Respiratory follow-up of patients with COVID-19 pneumonia

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ABSTRACT

The COVID-19 pandemic has led to an unprecedented surge in hospitalised patients with viral pneumonia. The most severely affected patients are older men, individuals of black and Asian minority ethnicity and those with comorbidities. COVID-19 is also associated with an increased risk of hypercoagulability and venous thromboembolism. The overwhelming majority of patients admitted to hospital have respiratory failure and while most are managed on general wards, a sizeable proportion require intensive care support. The long-term complications of COVID-19 pneumonia are starting to emerge but data from previous coronavirus outbreaks such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) suggest that some patients will experience long-term respiratory complications of the infection. With the pattern of thoracic imaging abnormalities and growing clinical experience, it is envisaged that interstitial lung disease and pulmonary vascular disease are likely to be the most important respiratory complications. There is a need for a unified pathway for the respiratory follow-up of patients with COVID-19 balancing the delivery of high-quality clinical care with stretched National Health Service (NHS) resources. In this guidance document, we provide a suggested structure for the respiratory follow-up of patients with clinicoradiological confirmation of COVID-19 pneumonia. We define two separate algorithms integrating disease severity, likelihood of long-term respiratory complications and functional capacity on discharge. To mitigate NHS pressures, virtual solutions have been embedded within the pathway as has safety netting of patients whose clinical trajectory deviates from the pathway. For all patients, we suggest a holistic package of care to address breathlessness, anxiety, oxygen requirement, palliative care and rehabilitation.

INTRODUCTION

The first reports of a novel respiratory virus which was subsequently shown to be a coronavirus, severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), emerged from Wuhan, China in December 2019.[1] The highly transmittable virus spread rapidly and on 11 March 2020, coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organisation. By 10 May 2020, there were over 4 million confirmed cases worldwide with over 280 000 deaths. In the UK alone by this date, there were over 215 000 confirmed cases and over 30 000 deaths.

The clinical manifestations of SARS-Cov-2 infection vary, ranging from asymptomatic carriage to atypical pneumonia, a hyperinflammatory phenotype, respiratory failure and acute respiratory distress syndrome (ARDS).[2–5] An unexpectedly high prevalence of venous thromboembolic (VTE) disease and pulmonary embolism (PE) has become apparent[6] and this is an important consideration for acute management and subsequent follow-up. Those most severely affected by COVID-19 are older men, individuals of black, Asian and minority ethnicity and those with comorbidities such as obesity, hypertension and diabetes.[2–4 7–9] By far, the the most common indication for admission to hospital is viral pneumonia and over 80% of hospitalised patients are cared for in general medical wards.[10] A smaller proportion of patients with more severe disease require additional ventilatory support and are admitted to high dependency and intensive care units (ICUs). In a Chinese study of 1099 hospitalised COVID-19 patients, 173 patients (16%) had severe disease based on American Thoracic Society (ATS) community-acquired pneumonia guidelines[11] and 55 (5%) required ICU admission.[2] The mortality associated with COVID-19 is considerable—in a large UK study, in-hospital mortality was 26% for patients on general wards rising to 32% in those requiring ICU care.[10] Depending on the series, COVID-19-related ICU mortality has been reported to be between 16% and 78%.[3 4 8 10 12–15]

As effective vaccines and treatments for SARS-Cov-2 emerge, a key objective will be to identify and proactively manage complications from the infection and support patients through the recovery phase with the goal of preserving their health status. In this guidance document, we provide a suggested structure to achieve these aims with a focus on the respiratory follow-up of patients with clinicoradiological confirmation of COVID-19 pneumonia.

This guidance has been adopted by the British Thoracic Society (BTS) and the British Society of Thoracic Imaging (BSTI) after wide consultation and peer review. It is available online (https://brit-thoracic.org.uk/about-us/covid-19-information-for-the-respiratory-community/).

COVID-19 PNEUMONIA IMAGING AND SPECIFIC RESPIRATORY COMPLICATIONS FOR CONSIDERATION

In typical cases of COVID-19 pneumonia, the chest X-ray (CXR) shows multiple bilateral peripheral opacities (figure 1A). In some patients, the morphological

