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# Long-term monitoring of patients with fibrotic interstitial lung disease: A Canadian Thoracic Society Position Statement

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**ABSTRACT**

Longitudinal monitoring of patients with fibrotic interstitial lung disease (ILD) is essential to identifying disease progression and guiding management decisions. There are no evidence-based clinical practice guidelines to inform decision-making for the appropriate components and frequency of monitoring patients with fibrotic ILD. This position statement summarizes the key components of long-term monitoring of fibrotic ILD, including the appropriate frequency of monitoring, specific symptoms and comorbidities to consider, and the objective testing that should be routinely performed. Key messages based on scientific literature review and consensus from a panel of ILD experts are provided to guide clinical practice.

**RÉSUMÉ**

La surveillance longitudinale des patients atteints de fibrose pulmonaire interstitielle est essentielle pour déterminer la progression de la maladie et guider les décisions de prise en charge. Il n'existe pas de lignes directrices de pratique clinique fondées sur des données probantes pour éclairer la prise de décision concernant les composantes et la fréquence de la surveillance appropriées des patients atteints de fibrose pulmonaire interstitielle. Cet énoncé de position résume les éléments clés de la surveillance fibrose pulmonaire interstitielle à long terme, y compris la fréquence appropriée de la surveillance, les symptômes particuliers et les comorbidités à tenir en compte, ainsi que les tests objectifs qui devraient être effectués en routine. Des messages clés fondés sur une revue de la littérature scientifique et le consensus d'un panel d'experts en fibrose pulmonaire interstitielle sont présentés pour guider la pratique clinique.

## Introduction

Fibrotic interstitial lung diseases (ILDs) are a heterogeneous group of disorders that can be related to underlying connective tissue disease (CTD), occupational or environmental exposures or an unknown cause. They are characterized by fibrosis of lung interstitium, progressive dyspnea, worsening lung function and poor prognosis.[1] Canadian Thoracic Society (CTS) Position Statements have been recently published on the diagnosis and management of fibrotic ILDs.[2,3]

Longitudinal monitoring of patients with fibrotic ILD is essential for identifying disease progression and guiding management decisions. There are no evidence-based clinical practice guidelines to inform decision-making for the appropriate components and frequency of monitoring patients with fibrotic ILD. The aim of this position paper is to provide evidence-based recommendations on the key components of long-term monitoring for the fibrotic ILD patient, and where evidence is lacking, to provide consensus expert opinions.

## Objectives

1. To summarize the current evidence on long-term monitoring of patients with fibrotic ILD.
2. To provide evidence-based or expert consensus recommendations for the long-term monitoring of patients with fibrotic ILD.

## Methods

### *Working group composition*

A working group of respirologists with expertise in the field of ILD was created within the CTS ILD Clinical Assembly.

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Two co-chairs (JHF and MK) selected committee members with the intent to represent the diversity of gender, geography, experience and expertise among Canadian ILD respirologists. Areas of expertise represented include general ILD, connective tissue disease, lung transplantation, occupational lung disease, clinical epidemiology and basic science. The primary target audiences for this statement include respirologists, internists, primary care physicians and allied-health care practitioners caring for patients with fibrotic ILD. Secondary target audiences include patients with fibrotic ILD, caregivers and advocates, and those making health policy decisions regarding fibrotic ILD.

### Literature search, evidence appraisal, and recommendations

This document was developed in accordance with the CTS requirements for a position statement (https://cts-sct.ca/guideline-library) and using the AGREE II checklist for guidance.[4] Eight questions regarding the long-term management of fibrotic ILD were selected by consensus using group discussion amongst the above described working group. Topics were chosen based on members' knowledge of the literature and gaps in existing guidance and prioritized according to clinical relevance and the lack of already available evidence-based recommendations. Each question was then formulated in the PICO (problem/population, intervention, comparison, outcome) format, where applicable, by the co-chairs with the final questions approved by all coauthors. Based on expertise, groups of coauthors were assigned to summarize the scientific literature for each PICO question using keyword searches, supplemented by manual search of bibliographies of identified literature. When formulating recommendations, given the lack of available evidence in most areas, committee members were surveyed to obtain expert opinions for some key questions, including the frequency of clinic visits, symptom monitoring and appropriate testing and frequency (Online Supplemental Table 1). Consensus was reached through teleconference and email correspondence and all authors agreed with the key messages presented in the following sections.

