the next section describes, the panel used its own expertise and the patient experience data to supplement the lack of an evidence base for this review question.

Trade-off between benefits and harms

Whilst the evidence presented was insufficient to directly inform knowledge of benefits and harms of different monitoring and referral options, the panel used their experience to consider benefits and harms when drafting recommendations.

The panel noted that people may need to be referred urgently to acute services for physical health symptoms, or to psychiatric services, to prevent potentially serious

consequences. The panel discussed appropriate tests which may need to be carried out as part of monitoring and follow-up; and agreed that these should be based on the person and their symptoms.

Based on limited evidence from one study in the review, the panel considered that a chest X-ray should be done if the person had not had one and there were continuing respiratory symptoms. The panel agreed that a chest X-ray should only be used as part of a holistic assessment to decide if referral or further care are needed. The panel also agreed that the lack of abnormal findings on a person's chest X-ray should not be used as a reason to not refer the person for further assessment and rehabilitation. The panel discussed that the chest X-ray should be done (if needed) before 12 weeks to help rule out any other pathology before the person moves onto a treatment pathway for post-COVID-19 syndrome.

The panel discussed the patient lived experience evidence, describing how some people were not offered tests, and how others were denied referral due to not having a positive SARS-CoV-2 test result. Since many people with ongoing symptoms of COVID-19 or post-COVID-19 syndrome will not have been tested, particularly those who had COVID-19 illness earlier in the pandemic, the panel recommended that access to services should not be restricted by the need for a positive test.

The panel discussed the need for prompt referral to avoid delaying support for people. The panel drew on their own expertise to conclude that the earlier people received help, the more effective the interventions Qualitative evidence based on patient lived experience evidence potentially suggested that people left without support may suffer worse anxiety and poorer mental health.

Whilst evidence on monitoring was lacking, the panel agreed that monitoring is important to enable support to be adapted, if people's symptoms or ability to carry out usual activities change. Evidence from patients' lived experience highlighted the importance of follow-up to access further care. The panel did not want to limit monitoring to specific tests or symptoms, or to a particular timeframe, because people with long-term effects of COVID-19 have a wide range of care needs. The panel considered that monitoring should be tailored to each person. Based on their own experience and the patient lived experience evidence, the panel agreed on the

value of people recording or tracking their symptoms, goals and progress. The panel were aware of digital tracking apps that could be used for self-monitoring and, although they acknowledged that these would not be suitable or accessible for everyone, they concluded that it would be useful to highlight these as potentially helpful approaches to recording symptoms.

Evidence from patients' lived experience suggested that some people struggled to access appropriate care, and some had experienced fragmented care. The panel agreed on the need to improve integration and coordination of care across different services. The panel agreed that having regular multidisciplinary meetings would help share information more efficiently and allow professionals to make decisions quickly about tests and referral. The patient experience evidence also described how people could benefit from continuity of care, and the panel agreed this should be an aim for well-integrated services.

The panel discussed potential active monitoring of symptoms which would be considered below a threshold for referral. They concluded that whilst it is important not to miss these symptoms, neither should all decisions be based on them.

The panel noted that thresholds in screening tools, whilst capturing symptoms where they are high in one area, may miss so-called 'pink flags', whereby a patient may be experiencing multiple relatively low-level symptoms (e.g. a little shortness of breath, fatigue) which may still indicate very significant illness, needing multidisciplinary team (MDT) input. The panel therefore concluded that it was crucial for the referral to be based on a holistic assessment, not just a checklist of symptoms.

The panel also discussed the need to consider symptoms which would raise concern over a patient's suitability for rehabilitation. Noting that, while patients will talk about their most current symptoms and be referred, symptoms might change by the time of the specialist/clinic appointment. It was discussed that patients may feel embarrassed if they have too many things to list, and not mention everything of potential significance. And so the panel agreed that it was essential for the healthcare professional to take these factors into account whenever carrying out assessments or rehabilitation.

Implementation and resource considerations

Much of the panel's discussion on implementation and resource is covered in the expert discussion in the evidence review on service models, which informed the recommendations on service organisation (rather than on monitoring and referral).

The panel discussed evidence from patients' lived experience describing challenges for GPs of addressing a wide range of people's symptoms, and a lack of coordinated care. As well as informing recommendations on service organisation, this informed recommendation 6.1 on planning and agreeing follow-up and monitoring.