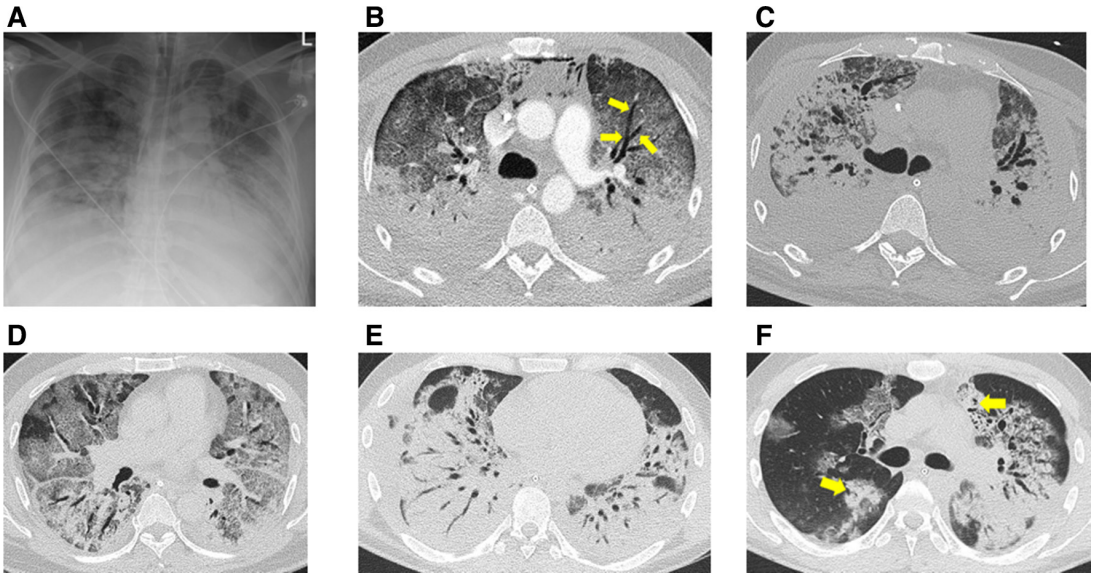

Figure 1 (A) Plain chest radiograph in a male patient with COVID-19 pneumonia referred for extracorporeal membrane oxygenation support. (B) CT images showing broadly symmetrical air space opacification with dependent dense parenchymal opacification and extensive ground-glass opacification with thickened interlobular and intralobular septa (the 'crazy-paving' pattern) in the non-dependent lung. Note that the airways are conspicuous against the ground-glass opacification but, importantly, taper normally (arrows) and have smooth walls. (C) CT performed 10 days later again showing widespread air space opacification but now with 'varicose' dilatation (non-tapering) of airways in the left upper lobe indicative of developing pulmonary fibrosis. (D) Classical 'crazy-paving' appearance in COVID-19. There is patchy but very extensive ground-glass opacification with superimposed fine thickening of interlobular and intralobular septa throughout both lungs. Relatively limited dense parenchymal opacification is present in the dependent lung bilaterally, likely to reflect variable combinations of the consolidated and atelectatic lung. (E) A patient with COVID-19-related acute respiratory distress syndrome (ARDS) with image section though the lower zones showing characteristic findings of ARDS with symmetrical air space opacification but with a gradient of increasing density from the ventral to the dorsal lung. (F) Image just below the carina demonstrating foci of non-dependent consolidation (*arrows*), conceivably denoting areas of organising pneumonia.

pattern of lung disease on CT scan with regions of ground-glass opacification and consolidation, which variably comprise foci of oedema, organising pneumonia and diffuse alveolar damage, are not too far removed from those in patients with an acute inflammatory pneumonitis (figure 1B–F). The radiological changes in COVID-19 pneumonia do not appear to resolve fully in all patients and in some, inflammation matures to form residual pulmonary fibrosis (figure 2).

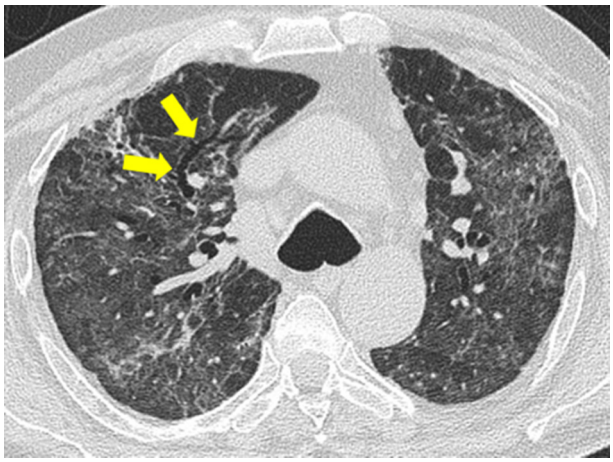

Figure 2 CT in COVID-19 extubated survivor: a study performed during recovery (26 days after onset of COVID-19 pneumonia). Image section at the level of the carina demonstrating widespread ground-glass opacification and considerable architectural distortion. There is definite CT evidence of fibrosis—note the varicose dilatation ('traction bronchiectasis') of the anterior segmental bronchus in the right upper lobe (arrows).

Predicting the likely respiratory consequences of COVID-19 is challenging but reviewing data from this and other coronavirus infections provides insights. There may be important parallels from the severe acute respiratory syndrome (SARS) outbreak of 2002–2003 caused by SARS-CoV and Middle East respiratory syndrome (MERS) first identified in 2012.[16–20] In a longitudinal CT study of 90 patients with COVID-19, 94% of individuals had residual changes on CT at discharge (median duration of 24 days after symptom onset) with ground-glass opacity the most common pattern.[21] At discharge, in a study of 110 patients with COVID-19, 91 (83%) of whom had a mild–moderate disease and 19 (17%) of whom had severe disease, almost half had impairment of the transfer factor of the lung for carbon monoxide (TLco).[22] The duration between onset of illness and pulmonary function testing ranged from an average of 20 days in mild cases to an average of 34 days in severe pneumonia. The TLco was lower in patients with severe disease and was more sensitive to disease severity than other lung function measures such as forced vital capacity (FVC) and total lung capacity (TLC). Interestingly in this study, and although still largely within normal ranges at an average of 83% predicted, the TLco/alveolar volume (Kco) was significantly lower in those with severe disease than those with mild to moderate COVID-19 possibly implying a degree of pulmonary vasculopathy.

