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Review Article

Breathing Back Better! A State of the Art on the Benefits of Functional Evaluation and Rehabilitation of Post-Tuberculosis and Post-COVID Lungs

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ABSTRACT

Currently, tuberculosis (TB) and COVID-19 account for substantial morbidity and mortality worldwide, not only during their acute phase, but also because of their sequelae. This scoping review aims to describe the specific aspects of post-TB and post-COVID (long-COVID-19) sequelae, and the implications for post-disease follow-up and rehabilitation.

In particular, evidence on how to identify patients affected by sequelae is presented and discussed. A section of the review is dedicated to identifying patients eligible for pulmonary rehabilitation (PR), as not all patients with sequelae are eligible for PR. Components of PR are presented and discussed, as well as their effectiveness.

Other essential components to implement comprehensive rehabilitation programmes such as counselling and health education of enrolled patients, evaluation of cost-effectiveness of PR and its impact on health systems as well as research priorities for the future are included in this scoping review.

Introduction

Both, tuberculosis (TB) and COVID-19 currently account for substantial morbidity and mortality worldwide. Both can lead to cure, naturally or following treatment. However, what actually happens to people after the two diseases are considered cured is still not fully known, and is presently attracting major clinical and scientific interest. The aim of this scoping review is to describe these specific post-diseases aspects, and the implications for post-disease follow-up and rehabilitation.

Post TB lung disease (PTLD)

Over the last decades National TB Control Programmes concentrated their efforts on diagnosis and treatment of cases of sputum smear positive TB. The main target was to curb TB transmission by early diagnosis and successful treatment of infectious cases.[1] This approach proved to be effective in reducing TB transmission and decreasing the burden of disease in many countries.

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Nevertheless, concentrating efforts on the urgent need to reduce transmission of disease had some consequences on the health of survivors. Programmes are following-up patients till the end of treatment (when patients are declared cured and/or successfully treated/dead/lost to follow-up). Monitoring/evaluation of health outcomes after the end of treatment is not done. Even if recognised by clinicians as PTLD, TB sequelae after the end of treatment have been studied only recently.[2–7] In fact, after TB treatment completion, a significant proportion of people (formally cured or not) present residual cough, weakness, dyspnoea, difficulties in climbing stairs or managing every-day or work activities. PTLD affects patients' quality of life (QoL) while increasing the risk of death.[2–7]

Experts convening at the First International Symposium on Post-TB disease defined PTLD as: 'Evidence of chronic respiratory abnormality, with or without symptoms attributable at least in part to previous (pulmonary) tuberculosis'.[8]

There is increasing evidence that up to 50% of TB patients (>70% among multidrug-resistant patients) report health problems consistent with PTLD after completion of treatment.[9–18] Thus, PTLD is likely to cause a considerable burden of disease globally, suggesting opportunities for prevention, management and rehabilitation. It has been estimated that 138–171 million TB survivors were alive in 2020, of whom nearly one fifth had been treated in the previous 5 years.[19] PTLD was estimated to account for approximately half of lifetime disability-adjusted life years (DALYs) caused by incident TB.[17,20,21] However, PTLD is currently not considered as a health consequence in global disease burden estimates.

Post-COVID

During the last two years the epidemic of the severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) infection caused COVID-19 in a significant proportion of those infected. The disease can cause pneumonia with variable degrees of severity, up to acute respiratory distress syndrome (ARDS) and death. It is well known that when ARDS occurs, whatever aetiology causes it, patients will later suffer from impaired lung function, reduced exercise capacity and quality of life for up to 5 years after the event.[22] Given the recent appearance of the disease in different waves, the consistency of its long-term consequences is not yet completely understood. Unfortunately, albeit slowly, its impact continues to grow.