The panel discussed the need for patient information, including advice for patients on trends in symptoms, management of symptoms, and when to call professionals. There needs to be good communication with patients, including how to manage subsequent symptoms if they occur. Panel members were concerned about the risk of patients who were not previously hospitalised becoming 'lost' in the system.

These discussions helped inform recommendations 6.2 (on shared decision-making) and 6.3 (on tailoring monitoring)

The panel noted there are likely to be waiting lists for referral into services and that people should be provided with clear information about what to expect, red flags and who to contact during this time. Patients could feel more empowered, with heightened sense of agency and control, if there are things they can do at home while waiting for referral, including potentially to aid their recovery.

The panel, considered, from their experience, that self-monitoring at home can be useful and is used in practice. However, the panel noted that it might not be suitable for everyone, and without the right information and support can cause unnecessary anxiety. People need good guidance to use equipment, interpret the results and understand when to contact a healthcare professional.

The panel therefore recommended (6.4) supported self-monitoring at home, if agreed as part of a person's assessment, and combined with clear instructions including on when to seek further help.

Other considerations

The panel noted the need to also ensure that any symptom scores do not miss out other people who present with less common symptoms, with a concern over potential inequalities. They noted that vulnerable groups, such as older people and people who are isolated may need proactive patient follow-up, together with accessible advice.

The panel discussed the need for co-ordinated care and communication when referring to specialist services.

Appendix 1 Methods used to develop the guidance

Please see the methods chapter for details on how this guideline was developed.

Appendix 2 Review protocols

Review question 6: What monitoring is helpful to assess deterioration or recovery in people with ongoing physical or mental health symptoms and problems carrying out usual activities, including work, education and leisure, following acute COVID-19?

Criteria	Notes
Population	Adults and children who are experiencing new or ongoing symptoms: • 4 to 12 weeks from onset of acute COVID-19 illness • 12 weeks from onset of acute COVID-19 illness
Interventions	Any type of monitoring for example, frequency of follow-ups
Comparators	Any or no comparator
Outcomes	• Symptom improvement (or worsening) • Mortality • Return to usual activities including work, education or leisure • Resumption of (informal) caring arrangements • Quality of life and/or Wellbeing • Healthcare utilisation, for example number of visits to A&E or increased need for social care support • Adverse events, e.g. side effects or unintended consequences
Settings	Any
Subgroups	• Groups as defined in the EIA for example, age, sex, ethnicity • Diagnosis of COVID-19 (e.g. confirmed or high clinical suspicion) • Duration of symptoms
Study types	Any The following study design types for this question are preferred. Where these studies are not identified, other study designs will be considered. • RCTs • Systematic reviews of RCTs and observational studies • Prospective and retrospective observational studies
Countries	Any
Timepoints	Any
Other exclusions	• Management of acute COVID-19 (symptoms experienced for up to 4 weeks) • Management of other conditions with similar features to post-COVID-19 syndrome, for example post-intensive care syndrome and myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome (ME/CFS)

	• Management of end-organ damage, which already has defined pathways of care.

Review question 7: What symptoms or signs indicate that referral to specialist care is needed for assessment or management of post-COVID-19 syndrome?