In a study of SARS survivors, 12 weeks after discharge, 36% of patients had residual CXR abnormalities and at 6 months, these were still present in 30% of the entire cohort, with airspace opacification and reticulation the predominant abnormalities.[23] CXR abnormalities were correlated with lung function test parameters including FVC, TLco and TLC but not with measures of

respiratory muscle strength. Six months from hospital discharge, 16% of patients had persistent impairment of TLco with the preservation of the Kco.[23] The implication, therefore, is that these CXR imaging abnormalities were physiologically relevant and related to parenchymal lung disease. Similarly, in MERS survivors, at a median follow-up point of 6 weeks (range 32–230 days), 36% of patients had residual CXR changes, the vast majority of which were due to pulmonary fibrosis.[16]

These data suggest that the majority of patients infected with coronaviruses are discharged from hospital with persisting radiological change but that (at least in SARS[23] and MERS[16]) by 12 weeks, approximately two-thirds of patients have full CXR resolution. The optimal time for follow-up imaging to assess for radiological clearance in COVID-19 is unknown. Current BTS guidelines recommend a repeat CXR 6 weeks after a (bacterial or viral) community-acquired pneumonia[24]; the rationale being to exclude primary bronchial neoplasms that can contribute to lobar or segmental pneumonia. The ATS does not recommend routine follow-up imaging for patients recovering satisfactorily from community-acquired pneumonia.[11] The patchy ground-glass opacification classically observed in COVID-19 pneumonia (figure 1A–F) is, however, much less suspicious of harbouring a malignancy, particularly in the context of a pandemic. A 6-week follow-up CXR is, therefore, not advised and the 12-week time point is considered to be optimal in providing sufficient time for imaging resolution while also ensuring that non-resolving changes are addressed sufficiently early. Given that persisting imaging abnormalities correlate with physiological impairment, it is likely that these patients are at a greater risk of long-term parenchymal lung disease and are the group in whom closer follow-up and further investigation are indicated.

Unlike the MERS and SARS outbreaks, acute COVID-19 infection is associated with a high prevalence of VTE disease[25–27] and in situ thrombosis. Indeed, patients remain hypercoagulable for a variable period of time and prolonged immobility in the most severely affected patients represents an additional VTE risk factor. It is increasingly appreciated that a number of patients are diagnosed with acute PE and deep vein thromboses de novo during the pneumonia recovery phase. Although the follow-up of COVID-19 pneumonia may hinge on the radiological resolution, it is crucial to be mindful of the high risk of PE in this group; this follow-up guidance should highlight to clinicians the need for prompt identification and treatment of acute PE and post-PE complications such as chronic thromboembolic disease and pulmonary hypertension (PH).

AIMS AND SCOPE OF GUIDANCE

Given the large numbers of patients admitted to hospital in a short period of time, the aims of this guidance are to ensure that patients are followed-up in a timely but practical manner, ensuring the early identification of respiratory complications integrating factors such as disease severity, likelihood of long-term respiratory sequelae and functional disability (box 1).

In this document, we provide a suggested structure for the respiratory follow-up of patients with clinicoradiological confirmation of COVID-19 pneumonia. We do not recommend routine imaging or respiratory follow-up for patients without pneumonia on imaging nor those in whom CXR changes have fully resolved on follow-up imaging during hospitalisation. Given that the risk of subsequent post-infectious complications in this patient group is unknown, we do however advise that such patients consult their general practitioner (GP) should they experience persistent, new or progressive respiratory symptoms that do not recover over the 6–12 weeks following their acute illness. The lack of a robust evidence base for this new disease means that in consultation with their patient, an individual clinician can and should choose to deviate from the pathway when required.

Box 1 Specific aims of COVID-19 pneumonia follow-up

- The early, medium and long-term respiratory complications of COVID-19 pneumonia are identified and affected patients are then followed-up by appropriate services.
- The most serious and potentially life-limiting complications of COVID-19 such as pulmonary fibrosis and pulmonary vascular disease are identified at the earliest possible stage without overinvestigating those patients who will make a full recovery.
- Acute patients' needs such as breathlessness, oxygen requirements, rehabilitation, palliative care/symptom management and psychosocial needs are identified and addressed at the earliest possible stage.
- Patients diagnosed with COVID-19 pneumonia who have made a full recovery are appropriately reassured that their chest X-ray changes have resolved.
- Respiratory, radiology and physiology resources are coordinated and used optimally and efficiently using virtual systems where feasible.
- Patients with hitherto undiagnosed pre-existing respiratory disease are opportunistically identified and managed as appropriate.
- At all points of patient contact, teams are reminded to undertake a 'post-COVID-19 holistic assessment' (box 3) of patient needs.

On discharge from hospital, all patients should be advised that if they develop progressive or new respiratory symptoms prior to their intended review date, they should seek advice either from their GP surgery or if appropriate by presenting to emergency services. Frail patients or those with a performance status of 3–4 who have made a good clinical recovery post-COVID-19 pneumonia may understandably decline to reattend for a follow-up CXR. Where patients do not wish to attend for a follow-up CXR, teams should review the case notes and consider a remote clinic consultation to establish patient wishes and individual needs for further follow-up.

Use of this follow-up guidance may lead to the detection of incidental lung cancers and if detected these should be actioned. If any imaging is suspicious for lung malignancy, patients should either have an early repeat CXR 6 weeks after hospital discharge or a thoracic CT scan as appropriate to check for resolution with referral to local cancer services for further assessment as clinically indicated.

FOLLOW-UP ALGORITHMS

With the intention of addressing these aims (box 1), we have defined two follow-up algorithms (figures 3 and 4) that integrate disease severity as well as the functional capacity of patients on discharge.