The post-COVID-19 phase is often difficult to define. Early studies aimed at defining and investigating symptoms and health consequences included hospitalised patients with short follow-up periods after discharge,[23–25] while only recent studies included community patients, never hospitalized for COVID-19.[26–29]

In 2021, the WHO defined post-COVID-19 sequelae as the presence of symptoms in a patient with a history of probable or confirmed SARS-CoV-2 infection, usually at least 3 months from the onset of COVID-19, with symptoms lasting more than 2 months and not explained by an alternative diagnosis.[30] Common symptoms used to diagnose this condition include fatigue, shortness of breath, cognitive dysfunction and other symptoms that generally have an impact on everyday functioning.[31] A recent systematic review and meta-analysis reported that 80% of patients surviving COVID-19 had one or more symptoms compatible with post-COVID-19 sequelae, such as fatigue (58%), and dyspnoea (24%).[32]

Sequelae can be mild, moderate or severe. Mild sequalae include persistent but reversible symptoms with no need for treatment. Moderate sequelae, although generally treatable and reversible, require active intervention in terms of diagnosis and treatment. Finally, severe sequelae, although rare, present with chronic organ failure, such as cardiovascular events including myocarditis, renal failure or pulmonary fibrosis.[33,34]

Post-COVID sequelae may affect several organs or body systems, but in this scoping review the focus will be on the lungs.

Pulmonary fibrosis is a known sequela of severe lung damage secondary to many aetiologies including respiratory infections.[35,36] Although the precise pathophysiological mechanisms underlying this complication remain unknown, the immune activation and alveolar epithelial injuries might lead to an aberrant reparative response with accumulation of fibroblasts and excessive deposition of collagen.[35] Of note, persistent radiological signs of pulmonary fibrosis can be observed after 3 months since acute phase of disease in previously hospitalized patients.[37,38]

Methodology

PTLD has reached internationally acknowledged relevance during the last few years,[1,8–10,12–15] thus we revised all international literature of the last 5 years searching on PubMed the following keywords: '*tuberculosis*', '*TB*', '*post-TB*' and '*sequelae*' or '*rehabilitation*'.

Since COVID-19 has been recently identified, we revised all international literature searching on PubMed the following keywords: '*tuberculosis*', '*TB*', '*post-TB*' and '*sequelae*' or '*rehabilitation*'.

The selection of relevant articles among those identified for both conditions started with reading the abstract. The second phase consisted on reading the whole text of the relevant articles. Additional articles were identified through accurate evaluation of references of the selected papers.

Identifying patients with sequelae

Post-TB sequelae

PTLD includes structural and functional lung sequelae, with varying severity, such as fibrosis, pleural thickening, cavitation, bronchiectasis, lung function deficits (obstruction, restriction and mixed patterns), pulmonary hypertension, and colonization and infection with *Aspergillus fumigatus*, non-tuberculous mycobacteria and other bacteria.[7,11,12,39,40] PTLD patients have a two-fold higher risk of spirometry abnormalities in comparison to the general population,[10] and approximately 10% of them have lost more than half of lung function.[41] As a consequence, persistent respiratory symptoms are common, and include residual cough, dyspnoea, wheeze, and reduced exercise capacity.[42]

In a cross-sectional study with 145 adults who completed TB treatment, 38% of participants had airflow obstruction, 58% low forced vital capacity (FVC), and the most frequent respiratory symptoms were wheeze (42%), dyspnoea (25%), and cough (19%).[39] Functional impairment is even more prevalent in drug-resistant TB cases.[43] In a prospective study with 405 patients in Malawi, 44% had bronchiectasis, and after 1 year, approximately 30% had respiratory symptoms and one in five had a decline of 100 mL in forced expiratory volume in one second (FEV_1).[44] In accordance with these findings, in a Brazilian cohort of PTLD patients followed-up for a mean time of 8.3 ± 4.9 years, a decline in FEV_1, FVC, total lung capacity (TLC), Diffusing Capacity for carbon monoxide (DLCO), and six-minute walking test (6MWT) was demonstrated.[45] The most important predictors of PTLD are generally a delay in diagnosis, multiple TB treatments, and drug-resistant TB.[11]