### Position statement review

In accordance with the CTS Guideline Production Methodology (https://cts-sct.ca/guideline-library), this position statement underwent an external review. External review was conducted by a national and an international ILD expert who were independently invited by the CTS to review this position statement. Each expert provided a detailed review and suggestions, and authors responded to these reviews in detail. Internal review was conducted by 3 members of the CTS Canadian Respiratory Guidelines Committee, who provided further feedback for consideration by authors. Original reviews and responses to reviews are posted along with the position statement and all authors' conflicts of interest at (https://cts-sct.ca/guideline-library). The CTS Executive approved the final document for publication.

### Updating this statement

In accordance with the CTS Living Guideline Model (https://cts-sct/guideline-library/methodology), this document will be regularly reviewed and updated as necessary. Reviews will occur at a minimum of every 3 years by members of the CTS ILD Clinical Assembly.

## Summary of evidence and key messages

### Monitoring of fibrotic ILD

**Q1. How often should patients with fibrotic ILD be assessed in a respirology clinic in order to optimize care?**

Most patients with fibrotic ILD should be regularly assessed in a respirology clinic to monitor and manage symptoms, disease progression, treatment side effects and development of comorbidities. Clinic visits facilitate decision-making surrounding initiation, alteration or discontinuation of ILD-targeted medications. Patients should also be assessed regularly to identify the need for lung transplant referral, and end-of-life planning. No literature evidence or clinical practice guidelines were identified in order to inform the appropriate frequency of routine clinic visits, and thus our recommendations are primarily based on expert consensus.

We recommend that patients with fibrotic ILD should typically be assessed at intervals of 3 to 6 months, depending on disease severity and rate of progression. More frequent monitoring may be required around the time of diagnosis and for individuals with disease progression or who are at high risk for progression. Risk factors for disease progression include older age, male sex, lower baseline forced vital capacity (FVC) and diffusing capacity (DLCO) and a usual interstitial pneumonia (UIP) pattern on chest computed tomography (CT).[5–9] Less frequent monitoring is often appropriate for those patients with a high likelihood of stability, such as those with mild and longstanding disease. Given the variability in disease behavior, the availability of an expedited clinical assessment for fibrotic ILD patients is ideal in the event of worsening symptoms. A shared-care model between ILD centers and local respirologists may provide faster access to appropriate expertise. Routine assessment by a general internist may be required for those patients without access to a respirologist.

**Monitoring of fibrotic ILD**

**Q1. How often should patients with fibrotic ILD be assessed in a respirology clinic in order to optimize care?**

**Key Messages:**

- We suggest that patients with fibrotic ILD should typically be monitored by a respirologist every 3-6 months, with less frequent monitoring appropriate in patients with mild and/or stable disease.
- We suggest alternating clinic visits with local respirologists or internists for those patients followed in ILD centers in a shared-care model, in order to facilitate timely patient care and efficient use of tertiary and quaternary care resources.

**Q2. In patients with fibrotic ILD, which symptoms should be routinely monitored in order to optimally assess disease progression, medication side effects, comorbidities and quality of life?**

At each visit, the severity of dyspnea and cough, functional capacity, and quality of life should be assessed in

patients with fibrotic ILD. Worsening dyspnea and exercise limitation are key markers of disease progression and important risk factors for mortality.[10–12] The optimal methods of measuring dyspnea and functional capacity are not known, with practical options including qualitative assessment based on clinical history or simple tools such as the Medical Research Council breathlessness scale.[13] Cough is associated with disease progression and worse quality of life, and may predict time to death or lung transplantation in patients with fibrotic ILD.[14–16] A qualitative approach to assessing cough severity and frequency is most practical in the clinic setting, with cough questionnaires not commonly used outside of a research environment. Similarly, the use of detailed quality of life questionnaires, such as the St. George's Respiratory Questionnaire or King's Brief Interstitial Lung Disease questionnaire, have not been studied in the routine clinical setting. As a result, we recommend considering dyspnea and cough severity, functional capacity impairment and an individual patient's perceptions on their overall quality of life when making decisions surrounding symptom management, use of ILD-targeted medications, and timing of referral to palliative-care and/or lung transplant. Additional studies are needed to determine whether more detailed patient reported outcome measures have clinical utility.[17–19] The specific pharmacologic and nonpharmacologic components of fibrotic ILD management are addressed in a separate CTS position paper.[3]