1. Patients admitted for hospital care with a clinicoradiological diagnosis of COVID-19 pneumonia who required ICU or high dependency unit (HDU) admission or were cared for in the ward with severe pneumonia (figure 3)

Patients with severe COVID-19 pneumonia and those discharged with acute care needs including the elderly, those with multiple

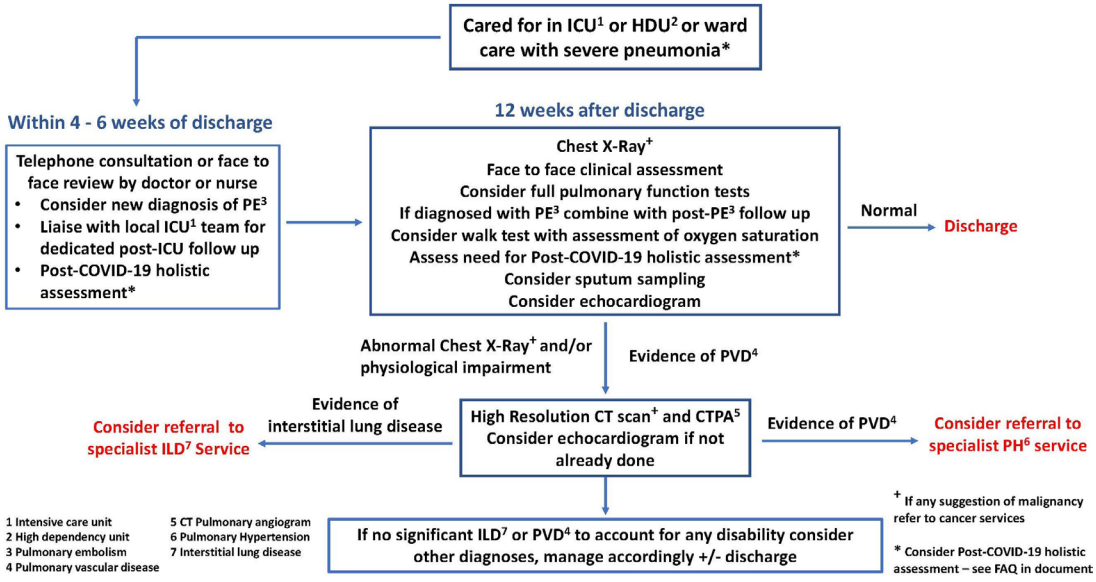

Figure 3 Respiratory follow-up algorithm for patients with COVID-19 pneumonia cared for in the ICU, HDU or those cared for on the ward with severe disease.

comorbidities and those with a lower performance status are also likely to be the most vulnerable and in need of more intensive medical, nursing, rehabilitation, psychological and social input. They are more likely to benefit from an earlier clinical review which in this algorithm is 4–6 weeks after discharge.

Severe disease is also associated with a higher likelihood of longer-term disability. During the SARS outbreak, patients requiring ICU admission experienced poorer longer-term outcomes with persisting radiological change and physiological impairment as compared with those cared for on general wards.[23] Although there was persistent lung function impairment, a prospective cohort study showed that the interstitial changes did not progress over time.[28]

Severe COVID-19 leads to ARDS.[29] The majority of patients with ARDS develop histopathological evidence of pulmonary fibrosis[30] and in survivors of ARDS, a significant proportion not only have CT evidence of residual pulmonary fibrosis but also functional impairment.[31 32] It is possible that some COVID-19 ICU survivors will experience persistent physiological impairment and radiological abnormalities although whether these are progressive remains to be seen.[33] There is some debate as to whether SARS-CoV-2-associated ARDS is phenotypically distinct from conventional ARDS, being characterised by profound hypoxaemia, relatively preserved lung compliance and significant ventilation/perfusion mismatch.[34] There is, however, a clearly emerging signal for endothelial dysfunction[35] with a high prevalence of pulmonary vascular dysfunction, thrombotic disease with PE and acute PH in the most severely affected patients. Some patients will be initiated on pulmonary vasodilators during the acute illness and will be discharged on therapy. These patients will require dedicated PH follow-up. Patients with organising pneumonia features and those in whom pulmonary

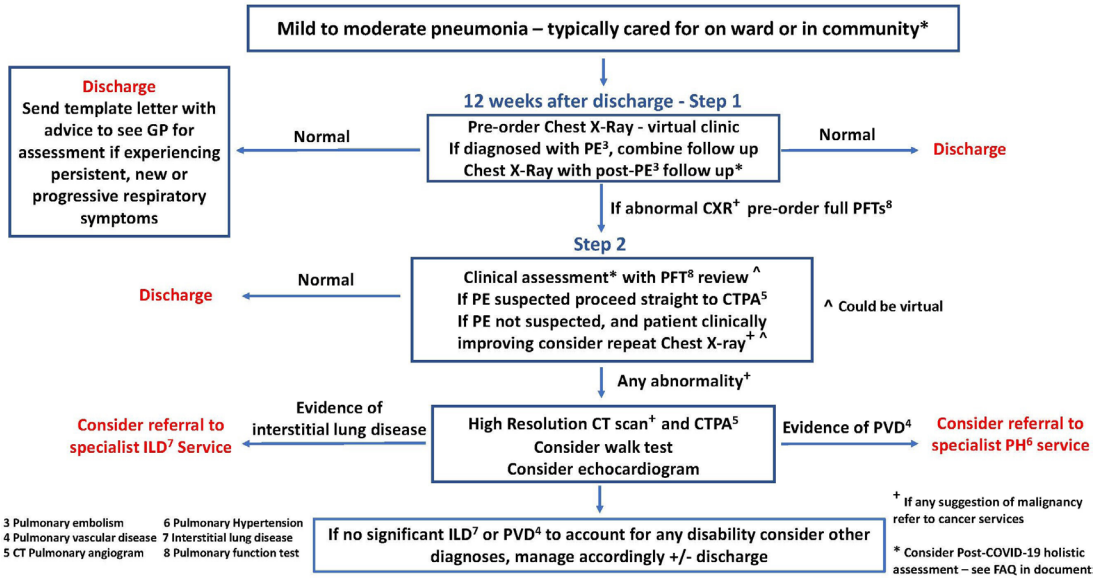

Figure 4 Respiratory follow-up algorithm for patients with mild to moderate COVID-19 pneumonia–typically cared for on the ward or in the community. GP, general practitioner.