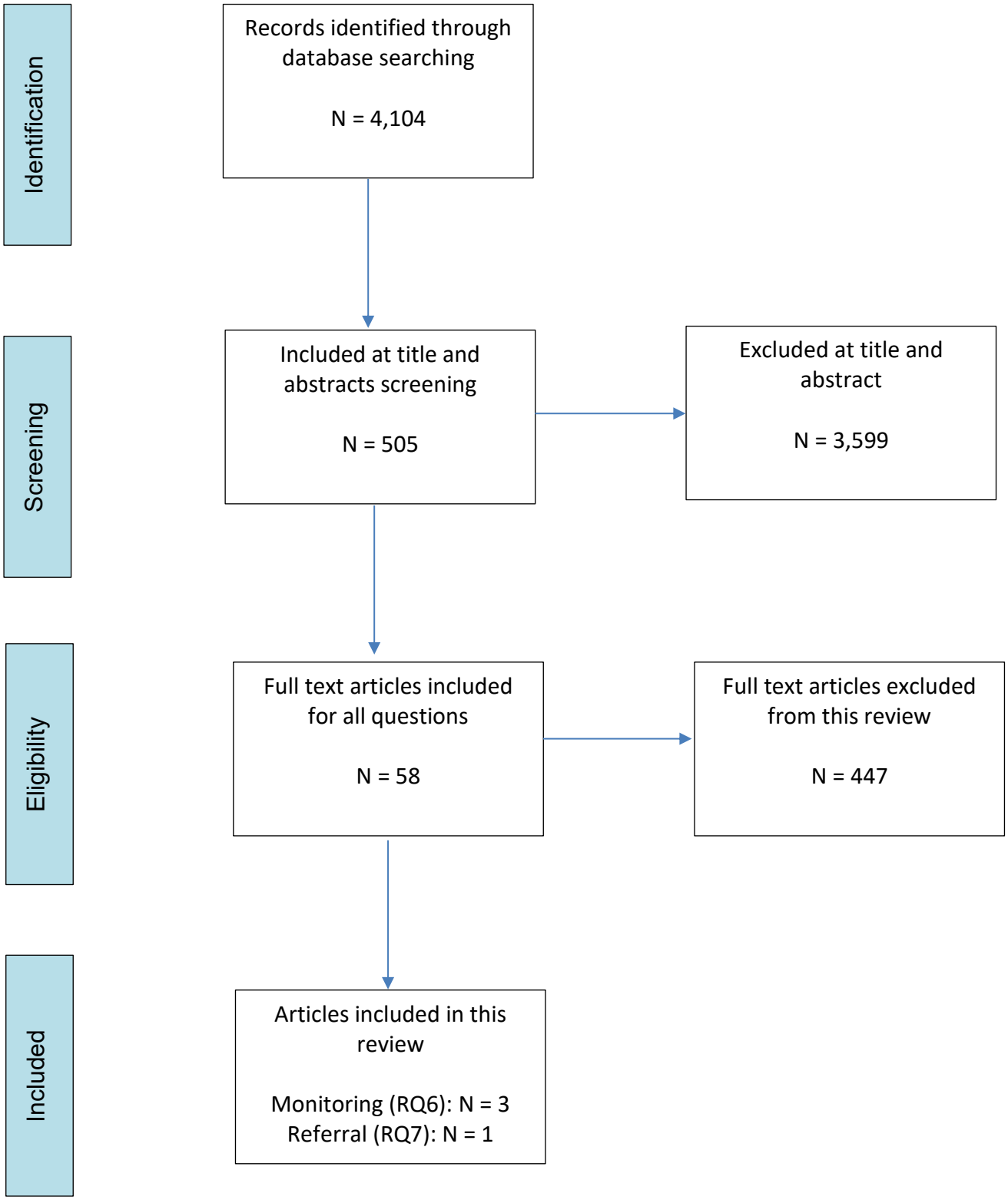
Criteria	Notes
Population	Adults and children who are experiencing new or ongoing symptoms: • 4 to 12 weeks from onset of acute COVID-19 illness • 12 weeks from onset of acute COVID-19 illness
Exposure	Critical symptoms or signs (e.g. red flags) that lead to referral
Comparators	Not applicable
Outcomes	• Number of referrals to specialist care • Association between symptoms and signs and referrals to specialist care
Settings	Any
Subgroups	• Groups as defined in the EIA for example, age, sex, ethnicity • Diagnosis of COVID-19 (e.g. confirmed or high clinical suspicion) • Duration of symptoms
Study types	Any The following study design types for this question are preferred. Where these studies are not identified, other study designs will be considered. Preferred: • Systematic reviews of cohort studies • Cohort studies (prospective or retrospective) • Cross-sectional studies
Countries	Any
Timepoints	Any
Other exclusions	See scope

Appendix 3 Literature search strategy

Database strategies

Please refer to the search history record for full details of the search.

Appendix 4 Study flow diagram



Appendix 5 Included studies

Review question 6: Monitoring

D'Cruz RF, Waller MD, Perrin F, et al. Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. ERJ Open Res 2020; in press (https://doi.org/10.1183/23120541.00655-2020).