Every patient completing TB treatment should be clinically evaluated to identify PTLD, ideally as soon as possible at the end of treatment.[1] Essential examinations/investigations recommended to identify post-TB sequelae include: clinical assessment (history, examination), chest imaging, in particular, chest X-ray and CT, where available and affordable, to detect fibrosis, cavities, pleural thickening, bronchiectasis, pulmonary hypertension, secondary bacterial and fungal infections; arterial blood gas analysis and/or pulse oximetry, pulmonary function testing (PFT), including 6MWT, spirometry, plethysmography and DLCO to detect obstructive, restrictive and mixed patterns; and cardiopulmonary exercise testing to assess the integrative responses of the cardiovascular, respiratory and musculoskeletal systems to incremental exercise in patients with PTLD and subjective evaluation (symptoms score and QoL questionnaire). In situations where all the examinations listed above cannot be performed, the following examinations/investigations should be prioritized: clinical history, symptom assessment and clinical examination; chest X-ray; spirometry; pulse oximetry; 6MWT; symptoms score and QoL questionnaire.[1,7–10,39,43,46–49]

Post-COVID-19 sequelae

COVID-19 can damage many organs, especially lung, heart, and brain. Patients surviving COVID-19 often experience persisting respiratory symptoms; abnormalities in PFT and chest CT images may persist for months after hospital admission.[50–53] Pulmonary dysfunction may occur even in patients with mild disease presentation.[54,55] Nevertheless, there is particular interest in long-term pulmonary sequelae in critical patients, i.e. those requiring intensive care unit (ICU) admission; among them a high prevalence of functional impairment and pulmonary structural abnormalities have been reported.[31,50,56,57]

The most commonly observed abnormalities are diffusion impairment, followed by restrictive ventilatory defects.[50] Lung function alterations have been reported at the time of discharge, and at 3, 6 and 12 months.[52,58–63] In a cohort of 110 patients in China,[58] reductions in FEV_1 were described in 13.6% of patients, FVC in 9.1%, TLC in 25%, and DLCO in 47.2% at the time of discharge. Persistent DLCO and TLC impairments were associated with the most severe SARS-CoV-2 cases.[58,60] At 3 months of follow-up, DLCO deficits were present in 25% of individuals in a retrospective multicentre cohort study.[59] Hellemons et al.[64] showed impaired FVC and DLCO in 25% and 63% of patients, respectively, at 6 weeks. These percentages have improved at 6 months to 11% and 46% for FVC and DLCO, respectively. In another study[61] that followed patients for 12 months after discharge, the authors noted a median DLCO of 77% of predicted at 3 months, 76% of predicted at 6 months, and 88% of predicted at 12 months. DLCO reductions (24–34%), restrictive defects (7–13%), and development of pulmonary fibrosis (19–26%) have been reported in several studies.[52,61–63]

The most important predictors of post-COVID-19 sequelae are older age, female sex, pre-existing comorbidities, and initial severity of the acute illness.[65] In addition, the risk of long-term symptoms is associated with elevated body mass index and more than five symptoms in their first week of disease. Fatigue (OR 2.83, CI 2.09–3.83) and dyspnoea (OR 2.36, CI 1.91–2.91) in the first week of the acute phase were associated with persistent symptoms 28 days after recovery.[66] Predictors of COVID-19-related pulmonary fibrosis include age, history of smoking or alcoholism, extent of lung injury, and length of mechanical ventilation.[56,67,68]

Essential examinations/investigations recommended to identify post-COVID-19 sequelae include: clinical history (persistent fatigue or respiratory symptoms; presence of comorbidities), evaluation of QoL (Euroqol five dimensions [EQ-5D]; Short-Form 36; St George's Respiratory Questionnaire), evaluation of functional status (Post-COVID-19 Functional Status [PCSF]; Functional Impairment Checklist [FIC]; Functional Independence Measure [FIM]; Barthel's Index), exercise capacity (Cardiopulmonary exercise test and/or 6MWT and/or One minute Sit to Stand Test and/or Maximal voluntary contraction and/or One Maximum Repetition and/or Short Physical Performance Battery), pulmonary function tests (spirometry with plethysmography, if available, and DLCO, blood gas analysis and/or pulse oximetry, and radiological evaluation (chest X-ray and CT, where available and affordable).

In situations where all the examinations listed above cannot be performed, the following examinations/investigations should be prioritized: clinical history; evaluation of QoL; evaluation of functional status; 6MWT; spirometry; pulse oximetry, and chest X-ray.