Box 2 Patients at highest risk of COVID-19 pneumonia complications

- All patients managed on intensive care unit or high-dependency unit.
- All patients discharged with a new oxygen prescription.
- All patients with protracted dependency on high inspired fractions of oxygen, continued positive pressure ventilation and bi-level non-invasive ventilation.
- Any other patient the discharging team has significant concerns about.

fibrosis has started to develop may have been treated with corticosteroids with a plan for weaning of the dose as an outpatient. These patients should be assessed by specialist interstitial lung disease (ILD) teams where possible.

We recommend that patients cared for in ICU or those with severe COVID-19 pneumonia (box 2) should undergo an early follow-up assessment at 4–6 weeks after discharge.

This should ideally take the form of a remote or virtual clinic consultation by either a respiratory doctor or nurse. A face-to-face clinical assessment by either a respiratory doctor, a nurse or a suitably trained allied healthcare professional can then be arranged should a virtual consultation not be deemed sufficient or suitable to assess specific patients. This appointment should include a post-COVID-19 holistic assessment (box 3).

Patients should then undergo a full clinical assessment at 12 weeks with a repeat CXR which should be compared with previous CXRs performed during the patient's hospitalisation. If the CXR changes have fully resolved by this point (or if there are only minor insignificant changes such as small areas of atelectasis) and the patient is asymptomatic having made a full recovery, then they can be considered for discharge. In some cases, a patient will be clinically improving but the CXR may still have persisting changes that require further assessment. In this scenario, clinicians should consider arranging a further CXR in 6–8 weeks to assess for clearance with remote or virtual follow-up assessment by a doctor or a nurse prior to discharge if progress remains satisfactory.

If the CXR changes have not satisfactorily resolved and/or the patient has ongoing respiratory symptoms, consider the following:

Box 3 Post-COVID-19 holistic assessment

- Assessment and management of breathlessness.
- Symptom or palliative care management where required.
- Assessment and management of oxygen requirements.
- Consideration of rehabilitation needs and onward referral where required.
- Psychosocial assessment and onward referral where required.
- Assessment and management of anxiety.
- Assessment and management of fatigue.
- Assessment and management of dysfunctional breathing.
- Assessment and management of postviral cough.
- Consideration of a new diagnosis of venous thromboembolic disease.
- Consideration of specific post-intensive care unit complications such as sarcopaenia, cognitive impairment and post-traumatic stress disorder.

- Full pulmonary function testing.
- Walk test with an assessment of oxygen saturation.
- Echocardiogram.
- Sputum sample if expectorating for microbiological analysis.
- Referral to rehabilitation services if not already done.
- A new diagnosis of PE or post-PE complications if diagnosed during the acute illness.

Patients with persistent significant radiological abnormalities on plain imaging or with any clinically significant functional deficit or respiratory symptoms should then proceed to a pre-contrast thin section volumetric high-resolution CT (HRCT) scan and a CT pulmonary angiogram (CTPA) to assess for the presence of ILD and PE. If there is evidence of clinically significant ILD such as organising pneumonia or pulmonary fibrosis, patients should be considered for referral to regional specialist ILD services.

Patients diagnosed with PE de novo during follow-up should be treated as per standard protocols and followed-up in local services. If there is evidence of significant PH during follow-up, patients should be considered for referral to a specialist PH service. Patients diagnosed with PE during the acute illness should, where possible, be followed-up in local clinics 12 weeks after discharge as per usual protocols. If there is no suspicion of residual thromboembolic disease or evidence of significant PH, patients should be considered for discharge from PE follow-up with clear advice to primary care teams about the intended length of anticoagulation treatment. Patients with evidence of significant PH or evidence of significant chronic thromboembolic disease with or without PH should be considered for referral to specialist PH services.

If there is evidence of physiological or functional impairment but no evidence of significant ILD or pulmonary vascular disease, other diagnoses should be considered and managed appropriately. Specifically, there may be a high prevalence of dysfunctional breathing and breathing pattern disorder—if this is suspected, consider referral to specialist physiotherapy services.

2. Patients with a mild to moderate clinicoradiological diagnosis of COVID-19 pneumonia who did not require ICU or HDU care—typically cared for on the ward or in the community (figure 4)

This group includes those discharged directly from the emergency department or medical assessment unit and not admitted to hospital despite a diagnosis of COVID-19 pneumonia. These patients should have a routine follow-up CXR at 12 weeks from hospital discharge ideally in a virtual clinic. The CXR should be compared with previous CXRs performed during the patient's hospitalisation. If the 12-week follow-up CXR demonstrates complete resolution (or minor insignificant changes such as atelectasis), the patient should be discharged from further follow-up. Patients in this group who experience persistent or progressive respiratory symptoms such as breathlessness, chest pain or cough should seek medical attention promptly in advance of the scheduled CXR review, as early acute post-COVID-19 complications such as PE, interstitial lung disease or secondary infection will require more urgent medical attention. It is expected that respiratory follow-up for a significant number of post-COVID-19 pneumonia will end at this point.