Greenhalgh, T., Knight, M. et al. (2020) Management of post-acute COVID-19 in primary care. BMJ 2020;370:m3026 http://dx.doi.org/10.1136/bmj.m3026

Salawu, Abayomi, Green, Angela, Crooks, Michael G et al. (2020) A Proposal for Multidisciplinary Tele-Rehabilitation in the Assessment and Rehabilitation of COVID-19 Survivors. International journal of environmental research and public health 17(13)

Review question 7: Referral

Greenhalgh, T., Knight, M. et al. (2020) Management of post-acute COVID-19 in primary care. BMJ 2020;370:m3026 http://dx.doi.org/10.1136/bmj.m3026

For reference: Relevant guidance not included formally in evidence review

Barker-Davies RM, O'Sullivan O, et al. Br J Sports Med 2020;54:949–959.

COVID Trauma Response Working Group Rapid Guidance: Screening and active monitoring for post-traumatic stress disorder (PTSD) and other mental health consequences in people recovering from severe COVID-19 illness. COVID Trauma Response Working Group. Version 1.5 (June 25, 2020). Available at: https://www.traumagroup.org/ (checked 11/12/20).

Spruit 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; in press (https://doi.org/10.1183/13993003.02197-2020).

Appendix 6 Evidence tables

Review questions 6: Monitoring; and 7: Referral

D'Cruz 2020 (Monitoring only)

Bibliographic reference/s	**D'Cruz RF, Waller MD, Perrin F, et al. Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. ERJ Open Res 2020; in press (https://doi.org/10.1183/23120541.00655-2020).**
Questions relevant to?	**Investigations** **Monitoring** **Risk Factors** **Signs and symptoms/prevalence**
Publication status	Accepted for publication
Study type	Cohort (prospective)
Quality	Low quality evidence CASP critical appraisal checklist (cohort studies): High risk of bias
Objective	To prospectively investigate clinical, radiological, functional, and psychological COVID-19 sequelae of severe COVID-19 pneumonia, and to identify factors associated with symptomatic and functional recovery
Study date	June to July 2020
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	Kings College Hospital, UK
Population (including n)	119 COVID-19 survivors who had been hospitalised with PCR-confirmed severe COVID-19 pneumonia
Time since acute COVID-19 illness	Median (IQR) times between hospital admission to follow-up assessment, and discharge to follow-up assessment were 76 (71 to 83) days and 61 (51 to 67) days, respectively (4 to 12 weeks grouping)
Investigations	• Chest radiography • Symptom questionnaires • Mental health screening • Physiological testing • Computed tomography and pulmonary angiography (CTPA)
Baseline characteristics	**Age (years)**: Mean 58.7 SD 14.4 **Sex**: Female 45/119 (37.8%); Male 74/119 (62.2%) **Ethnicity**: White 36/119 (30.3%); Black 52/119 (43.7%); Asian 18/119 (15.1%); Mixed race 5/119 (4.2%); Other 8/119 (6.7%) **BMI (kg/m^2):** 30.0 (25.9 to 35.2) **Comorbidities:** Any CVD 63/119 (52.9%); Diabetes 41/119 (34.5%); Immunosuppressed 16 (13.4%); Obstructive lung disease 13/119 (10.9%), Malignancy 12/119 (10.1%); End stage renal failure 8/119 (6.7%); Thyroid disease 7/119 (5.9%); Mental health condition 6/119 (5%); Cerebrovascular disease 5/119 (4.2%).
Inclusion and exclusion criteria	• Aged 18 years and above