Identifying patients eligible for pulmonary rehabilitation (PR)

Post-TB patients

Clinical Standards on PTLD recommended that former TB patients with clinical and radiological signs and symptoms consistent with post-TB sequelae should be evaluated for PR.[1] Patients with functional impairments such as reduced pulmonary function (airflow obstruction or restriction or mixed abnormalities, and/or impaired diffusing capacity for carbon monoxide), abnormal blood gas ($PaO_2 < 80$ mmHg and/or $PaCO_2 > 45$ mmHg and/or nocturnal and exercise-induced desaturation), and reduced exercise capacity should also benefit from PR. In addition, PR can be indicated in the presence of comorbidities, like chronic obstructive pulmonary disease, asthma, bronchiectasis, pulmonary fibrosis, and pulmonary hypertension. PR is also beneficial for patients with at least one hospitalization or two exacerbations in the last 12 months, and impairment in QoL.[1]

Post-COVID-19 patients

Clinical Standards on post-COVID-19 sequelae recommend that every patient with previous history of COVID-19, lung function impairment (airflow obstruction or restriction or mixed and/or impaired DLCO), reduced exercise tolerance and related impairment in QoL and other relevant signs or symptoms (fatigue or exhaustion or asthenia or weakness; respiratory symptoms [dyspnoea, cough, chest pain]; $PaO_2 < 80$ mmHg and/or $PaCO_2 > 45$ mmHg and/or exercise-induced desaturation) should be evaluated for PR.

Debeaumont et al. evaluated COVID-19 patients, 6 months after their discharge from the hospital, and showed that persistent dyspnoea was associated with reduced physical fitness.[69] Those patients should benefit from PR. In addition, patients who had severe acute illness, and those with abnormal chest X-ray or CT or reduced DLCO will probably need early and effective respiratory rehabilitation.[70]

Post-ICU patients with COVID-19 should be a target population for rehabilitation.[55] Patients with severe lung impairment during COVID-19 acute illness are prone to pulmonary function tests and 6MWT alterations, and are a subgroup of patients that could also benefit from PR.[71]

Components of pulmonary rehabilitation

Pulmonary rehabilitation programmes cannot be planned without considering local organisation of health services. They should also be organised according to feasibility, effectiveness and cost-effectiveness criteria.

Knowledge on PR is mostly derived from experiences in chronic respiratory diseases, especially chronic obstructive pulmonary disease (COPD). In this setting, PR showed to be relatively more cost-effective than pharmacotherapy.[72] There are obviously notable differences between these conditions, PTLD and/or post-COVID.

Any programme, to qualify as PR, should have some minimum and unavoidable requirements. These include comprehensive baseline and post-PR outcome measurements, a structured and supervised exercise training programme, an education/behavioural

Table 1
Proposed components of a pulmonary rehabilitation programme for PTLD or for COVID survivors.