For patients with significant persisting CXR abnormalities at 12 weeks;

- Arrange to see the patient at a face-to-face outpatient clinic setting.
- Organise full pulmonary function tests.

- If more than 6 weeks have passed since the first CXR, consider repeating the CXR on arrival to the outpatient setting as in some patients the abnormalities may have resolved between these two time points.

If the second CXR has cleared or has non-significant findings, radiological follow-up ends and the patient can be considered for discharge if they have recovered satisfactorily. Patients with persistent significant abnormalities on the second CXR and/or abnormal pulmonary function tests and/or significant unexplained breathlessness will require further investigations which may include the following:

- Precontrast thin section volumetric HRCT and CTPA to assess for the presence of ILD and PE.
- Walk test with an assessment of oxygen saturation.
- Echocardiogram if PH is suspected following pulmonary function testing and CT.

In the event that specific abnormalities such as ILD or PH are identified, patients should be considered for referral to regional specialist services. Patients diagnosed with PE de novo during follow-up should be treated as per usual protocols and followed-up in local services. Patients diagnosed with PE during the acute illness should be followed-up where possible in local clinics 12 weeks after discharge. If there is no residual thromboembolic disease or evidence of PH, patients should be discharged. Patients with evidence of PH or evidence of significant chronic thromboembolic disease with or without PH should be referred to specialist PH services. Any patient with post-COVID-19 pneumonia who is attending a post PE follow-up should have that visit coordinated with their pneumonia follow-up review where possible. A CXR should be offered on arrival to assess for resolution. If the CXR continues to show significant non-resolution, further investigations as before should be considered.

If there is evidence of physiological or functional impairment but no evidence of significant ILD or pulmonary vascular disease, other diagnoses should be considered. As previously, if dysfunctional breathing is suspected, then consider referral to specialist physiotherapy services.

PE AND POST-PE FOLLOW-UP

Patients diagnosed with PE during the acute illness should have post-PE follow-up as per local protocols. Patients should be considered for referral to specialist PH services where appropriate if PH is suspected or significant chronic thromboembolic disease demonstrated. If there is no evidence of chronic thromboembolic PH or significant residual thromboembolic disease, in light of the strongly provoked nature of the PE, discontinuation of anticoagulation after 3 months of therapy can be considered.[36] Further details are provided in the BTS VTE guidance (https://brit-thoracic.org.uk/about-us/covid-19-information-for-the-respiratory-community). Patients may remain hypercoagulable for some time after the acute illness and so extended thromboprophylaxis on discharge should be considered and there should be a high index of suspicion for the diagnosis of acute PE during the follow-up period. In those with PE who remain symptomatic, echocardiography and pulmonary vascular imaging modalities such as ventilation/perfusion (V/Q) scanning and CTPA form the mainstay of assessment for post-PE complications. It should be noted that V/Q scanning has limitations for patients with structural lung disease, which may be more likely in the aftermath of mechanical ventilation.

D-Dimer is a non-specific acute phase reactant that may be elevated in acute inflammatory illnesses, pneumonia and other causes of sepsis. Elevated levels are common in acute COVID-19 and are associated with poorer outcomes. Guan *et al* observed elevated D-dimer levels in 46% of patients in a series of 1099 patients,[2] whereas in a study of 183 patients with COVID-19 pneumonia, Tang *et al* observed higher D-dimer levels (median 2120 µg/L vs 610 µg/L) in non-survivors compared with survivors.[37] Although significantly elevated levels are more likely to be associated with VTE than more modestly elevated levels,[25 38] it is not possible to identify a threshold that can be used to non-invasively diagnose thrombus and a decision to proceed to diagnostic imaging should be based on overall clinical assessment. Acute thrombus can be excluded, however, in patients with normal D-dimer levels who do not have a high clinical probability of VTE.[39] There is no role for the routine measurement of D-dimer in patients being followed-up post-discharge. D-dimer may be useful in the investigation of possible acute PE in patients who develop acute new or worsening breathlessness. It should not be used to exclude suspected chronic thromboembolic disease and PH. Although there is some limited utility, outwith of COVID-19, in measuring convalescent D-dimer levels to refine decision-making regarding duration anticoagulation, there are no data to support this approach in patients following COVID-19 infection.[40]

GENERAL ISSUES TO CONSIDER DURING FOLLOW-UP

COVID-19, particularly severe disease, often leads to a wide range of sequelae that require dedicated follow-up. Renal dysfunction is common[3] and acute cardiac presentations of COVID-19 including myocarditis are well recognised.[41 42] Screening questionnaires utilising the Hospital Anxiety and Depression Scale may identify those in whom referral for psychological support is required.[43] Cognitive, psychiatric and physical complications including critical care neuromyopathy and post-tracheostomy care, collectively termed post intensive care syndrome[44] are often addressed in dedicated post-ICU clinics, which were first developed in the UK.[45] Other countries have recently started to replicate this approach to post-ICU care but it is estimated that in the UK, the country in which these clinics are most widely adopted, only approximately 30% of patients discharged from ICU are currently followed-up in this way.[46] Furthermore, patients requiring extracorporeal membrane oxygenation support are seen in dedicated follow-up clinics and so it will be important for respiratory and critical care teams to liaise closely ensuring that follow-up clinics are rationalised to avoid duplication of work.