	• PCR-confirmed COVID-19 by naso- and oro-pharyngeal swab between 5th March and 28th May 2020 • Severe COVID-19 pneumonia defined as requiring hospitalisation for ≥48 hours and a fraction of inspired oxygen (FiO_2) of ≥40% or intensive care unit (ICU) admission
Follow up	Face to face assessment 4 to 6 weeks post discharge
Main results	**At follow-up:** There was no relationship between age groupings and persistent post-COVID symptoms, self-reported functional disability, or physiological impairment. **Breathlessness**: (Medical Research Council Breathlessness Scale, mMRC): • 55/115 (46.2%) had not returned to pre-COVID mMRC • Of these, 11/55 (20%) had no pre-existing comorbidity • Comorbid obstructive lung disease was associated with failure of mMRC recovery to baseline (OR 5.06 95%CI 1.33 to 19.2) **Post-COVID Functional Status (PCFS)**: • ≥2 in 47/115 (40.9%) • Comorbid obstructive lung disease was associated with PCFS ≥2 (OR 2.84 95%CI 1.01 to 7.98) **Persistent symptoms:** • Median 4 IRQ (2-5) • 11% reported no persistent symptoms • Burdensome breathlessness (numerical rating scale, NRS ≥4): 37/115 (32.2%) • Persistent cough (NRS ≥1): 49/115 (42.6%) • Burdensome cough (NRS ≥4): 8/115 (7%) • Fatigue: 78/115 (67.8%) • Sleep disturbance: 65/115 (56.5%) • Pain (commonly reported in shoulder, chest, lower limbs and back): 57/115 (49.6%) • Pre-morbid obstructive lung disease was associated with persistent (NRS ≥1) breathlessness (OR 8.04 95%CI 0.19 to 21.4) and cough (OR 3.43 95% CI 0.98 to 12.0), but not burdensome (NRS ≥4) breathlessness or cough (OR 1.97 95%CI 0.60 to 6.47 and OR 2.27 95% CI 0.38 to 13.7, respectively) • There were no associations between the presence or absence of pre-existing comorbidities and persistent fatigue, sleep disturbance or pain **Mental health outcomes:** • PHQ-9 score ≥9: 20/115 (18%) • GAD-7 score ≥9: 25/113 (22.1%) • Trauma screen questionnaire ≥6: 28/113 (24.8%) • 6-item Cognitive impairment test ≥8: 21/97 (21.6%) **Physiological outcomes:** • 4-metre gait speed (4MGS): 44/115 (38.3%) had a 4MGS <0.8m/s; 71/115 (61.7%) • Sit to stand (STS): The number of repetitions performed were below the 2.5 percentile in 56/109 (52%) • There were no adverse events during physiological testing. • There were no associations between pre-morbid obstructive lung disease and physiological functional impairment (OR 0.68 95%CI 0.16 to 2.95)

	• Cardiovascular disease was associated with a 4MGS <0.8 m/s (OR 3.95 95%CI 0.42 to 2.49). **Chest radiography** • Evidence of COVID-related lung disease (RALE score >4): 15/119 (13%) **CTPA (for patients with abnormal chest radiography, persistent respiratory symptoms, or exercise desaturation)** • Features of COVID-related interstitial lung disease and/or airways disease: 42/56 (37.5%) • No pulmonary emboli were identified on CT pulmonary angiography • Presence of COVID-related CT abnormalities were associated with mental health screening questionnaires (PHQ-9 ≥9, GAD-7 ≥9 and/or Trauma Screening Questionnaire ≥6) (χ^2 =3.98 p=0.046 95%CI -0.56 to -0.02) but not with any measure of patient reported or physiological functional impairment • Only 21% of patients with abnormal CT findings also had an abnormal follow-up chest radiograph • 78% of those with ≥4% desaturation during STS also had abnormal CT findings • 33 patients had a normal chest radiograph (RALE score 0-4) and an abnormal CT • 9 patients had both an abnormal chest radiograph (RALE score >4) and abnormal CT • Amongst those with abnormal CT scans, presence or absence of radiographic abnormalities was not predictive of any patient-reported or physiological outcome measure **Summary:** Persistent symptoms, adverse mental health outcomes and physiological impairment are common 2 months after severe COVID-19 pneumonia. Follow-up chest radiograph is a poor marker of recovery, therefore holistic face-to-face assessment is recommended to facilitate early recognition and management of post-COVID sequelae
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	**Statistical analysis:** Group comparisons were performed using independent t-tests and Chi square (χ^2) tests. Ordinal logistic regression modelling was used to identify factors associated with measures of COVID-19 recovery. **Limitations:** • Unable to perform lung function testing in serial patients due to decontamination procedures required, limiting conclusions on respiratory sequelae • Conventional field walking tests to evaluate exercise capacity (6-minute walk test (6MWT), incremental shuttle walk test (ISWT)) were impractical in the clinic setting. • Authors devised their own definition of “severe” COVID-19 pneumonia which may have missed some patients with persistent symptoms or functional disability. • Data collected from a single, urban teaching centre which may limit generalisability **Funding:** This study received no specific funding or grant from any agency in the public, commercial, or not-for-profit sectors. RFD is funded by a National Institute for Health Research (NIHR) Doctoral Research Fellowship (RFD)

Additional references	None

Greenhalgh 2020 (Monitoring and referral)