	Methods		
Components	Indication	Interventions	Adoptions to special settings and situations
Aerobic exercise: Endurance Training (limited evidence on COVID)[1,8,9,31,78,81,82,88]	- Impaired exercise capacity, limited by dyspnoea, fatigue and or other symptoms. - Restriction in daily life activities.	• Treadmill and/or cycle-ergometer • 30 min. 2–5 times/week for 4–8 weeks • Continuous or interval training • Low-Intensity (40–60%) or Hight-Intensity (60–80%) set according to - maximal heart rate (220-age) or - maximal oxygen consumption or - the equation of Luxton or - symptom limited (target Borg scale ≤4) • In- or out-patients or tele-monitoring • Suggest maintenance program	• Free walks 30 min. 2–5 times/week for 4–8 weeks • Intensity set according to perceived symptoms (target Borg scale ≤4) • Out-patients or home setting • Suggest maintenance program
Strength training: Upper and lower extremities (limited evidence on TB and COVID)[1,9,31,78,81,82,88]	Sarcopenia, reduced strength of peripheral muscles. Lower muscle weakness with risk for falls. Impaired activities of daily living involving the upper extremities (including dressing, bathing, and household tasks)	• free weights (dumbbells and ankle-brace) • 20–30 min. 2–5 times/week for 4–8 weeks • 2–3 set of 6–12 repetitions • Intensity set to 80% of MVV or 1MR and/or adjusted on perceived muscles fatigue (target Borg scale ≤4) • In or out-patients or tele-monitoring Suggest maintenance program	• free weights (dumbbells and ankle-brace) • 20–30 min. 2–5 times/week for 4–8 weeks 2–3 set of 6–12 repetitions • Intensity set according to perceived muscles fatigue (target Borg scale ≤4) • Out-patients or home setting • Suggest maintenance program
Inspiratory muscle training (limited evidence on TB and COVID)[1,79,96]	Impaired respiratory muscle function, altered respiratory mechanics, decreased chest wall compliance or pulmonary hyperinflation	• load threshold devices, seated and using a nose clip • Intensity/load set at 30–60% of maximal inspiratory pressure • Interval training, 3 sets with10 breaths followed by 1-minute break between each set. • 15–20 min. 2–5 times/week for 4–8 weeks	Not applicable
Calisthenics and stretching exercises (limited evidence on TB and COVID)[31,79,82]	Impaired daily life activities	• Calisthenics exercises • Stretching exercises • Nordic walking or Aqua fitness or home exercise • 2–5 times per week for 30 min	• Calisthenics exercises • Stretching exercises • Home exercises • 2–5 times per week for 30 min
Respiratory exercise (limited evidence on TB and COVID)[31,78,79,82]	Dynamic hyperinflation Resting tachypnea Dyspnoea	• Adaptive breathing strategies • yoga breathing • pursed-lips breathing • computer-aided • breathing feedback • 2–4 times per week for 30 min each	• Adaptive breathing strategies • yoga breathing • pursed-lips breathing • computer-aided • 2–4 times per week for 30 min each
Education (limited evidence on TB and COVID)[31,78]	Impaired/reduced self-efficacy and collaborative Self-Management	• Structured and comprehensive educational programmes • Age specific, gender-sensitive, delivered in the local language and extended to family and/or care-givers • Individual or group sessions • 15–60 min. • Importance of physical activity and exercise to improve quality of life • Maintaining results achieved with pulmonary rehabilitation (follow-up plan) • Advantages/importance of smoking cessation and risk of comorbidities (e.g., diabetes, etc.) • Importance of adhering to medical prescriptions in terms of management of comorbidities and vaccinations • Achieving an optimal healthy life style	• Structured and comprehensive educational programmes • Age specific, gender-sensitive, delivered in the local language and extended to family and/or care-givers • Individual or group sessions • 15–60 min. • Importance of physical activity and exercise to improve quality of life • Maintaining results achieved with pulmonary rehabilitation (follow-up plan) • Advantages/importance of smoking cessation and risk of comorbidities (e.g., diabetes, etc.) • Importance of adhering to medical prescriptions in terms of management of comorbidities and vaccinations • Achieving an optimal healthy life style
Psychological support (limited evidence on COVID)[1,31,78,80,81,105,105]	Depression, anxiety and cognitive dysfunction	• Psychological assessment • Psychological support • Relaxation technique • Consider self-help group	• Psychological assessment • Psychological support • Relaxation technique • Consider Self-help group
Airway clearance techniques (limited evidence on COVID)[1,31,78,97]	Difficult to remove secretions or mucous plugs. Frequent bronchial exacerbations (≥2/year). Concomitant diagnosis of bronchiectasis.	• Choose the technique suitable for the subject among those available, based on respiratory capacity, mucus rheology, collaboration and patient preferences • 15–30 minutes one or more times/day • Choose the duration of treatment based on chronic (long term) or acute problem (short term) • Suggest maintenance program when needed	• Choose the technique suitable for the subject among those available, based on respiratory capacity, mucus rheology, collaboration and patient preferences • 15–30 minutes one or more times/day choose the duration of treatment based on chronic (long term) or acute problem (short term) • Suggest maintenance program when needed

Table 1 (*Continued*)