Experience from the SARS outbreak suggested definitive evidence of coinfection with other microorganisms in a subset of patients, including disseminated invasive aspergillus infection and cytomegalovirus, with a prevalence as high as 15% in one postmortem cohort.[47 48] Systemic corticosteroid treatment was speculated to have contributed to some of these cases. In critically ill patients with COVID-19, it has been suggested that the prevalence of invasive aspergillosis is as high as 25%.[49] We recommend, therefore, that clinicians have a high index of suspicion for bacterial and fungal coinfection. Careful microbiological sampling and analysis are required to ensure that infective complications are addressed as early as possible.

Pulmonary rehabilitation is already established as a key management strategy in those with chronic respiratory disease, designed to optimise patients' exercise capacity, breathlessness, health status and psychological well-being.[50] A study investigating the pulmonary function and exercise capacity in a group of SARS survivors showed that although residual mild pulmonary function defects were detected in over half of recovered SARS patients at 3 months after hospital discharge, 41% had impaired exercise capacity that could not be accounted for by

ventilatory limitation.[51] Critical illness muscle weakness and deconditioning are likely to be contributing factors.[52] Rehabilitation services are currently under national review after the COVID-19 outbreak and are expected to offer comprehensive assessments, including psychosocial assessments where appropriate, for patients who prefer web-based, self-directed rehabilitation at home (https:///www.bts-thoracic.og.uk/about-us/covid-19-information-for–the-respiratory-community/).

Respiratory teams are advised to seek additional resources to support the delivery of post-COVID-19 follow-up work. Respiratory services have in most places already shouldered much of the responsibility for the care of patients with acute COVID-19. They will be key in delivering ongoing acute care with further surges predicted against a backdrop of 'chronic COVID-19 activity' as the infection persists within the population at a lower incidence level. Like other medical specialities, they also have a backlog of outpatient activity to address in a new working environment that is 'COVID-19 safe' but 'COVID-19 slow', for example, when considering access to imaging, physiology and bronchoscopy. With an appreciation that models of care will by necessity evolve to adapt to the post-COVID era, possible virtual solutions have been embedded within this guidance at multiple points. Respiratory community teams will play an important part in the early and indeed longer-term care of patients discharged from hospital, for example, when considering ongoing oxygen requirements, identification of rehabilitation needs, management of dysfunctional breathing and mental health assessment.

Summary

COVID-19 is a unique and novel infection that has already demonstrated a range of perplexing clinical syndromes—it's legacy will be felt long after the pandemic has passed. It is vital that the respiratory community is primed to detect and manage the long-term consequences of the infection and has sufficient resources to deliver it. This clinical guidance has been developed through expert consensus and then extensive peer review by a number of specialist advisory groups and experts at the BTS and the BSTI. Coordinated national guidance will facilitate data collection, research and audit, allowing the respiratory community to learn more about COVID-19 as well as ensuring that the clinical follow-up pathway can be iterated where required for future peaks of the infection. The use of the standardised BSTI CXR and CT reporting codes will facilitate data collection for audit and research purposes (online supplementary appendix 1 and 2). As the National Health Service starts to recover from the first peak of the COVID-19 pandemic and with high-quality patient care as a central principle, we envisage that this guidance will help to protect precious resources whilst minimising the long-term health effects related to the respiratory complications of this devastating disease.

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REFERENCES

1 Zhu N, Zhang D, Wang W, *et al*. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;382:727–33.
2 Guan W-jie, Ni Z-yi, Hu Y, *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med Overseas Ed* 2020;382:1708–20.
3 Yang X, Yu Y, Xu J, *et al*. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020;8:475–81.
4 Grasselli G, Zangrillo A, Zanella A, *et al*. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA* 2020. doi:10.1001/jama.2020.5394. [Epub ahead of print: 06 Apr 2020].
5 Mehta P, McAuley DF, Brown M, *et al*. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020;395:1033–4.