In those patients with fibrotic ILD receiving treatment with antifibrotic or immunosuppressive medications, routine symptom monitoring should include assessment of medication tolerability, side effects and complications. The symptoms are therapy-specific but can include nausea, vomiting, diarrhea, fatigue, weight loss, (pirfenidone, nintedanib and some steroid sparing medications, such as, azathioprine, cyclophosphamide and mycophenolate) and complications such as infections (immunosuppressants such as prednisone and steroid sparing medications).

Assessment of additional symptoms should be considered at each clinic visit on an individualized basis. These may include alternative contributors to dyspnea and cough (e.g., infection, coronary artery disease (CAD), pulmonary vascular disease (PVD), heart failure, gastroesophageal reflux disease (GERD)), potential clues to the etiology of ILD (e.g., environmental triggers, CTD symptoms) and features of other common comorbidities. Comorbid conditions such as CAD, GERD, depression and anxiety are common in patients with fibrotic ILD, with as many as 30% of idiopathic pulmonary fibrosis (IPF) patients having 4 or more comorbidities[20–24] The role of screening for PVD, lung cancer and obstructive sleep apnea (OSA) in patients with fibrotic ILD is discussed later in this document.

**Monitoring of fibrotic ILD**

**Q2. In patients with fibrotic ILD, which symptoms should be routinely monitored in order to optimally assess disease progression, medication side effects, comorbidities and quality of life?**

**Key messages:**

- In patients with fibrotic ILD, we suggest that clinicians monitor symptoms routinely, including qualitatively assessing dyspnea, cough, functional capacity and quality of life.
- In patients with fibrotic ILD on medical therapy, we suggest that clinicians routinely screen for medication side effects and tolerability.
- In patients with fibrotic ILD, we suggest that clinicians consider the potential contribution of comorbidities, given the high prevalence of coronary artery disease, pulmonary vascular disease, gastroesophageal reflux disease, depression and anxiety in this population.

(*continued*)

**Q3. What testing should be performed for routine monitoring of patients with fibrotic ILD in order to detect disease progression?**

We recommend routine testing of forced vital capacity (FVC) and diffusing capacity (DLCO) every 3 to 6 months to monitor for disease progression given their strong association with symptoms and mortality, frequent use as clinical trial endpoints, and mandated reporting for reimbursement of some ILD medications. We recommend six-minute walk test (6MWT) or walking oximetry be performed at 6–12-month intervals, although testing frequency will vary depending on availability, disease severity, and rate of progression.

We recommend performing chest computed tomography (CT) periodically in order to monitor for disease progression and assist with decision making surrounding treatment initiation or intensification, usually at intervals of 2 to 3 years in otherwise stable patients with no evidence of symptom or pulmonary function worsening. We do not recommend routine echocardiography for the majority of fibrotic ILD subtypes outside the setting of a suspicion of pulmonary hypertension (PH) and/or suspected cardiac dysfunction. Existing clinical practice guidelines recommend regular screening echocardiography in ILD patients at high risk of developing PH (e.g., annually in systemic sclerosis) and during lung transplant evaluation. Repeat autoimmune serology testing is suggested for patients with previously negative serology in the setting of new features suggestive of CTD. Treatment-specific monitoring is required for many ILD medications. For example, antifibrotic medications require regular testing of hepatic function. Several immunosuppressant medications (e.g., azathioprine, mycophenolate, cyclophosphamide) also require routine laboratory monitoring which often includes complete blood count, renal (creatinine) and hepatic function tests (alanine aminotransferase, alkaline phosphatase, gamma-glutamyl-transferase, bilirubin).