Methods			
Components	Indication	Interventions	Adoptions to special settings and situations
Long term oxygen therapy (limited evidence on TB and COVID)[1,78,98,99]	Resting hypoxemia despite stable condition and optimal medical therapy (partial pressure of oxygen < 7.3 kPa (<55 mmHg) or ≤8 kPa (≤60 mmHg) with evidence of peripheral oedema, polycythaemia (haematocrit ≥55%) or pulmonary hypertension).	Titrate oxygen flow that maintain oxygen saturation >92–93%. • Long term oxygen therapy should be initiated on a flow rate of 1 L/min and titrated up in 1 L/min increments until oxygen saturation >90%. An arterial blood gas analysis should then be performed to confirm that a target partial pressure of oxygen ≥8 kPa (60 mm Hg) at rest has been achieved. • Ambulatory and nocturnal oximetry may be performed to allow more accurate flow rates to be ordered for exercise and sleep, respectively during rest, sleep and exertion. • Provide formal education to patients referred to home • Schedule periodic re-assessment at 3 months	Titrate oxygen flow that maintain oxygen saturation > 92–93%. • Long term oxygen therapy should be initiated on a flow rate of 1 L/min and titrated up in 1 L/min increments until oxygen saturation > 90% at rest has been achieved. • Non-hypercapnic patients initiated on long term oxygen therapy should increase their flow rate by 1 L/min during sleep in the absence of any contraindications. • Ambulatory oximetry may be performed to allow more accurate flow rates to be ordered for exercise • Provide formal education to patients referred to home • Schedule periodic re-assessment at 3 months
Long-term nocturnal non invasive mechanical ventilation (limited evidence on TB and COVID)[1,77,100]	Chronic stable hypercapnia (partial pressure of carbon dioxide >6–8 kPa (45–60 mmHg)), despite optimal medical therapy. non-invasive ventilation could be applied during aerobic training in case of severe breathlessness or reduced exercise resistance.	• Not initiating long-term non-invasive ventilation during an admission for acute on-chronic hypercapnic respiratory failure, favoring reassessment at 2–4 weeks after resolution • Titrate non-invasive ventilation setting • Titrate mask • Plan education • Consider non-invasive ventilation during exercise • Schedule an educational meeting and verifies the ability of the subject and/or a caregiver to manage the non-invasive ventilation at home	• Probably not applicable
Nutritional support (limited evidence on COVID)[1,78,101–103]	Body composition abnormalities	• Nutritional assessment • Tailored treatment from foods and medical supplements	• Nutritional assessment • Tailored treatment from foods and medical supplements • Need for financial incentives and transportation access should be evaluated

programme intended to foster long-term health-enhancing behaviour, and provision of recommendations for home-based exercise and self or supervised physical activity programmes.[1,73]

Some evidence on effectiveness of PR programmes targeting PTLD patients exists only in selected settings with adequate resources, logistics, and expert healthcare providers.[74–77] Recently, a few positive experiences of PR programmes targeting post-COVID patients have been reported.[31,78–85] Depending on the residual individual deficits in post-COVID patients, PR should be offered with the objective to improve respiratory, physical and psychological impairments.[31,78,86–88]

PR programmes should be adapted to the context and resources available to make them as accessible as possible for those benefiting from it (including children and adolescents) in different settings.[9,89–95] The core components of a PR programme are summarised in Table 1.[96–105]

The Global Tuberculosis Network (GTN) is monitoring PR pilot testing activities and it will share the results when available.

Evaluation of effectiveness of pulmonary rehabilitation

Implementation of a rehabilitation programme implies a plan to evaluate its effectiveness. The main recommendation is generally to compare the core variables before and after rehabilitation.[1]

As previously discussed, on completion of TB treatment or at discharge from hospital post COVID, before starting a PR programme tailored to a patient's needs, a comprehensive assessment is necessary. Therefore, having a baseline assessment, i.e., before programme, the simplest way to evaluate the effectiveness of PR is to compare the core variables at baseline vs. at the end of the programme.[74–76,89] The minimal evaluation set includes the patient's functional exercise capacity, dyspnoea and health status.[8,9,17] If possible, a series of health outcomes including social, economic and psychological impact should be evaluated in clinical studies.[8,17]

The most popular tool to measure exercise capacity is the 6MWT.[73–75,90] Nevertheless, the cardiopulmonary exercise test or the incremental shuttle walk test and the 5 repetition 'sit to stand' test are recommended, too.[89,106] Regarding PTLD patients, PR has proven to significantly improve the distance covered during the 6MWT (by approximately 35–45 m), an improvement comparable to that observed in subjects with COPD.[107] QoL evaluation is extremely important, but it is usually measured by questionnaires, with inter-studies variability. Nevertheless, the questionnaires whose use actually show significant improvement were the St George's Respiratory Questionnaire, the Short Form Health Survey 36 and the Clinical COPD questionnaire.[107–109] Similarly, the clinical evaluation based on symptoms (dyspnoea, chest pain, haemoptysis and cough) employed different scales. Unfortunately, no data are available on other strong outcomes such as mortality and morbidity.