6 Middeldorp S, Coppens M, van Haaps TF, *et al*. Incidence of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost* 2020. doi:10.1111/jth.14888. [Epub ahead of print: 05 May 2020].
7 Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. *JAMA* 2020;323:1335.
8 Richardson S, Hirsch JS, Narasimhan M, *et al*. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the new York City area. *JAMA* 2020. doi:10.1001/jama.2020.6775. [Epub ahead of print: 22 Apr 2020].
9 Gold JAW, Wong KK, Szablewski CM, *et al*. Characteristics and Clinical Outcomes of Adult Patients Hospitalized with COVID-19 - Georgia, March 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:545–50.
10 Docherty AB, Harrison EM, Green CA, *et al*. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;369:m1985.
11 Metlay JP, Waterer GW, Long AC, *et al*. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American thoracic Society and infectious diseases Society of America. *Am J Respir Crit Care Med* 2019;200:e45–67.
12 Wang D, Hu B, Hu C, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020. doi:10.1001/jama.2020.1585. [Epub ahead of print: 07 Feb 2020].
13 Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506.
14 Arentz M, Yim E, Klaff L, *et al*. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington state. *JAMA* 2020. doi:10.1001/jama.2020.4326. [Epub ahead of print: 19 Mar 2020].
15 Zhou F, Yu T, Du R, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054–62.
16 Das KM, Lee EY, Singh R, *et al*. Follow-Up chest radiographic findings in patients with MERS-CoV after recovery. *Indian J Radiol Imaging* 2017;27:342–9.
17 Das KM, Lee EY, Langer RD, *et al*. Middle East respiratory syndrome coronavirus: what does a radiologist need to know? *AJR Am J Roentgenol* 2016;206:1193–201.
18 Das KM, Lee EY, Al Jawder SE, *et al*. Acute middle East respiratory syndrome coronavirus: temporal lung changes observed on the chest radiographs of 55 patients. *AJR Am J Roentgenol* 2015;205:W267–74.
19 Ketai L, Paul NS, Wong K-takT. Radiology of severe acute respiratory syndrome (SARS): the emerging pathologic-radiologic correlates of an emerging disease. *J Thorac Imaging* 2006;21:276–83.
20 Hosseiny M, Kooraki S, Gholamrezanezhad A, *et al*. Radiology perspective of coronavirus disease 2019 (COVID-19): lessons from severe acute respiratory syndrome and middle East respiratory syndrome. *AJR Am J Roentgenol* 2020;214:1078–82.
21 Wang Y, Dong C, Hu Y, *et al*. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: a longitudinal study. *Radiology* 2020;200843:200843.
22 Mo X, Jian W, Su Z, *et al*. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J* 2020;55. doi:10.1183/13993003.01217-2020. [Epub ahead of print: 18 Jun 2020].
23 Hui DS, Joynt GM, Wong KT, *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;60:401–9.
24 Lim WS, Baudouin SV, George RC, *et al*. Bts guidelines for the management of community acquired pneumonia in adults: update 2009. *Thorax* 2009;64 Suppl 3:iii1
25 Cui S, Chen S, Li X, *et al*. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost* 2020;18:1421–4.
26 Klok FA, Kruip M, van der Meer NJM, *et al*. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res* 2020.
27 Wichmann D, Sperhake J-P, Lütgehetmann M, *et al*. Autopsy findings and venous thromboembolism in patients with COVID-19. *Ann Intern Med* 2020. doi:10.7326/M20-2003. [Epub ahead of print: 06 May 2020].
28 Zhang P, Li J, Liu H, *et al*. Long-Term bone and lung consequences associated with hospital-acquired severe acute respiratory syndrome: a 15-year follow-up from a prospective cohort study. *Bone Res* 2020;8:8.
29 Marini JJ, Gattinoni L. Management of COVID-19 respiratory distress. *JAMA* 2020. doi:10.1001/jama.2020.6825. [Epub ahead of print: 24 Apr 2020].
30 Thille AW, Esteban A, Fernández-Segoviano P, *et al*. Chronology of histological lesions in acute respiratory distress syndrome with diffuse alveolar damage: a prospective cohort study of clinical autopsies. *Lancet Respir Med* 2013;1:395–401.
31 Herridge MS, Tansey CM, Matté A, *et al*. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med* 2011;364:1293–304.
32 Masclans JR, Roca O, Muñoz X, *et al*. Quality of life, pulmonary function, and tomographic scan abnormalities after ARDS. *Chest* 2011;139:1340–6.
33 George PM, Wells AU, Jenkins RG. Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy. *Lancet Respir Med* 2020. doi:10.1016/S2213-2600(20)30225-3. [Epub ahead of print: 15 May 2020].
34 Gattinoni L, Coppola S, Cressoni M, *et al*. Covid-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med* 2020.
35 Copin M-C, Parmentier E, Duburcq T, *et al*. Time to consider histologic pattern of lung injury to treat critically ill patients with COVID-19 infection. *Intensive Care Med* 2020;46:1124–6.
36 Konstantinides SV, Meyer G, Becattini C, *et al*. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European respiratory Society (ERS). *Eur Heart J* 2020;41:543–603.
37 Tang N, Li D, Wang X, *et al*. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 2020;18:844–7.
38 Leonard-Lorant I, Delabranche X, Severac F, *et al*. Acute pulmonary embolism in COVID-19 patients on CT angiography and relationship to D-dimer levels. *Radiology* 2020;201561.
39 Konstantinides SV, Meyer G, The MG. The 2019 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2019;40:3453–5.
40 Palareti G, Cosmi B, Legnani C, *et al*. D-Dimer testing to determine the duration of anticoagulation therapy. *N Engl J Med* 2006;355:1780–9.
41 Akhmerov A, Marbán E. COVID-19 and the heart. *Circ Res* 2020;126:1443–55.
42 Guo T, Fan Y, Chen M, *et al*. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020.
43 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–70.
44 Rawal G, Yadav S, Kumar R. Post-intensive care syndrome: an overview. *J Transl Int Med* 2017;5:90–2.
45 Colbenson GA, Johnson A, Wilson ME. Post-intensive care syndrome: impact, prevention, and management. *Breathe* 2019;15:98–101.
46 Teixeira C, Rosa RG. Post-intensive care outpatient clinic: is it feasible and effective? A literature review. *Rev Bras Ter Intensiva* 2018;30:98–111.
47 Wang H-jun, Ding Y-qing, Xu J, *et al*. Death of a SARS case from secondary Aspergillus infection. *Chin Med J* 2004;117:1278–80.
48 Hwang DM, Chamberlain DW, Poutanen SM, *et al*. Pulmonary pathology of severe acute respiratory syndrome in Toronto. *Mod Pathol* 2005;18:1–10.
49 Koehler P, Cornely OA, Böttiger BW, *et al*. COVID-19 associated pulmonary aspergillosis. *Mycoses* 2020;63:528–34.
50 Bolton CE, Bevan-Smith EF, Blakey JD, *et al*. British thoracic Society guideline on pulmonary rehabilitation in adults. *Thorax* 2013;68 Suppl 2:ii1–30.
51 Ong K-C, Ng AW-K, Lee LS-U, *et al*. Pulmonary function and exercise capacity in survivors of severe acute respiratory syndrome. *Eur Respir J* 2004;24:436–42.
52 Herridge MS. Long-Term outcomes after critical illness. *Curr Opin Crit Care* 2002;8:331–6.