**Monitoring of fibrotic ILD**

**Q3. What testing should be performed for routine monitoring of patients with fibrotic ILD in order to detect disease progression?**

**Key messages:**

- In patients with fibrotic ILD, we suggest that clinicians measure FVC and DLCO regularly, typically every 3 to 6 months, but less frequent testing may be appropriate in patients with either mild disease or demonstrated stability.
- In patients with fibrotic ILD, we suggest that clinicians measure 6MWT or walking oximetry regularly, typically every 6 to 12 months, although testing frequency varies depending on local availability, disease severity and rate of progression.
- In patients with fibrotic ILD, we suggest that clinicians consider follow-up chest computed tomography, every 2 to 3 years to assess for disease progression in otherwise stable patients.
- In patients with fibrotic ILD, we do not recommend screening echocardiography except in patients at high risk for pulmonary hypertension or undergoing lung transplant evaluation.
- In patients with fibrotic ILD, we do not recommend repeat autoimmune serology once negative, unless there are features suggestive of a connective tissue disease.

**Q4. How should disease progression be defined in patients with fibrotic ILD in order to guide management decision making?**

Recognizing disease progression in patients with fibrotic ILD is essential to guide management and prognostication. Progression can be identified based on worse symptoms or functional capacity, worsening physiologic testing or chest imaging and/or the occurrence of adverse clinical outcomes such as respiratory hospitalization or death. The majority of data defining disease progression come from studies of patients with IPF which may not be applicable to non-IPF fibrotic ILDs. No single variable performs ideally to define progression, and the most accurate determination of disease progression is achieved from composite outcomes that include symptoms, physiology, imaging, and event-driven endpoints (e.g., hospitalization).

Change in FVC remains the most commonly recommended marker of disease progression, with numerous studies confirming that a relative or absolute 10% decline over 6 to 12 months independently predicts mortality.[10,25–30] The minimal important difference (MID) in FVC is estimated at 2–6% in IPF.[31] DLCO can be influenced by multiple factors and is thus not an ideal single measure of ILD progression;[10,25,32] however, DLCO is strongly and independently associated with mortality, suggesting that there is clinical utility to its routine measurement.[10,32] Patients with combined pulmonary fibrosis and emphysema have a relatively preserved FVC that typically declines at a slower pace than in fibrotic ILD patients without emphysema, making FVC a less reliable measure of disease progression in this sub-population.[33–36] Additional monitoring modalities, such as chest CT are often required to assess disease progression in these patients.

The 6MWT is a simple, reliable, and valid tool for assessing functional capacity in patients with fibrotic ILD, providing valuable information on disease status and clinical deterioration.[37] Baseline 6-minute walk distance (6MWD) and the change over 6 and 12 months are independent predictors of mortality in IPF.[38,39] A $>50$ m decline in 6MWD over 24 weeks is associated with a 2-3x increased risk of death.[40,41] A nadir peripheral oxygen saturation $\leq$88% during a 6MWT is associated with increased mortality, suggesting that development of exertional hypoxemia is an important indicator of disease progression in fibrotic ILD.[42] The MID of the 6MWD in IPF ranges from 22 to 45 m.[39,40,43–46] In patients with CTD-related fibrotic ILD, the utility of the 6MWT may be limited by extrapulmonary issues, such as arthritis and/or myopathy.

Longitudinal radiographic evaluation of patients with fibrotic ILD is less established for detecting disease progression.[47,48] Plain radiography has insufficient sensitivity to demonstrate subtle disease progression. Frequent use of CT is limited by the current radiation dose, but can be done every few years to confirm or exclude the presence of disease progression in patients with otherwise stable metrics.

Recent clinical trials in non-IPF fibrotic ILD have defined progressive disease based on a single parameter or a combination of the following: worsening respiratory symptoms, lung function decline and worsening fibrosis on chest imaging.[49,50] Additional research is needed to evaluate the role of this definition in routine clinical practice.

Data which were derived from large cohorts studied under very standardized research settings can be challenging to apply to an individual in the clinic. An isolated worsening of one feature (e.g., 10% decline in FVC, 15% decline in DLCO, 50 m decline in 6MWD) may herald an important clinical change, but should be repeated and confirmed by a second observation. Smaller changes should similarly be corroborated with other measures or prompt a short-interval ($\leq$ 3 months) reassessment. In patients with uncertain evidence of progression, alternate etiologies of worsening (e.g., respiratory muscle weakness) should be excluded prior to making major treatment decisions.