Follow-up

Monitoring of patients undergoing PR is important during PR and at its end, this should occur with a formal evaluation. The impact of PR needs to be assessed also in the longer term since the early (end of programme) evaluation could miss clinical problems arising later and miss if the benefits achieved after PR are maintained and for how long. Any follow-up has to be arranged based on local feasibility and organisation of health services. In fact, for TB, individuals completing an episode of TB treatment, especially those with residual pulmonary sequelae (e.g. residual cavitations), and/or affected by other infections (e.g., aspergilloma and/or non-tubercular mycobacteria) remain at elevated risk of recurrent TB.[110,111] Recurrence may occur due to endogenous reactivation or following exogenous reinfection.[112,113]

Special considerations

Patients with sequelae, but without apparent need (or with contra-indications) for PR have a lower priority. However, if feasible, their follow-up can also be considered. In consideration of the risk of recurrence PTLD patients have, infection control and prevention measures (and reassessment of the patient's potential contagiousness) are recommended during all steps of the process.

Counselling & health education

Every patient who participates in a PR programme should undergo counselling/health education. Patients should be counselled about their disease, available treatments, benefit of healthy lifestyle, and smoking avoidance. Booklets, videos, and telehealth can be used for patient education, and the patient's family should be encouraged to participate. Counselling/health education should include a follow-up plan to maintain the results achieved with PR[1,114] (Table 2).

Table 2
Recommended topics for counselling/health education.

- Basic principles of disease: epidemiology, clinical aspects, transmission, diagnosis, and treatment
- Simple concepts of infection control (e.g. how long will they be considered contagious)
- Common symptoms they might experience after acute disease (post-COVID-19 or post-TB)
- How to monitor and manage their symptoms at home, and when they should go to a health facility/call a doctor
- Support for lifestyle interventions, such as physical activity, adequate nutrition, and smoking cessation
- Management of comorbid physical and mental health conditions
- Risks of reinfection and how they can manage this risk
- Address stigmatization of their COVID-19/TB infection and ongoing symptoms
- Maintaining results achieved with pulmonary rehabilitation (follow-up plan)

Evaluate cost-effectiveness and impact on health systems

PR is one of the most cost-effective interventions in patients with COPD, resulting in substantial cost savings through the prevention of readmission.[115–117] Although PR is associated with significant improvements in pulmonary function in post-TB patients,[7] and could accelerate the recovery of lung disease in post-COVID-19 patients,[118] there is a need for randomized-controlled trials to identify effective and cost-effective strategies to deliver PR in different settings and populations.[1]

In addition to cost-effectiveness, we have to consider the feasibility of PR programmes in low and high burden countries. In fact, the idea inspiring the recently published reference document[1] was to generate universal standards, offering to countries/settings an

Table 3
Research priorities.