Bibliographic reference/s	**Greenhalgh, T., Knight, M., et al. (2020) Management of post-acute COVID-19 in primary care. BMJ 2020;370:m3026 http://dx.doi.org/10.1136/bmj.m3026**
Questions relevant to?	Risk factors, signs and symptoms, investigations, interventions, referral
Publication status	Published
Study type	Narrative review and expert opinion
Quality	Low / very low CASP critical appraisal checklist (systematic reviews): High risk of bias
Objective	This article provides a practice guide for primary care clinicians, relating to the patient who has a delayed recovery from an episode of COVID-19 that was managed in the community or in a standard hospital ward.
Study date	11/8/20
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	International/primary care
Population (including n)	Patients who have a delayed recovery from an episode of COVID-19 that was managed in the community or in a standard hospital ward.
Time since acute COVID-19 illness	For the purposes of the article the authors define post-acute COVID-19 as extending beyond three weeks from the onset of first symptoms and chronic COVID-19 as extending beyond 12 weeks.
Interventions/ Prognostic factors	Medical and self-management (see main recommendations)
Baseline characteristics	N/A
Inclusion and exclusion criteria	Inclusion: patients who have a delayed recovery from an episode of COVID-19 that was managed in the community or in a standard hospital ward.
Follow up	N/A but cites advice from British Thoracic Society guidance on follow-up of COVID-19 patients who have had a significant respiratory illness proposes community follow-up with a chest x ray at 12 weeks and referral for new, persistent, or progressive symptoms.
Main recommendations	Recommended clinical assessment: • Full history from date of first symptoms • Nature and severity of current symptoms • Examination e.g. temperature, heat rate and rhythm, blood pressure, respiratory examination, functional status, pulse oximetry, clinical testing if indicated. Recommended Investigations if indicated: • Blood tests should be ordered selectively and for specific clinical indications after a careful history and examination; the patient may not need any. • Anaemia should be excluded in the breathless patient. • Lymphopenia is a feature of severe, acute COVID-19.

	• Elevated biomarkers may include C reactive protein (for example, acute infection), white cell count (infection or inflammatory response), natriuretic peptides (for example, heart failure), ferritin (inflammation and continuing prothrombotic state), troponin (acute coronary syndrome or myocarditis) and D-dimer (thromboembolic disease). Troponin and D-dimer tests may be falsely positive, but a negative result can reduce clinical uncertainty. • Further research is likely to refine the indications for, and interpretation of, diagnostic and monitoring tests in follow-up of COVID-19. • For patients who were not admitted to intensive care, British Thoracic Society guidance on follow-up of COVID-19 patients who have had a significant respiratory illness proposes community follow-up with a chest x ray at 12 weeks and referral for new, persistent, or progressive symptoms. For those with evidence of lung damage (such as persistent abnormal chest x ray and oximeter readings), referral to a respiratory service is recommended. • subsequent early referral to pulmonary rehabilitation probably aids recovery. Recommended medical management: • Symptomatic treatment e.g. treating fever with paracetamol, cough with breathing control exercises • Optimise control of long-term conditions • Listening and empathy • Consider antibiotics for secondary infection • Treat specific complications as indicated Recommended self-management: • Daily pulse oximetry and safety netting advice • Attention to general health • Rest and relaxation • Self-pacing and gradual increase in exercise if tolerated • Set achievable targets Recommended safety netting and referral: • The patient should seek medical advice if concerned e.g. worsening breathlessness, PaO2<96%, unexplained chest pain, new confusion, focal weakness. • Specialist referral may be indicated based on clinical findings e.g.: o Respiratory – if suspected pulmonary embolism or severe pneumonia o Cardiology – if suspected myocardial infarction, pericarditis, myocarditis or new heart failure o Neurology – if suspected neurovascular or acute neurological event.
Comments (e.g. source of funding, statistical analysis, any major limitations, or	The authors used a pragmatic approach based on indirect evidence from SARS and MERS, early editorials and consensus based guidance on COVID-19, a living systematic review, early reports of telerehabilitation (support and exercise via video link), and their own clinical experience. Limitations: no direct evidence was identified

issues with studies)	
Additional references	N/A

Salawu 2020 (Monitoring only)