	Research priority		Proposed type of study
	TB	COVID	
1.	To describe the frequency and severity of PTLD in different populations and subgroups of TB patients over time since the completion of TB treatment, including in children and adolescents	To describe the frequency and severity of post-COVID disease in different populations and subgroups of COVID survivors over time since hospital discharge or viral clearance, including in children and adolescents	Cross-sectional studies, cohort studies
2.	To identify risk factors for severe PTLD and associated poor health outcomes, including increased mortality	To identify risk factors for severe post-COVID and associated poor health outcomes, including increased mortality	Cohort studies (case-control studies)
3.	To quantify the health and economic impact of PTLD at the individual and population level, including the impact of managing PTLD on health systems	To quantify the health and economic impact of post-COVID at the individual and population level, including the impact of managing post-COVID on health systems	Health economic/mathematical modelling studies
4.	To identify feasible, accurate and cost-effective tools to evaluate patients at the end of TB treatment for their risk of PTLD and subsequent poor health outcomes	To identify feasible, accurate and cost-effective tools to evaluate patients at the end of hospitalization and/or at viral clearance for their risk of post-COVID and subsequent poor health outcomes	Diagnostic accuracy studies, diagnostic randomised-controlled trials
5.	To develop optimal approaches and algorithms to diagnose and manage PTLD, and to discriminate between PTLD and recurrent TB	To develop optimal approaches and algorithms to diagnose and manage post-COVID	Diagnostic accuracy studies, diagnostic randomised-controlled trials
6.	To identify effective and cost-effective strategies to prevent PTLD during anti-TB treatment, including, for example, adjuvant therapies and interventions to reduce concomitant risk factors for poor lung health outcomes (e.g., smoking cessation programmes)	To identify effective and cost-effective strategies to prevent post-COVID during hospitalization or home treatment/care, including, for example, adjuvant therapies and interventions to reduce concomitant risk factors for poor lung health outcomes (e.g., smoking cessation programmes)	Randomised-controlled trials
7.	To identify effective and cost-effective strategies to deliver pulmonary rehabilitation in specific sub-groups (using standard measures of minimum clinically important difference), including individual patient follow-up in different settings and populations	To identify effective and cost-effective strategies to deliver pulmonary rehabilitation in specific sub-groups (using standard measures of minimum clinically important difference), including individual patient follow-up in different settings and populations	Randomised-controlled trials
8.	To investigate the role of patient education programmes in improving long-term health outcomes post-TB	To investigate the role of patient education programmes in improving long-term health outcomes post-COVID	Randomised-controlled trials
9.	To investigate the role of social protection and support programmes in improving health outcomes and quality of life among former TB patients	To investigate the role of social protection and support programmes in improving health outcomes and quality of life among COVID survivors	Randomised-controlled trials
10.	To identify a set of standard indicators for the surveillance of PTLD that are feasible to implement within national TB programmes	To identify a set of standard indicators for the surveillance of post-COVID that are feasible to implement within national health programmes	Operational research studies

TB: tuberculosis; PTLD: post-TB lung disease; COVID: coronavirus disease.

ideal guide where to go, although not all countries or settings are immediately able to meet them.

COVID-19 has impacted healthcare systems globally, with many services reduced or temporarily cancelled.[119] In this sense, several PR programmes had to be adapted to ensure their continuity. Due to social distancing, and movement restrictions preventing attendance to in- or outpatient PR programmes, traditional face-to-face rehabilitation needs to be adapted through the use of tele-rehabilitation.[114,120–122] It has been shown that tele-rehabilitation is as effective as traditional PR, and could alleviate burden on health systems.[123] However, PR programmes should have a plan to work with a limited rehabilitation team.[114] In a Northern Italian rehabilitation hospital, organizational changes were required to overcome work overload during COVID-19 pandemic. Remodelled tasks, development of algorithms on patient management, and use of online communications systems helped to relieve the workload.[124]

Research priorities for the future

There is obviously a strong need for extensive research on the epidemiology, assessment and management of both PTLD and post-COVID in adults and children to gain a better understanding on the two diseases and to guide the development of future standards and guidelines. Political commitment and appropriate funding mechanisms will be essential to enable research in these fields in the forthcoming years. Key research priorities are highlighted in Table 3.

Among others, the priority studies needed to respond the main research questions include cohort, case–control, cross-sectional, diagnostic accuracy and operational research studies, as well as randomized controlled trials.

Conclusions

Several patients continue to require care after completing TB treatment or after recovering from acute COVID.[1,32–34,125,126] There is increasing evidence on the PR interventions useful for PTLD; however, full implementation of these programmes is still lagging behind. Beyond implementing what is already acknowledged as effective, there is currently a strong need to investigate additional PR interventions in PTLD and to accumulate the increasing evidence on approaches to PR in post-COVID disease. Research priorities set to improve our understanding of the measures that will prove to be most effective (and cost-effective) to prevent, detect and treat PTLD and post-COVID are listed in this scoping review. Since the evidence currently available is modest, periodical evaluation on PR in these two conditions is mandatory to guide clinicians, TB programme managers and public health officers towards evidence-based planning and implementation of adequate measures to assess and manage them.

Conflict of interest

The authors declare that they have no conflict of interest.

Appendix A Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.arbres.2022.05.010.

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