Bibliographic reference/s	**Salawu, Abayomi, Green, Angela, Crooks, Michael G et al. (2020) A Proposal for Multidisciplinary Tele-Rehabilitation in the Assessment and Rehabilitation of COVID-19 Survivors. International journal of environmental research and public health 17(13)**
Questions relevant to?	**Monitoring, Service models**
Publication status	Published
Study type	Narrative review and pathway model description
Quality	Very low-quality evidence Checklist not applicable – as model, not incorporating quantitative results
Objective	To propose a model of a care pathway to mitigate against the impact on the rehabilitation services due to the response of the UK National Health Service in managing the COVID-19 crisis. The care pathway aims to evaluate the post recovery rehabilitation and the clinical needs of patients following infection with the SARS-Cov-2 virus.
Study date/	Not reported (published 7/7/20)
COVID-19 prevalence (high/low) if reported	Not reported
Country/ Setting	UK
Population (including n)	COVID-19 patients requiring critical care/non-invasive respiratory support COVID-19 patients not requiring critical care/non-invasive respiratory support
Time since acute COVID-19 illness	4 to 6 weeks and 12 weeks post discharge
Interventions/ Prognostic factors	Multi-disciplinary tele-rehabilitation
Baseline characteristics	Not reported
Inclusion and exclusion criteria	Not reported
Follow up	4 to 6 weeks and 12 weeks post discharge
Main results	Recommended pathway: • The care pathway aims to evaluate the post recovery rehabilitation and the clinical needs of patients following infection with the SARS-Cov-2 virus. • The pathway has an embedded multidisciplinary tele-rehabilitation component to assess and deliver therapy to patients based on the identified needs. • Discharged COVID-19 patients will be managed along two streams based on whether they had intensive care input with respiratory

	support: mechanical ventilation, CPAP (continuous positive airway pressure) or high flow nasal oxygen (Stream 1), or not (Stream 2). • Electronic coding will enable patients who had a hospital admission where they tested positive for COVID-19 to be identified to a pathway administrator. • The codes also identify which patients require intensive respiratory support (i.e., stream 1) from those who are able to remain on a ward (stream 2). • The pathway administrator will receive weekly updates and then book patients into the appropriate assessment clinics. • The pathway will incorporate two assessment points at four-to-six weeks and 12 weeks where clinicians make contact remotely with the patients. • The 4 to 6 week assessment will be used to identify suitable patients who may benefit from a tele-rehabilitation program and providing them with the opportunity to enrol. A multidisciplinary rehabilitation telephone screening tool will be used for the rehabilitation assessment at the four-to-six weeks post discharge. The telephone screening tool is based on the domains of the ICF. • The screening tool was further modified to explore key medical and functional sequelae of COVID-19, as identified in the various guidelines issued by the UK professional bodies for rehabilitation medicine, respiratory medicine, intensive care medicine, and allied healthcare professionals. • Bespoke interventions tailored to individual circumstances will be provided based on the assessment. • The tele-rehabilitation therapy programme suite will incorporate the core principles of PR of reducing anxiety relating to breathlessness and additionally optimise the aerobic capacity, strength, endurance, and functional ability of the patients. There will also be an early focus on managing fatigue and pacing since profound fatigue appears to be a distinct limiting factor in the recovery of these patients. • The pathway was designed to be adaptable, and, as further evidence of clinically effective therapy and treatment of COVID-19 emerges, these programs and apps could be added to the pathway The program will use attend anywhere® an NHS digital-approved secure video conferencing platform to deliver structured exercises • Supervised exercise sessions will be provided two times each week. Activities will be commenced at mild intensity with progression over subsequent weeks to moderate intensity as tolerated by trained therapists to patients identified as requiring such intervention. • The rehabilitation process is a continuous interactive process that requires the frequent monitoring of the patient's functional ability, which is used to guide and adjust therapy delivery based on the patient's progress. • The screening assessment tool was piloted in 2 UK regions as part of a quality improvement program to allow for feasibility and a comparison of data trends.
Comments (e.g. source of funding, statistical analysis, any major limitations, or issues with studies)	Other relevant information is presented relevant to service models. **Limitations:** The proposal was based on the clinical experience of the authors and the local/regional service circumstances. No validation data was presented. Further research is needed to validate the model.
Additional references	N/A

Appendix 7 Excluded studies

Please refer to the full list of excluded studies for this guideline.