**Monitoring of fibrotic ILD**

**Q4. How should disease progression be defined in patients with fibrotic ILD in order to guide management decision making?**

**Key Messages:**

- In order to identify disease progression in patients with fibrotic ILD, we suggest that clinicians integrate multiple parameters, including symptoms, physiological measurements and radiological findings.
- In patients with fibrotic ILD, we suggest that clinicians contextualize worsening in a single domain (or measure) with other domains and/or repeat measurements in the short-term ($\leq$ 3 months) to confirm evidence of disease progression.

## *Treatment decisions*

**Q5. How should disease progression influence the decision to start, stop or change medications in patients with fibrotic ILD?**

Pharmacotherapy aimed at stabilizing or slowing the decline in lung function and the evidence supporting those treatments are summarized in the previous CTS position paper on the comprehensive management of ILD.[3] Initiation of anti-fibrotic therapy should be considered in all treatment-naïve patients with IPF, but may not be appropriate in some situations. In patients who continue to progress despite the use of medication, it can be difficult to establish if patients are "failing" on current therapy or if their observed progression has been attenuated from an even more rapid course that would have occurred without therapy. This poses significant challenges to clinicians who struggle to decide if therapy should be continued, modified or discontinued in the setting of disease progression.

A post-hoc analysis of patients who had a $\geq$10% decline in FVC in the pirfenidone and placebo arms of the ASCEND and CAPACITY studies, found continued pirfenidone treatment was associated with a lower risk of FVC decline $\geq$ 10% or death in the subsequent 6 months as compared to placebo (5.9% vs. 27.9%, relative difference 79.8%).[51] These results suggest it may be appropriate to continue therapy in some patients despite evidence of disease progression. In patients requiring discontinuation of their initial anti-fibrotic due to intolerability, many will be able to tolerate the alternative anti-fibrotic agent with subsequent stabilization of their lung function.[52] In patients with IPF who have had progression of their disease despite tolerating

moderate-to-high doses of their initial anti-fibrotic therapy for more than 6 months, switching from one medication to the other has never been assessed in a prospective randomized controlled trial, and thus very little is known about the efficacy of this strategy. Decisions about switching anti-fibrotic agents should be made on a case-by-case basis with a high priority placed on patient preferences regarding side effect profiles.

Trials of add-on (combination) anti-fibrotic therapy have demonstrated that adverse effects are additive, and although these may be acceptable to some patients, these trials were inadequately powered to demonstrate benefit.[53,54] Such studies are needed prior to endorsing the use of combination therapy outside of the clinical trial context. Currently, combination anti-fibrotic therapy is not approved in Canada.

Stopping anti-fibrotic therapy altogether may be appropriate in some cases, especially when patients have significant drug-induced adverse effects in the face of ongoing disease progression. There are rare reports of accelerated progression of IPF following discontinuation of anti-fibrotic medication,[55] although there are limited data on this possible phenomenon and this may be an acceptable risk if the primary goals of care are palliation of symptoms.

Many non-IPF fibrotic ILDs are progressive diseases that lead to worsening lung function, dyspnea, and quality of life. Some patient and disease-related characteristics such as age, sex, severity of lung function impairment, specific auto-antibody profiles and radiological/histopathological pattern can help predict prognosis.[7,56,57] Patients with a high risk of adverse outcome or clear evidence of progressive disease should be considered for early pharmacotherapy. Decisions regarding which therapy to use in which patient is often based on expert opinion rather than high-quality data. In the setting of clear disease progression on one treatment, switching or adding a medication is often considered. A multidisciplinary approach combining rheumatology and respirology specialists for patients with CTD-ILD is essential to ensure that the chosen medication regime is appropriate for both the pulmonary and extra-pulmonary manifestations of disease.[58]

**Treatment decisions**

**Q5. How should disease progression influence the decision to start, stop or change medications in patients with fibrotic ILD?**

**Key Messages:**

- In patients with IPF, we suggest that clinicians discuss initiation of an anti-fibrotic medication at the time of diagnosis and place a high priority on individual patient preference regarding risk of future disease progression (worsening) vs. side effect profile when making treatment decisions.
- In patients with IPF with disease progression on therapy, it is reasonable to either continue or switch antifibrotic medication. This decision should be made on an individual basis, placing a high priority on patient preferences regarding side effect profile. Add on or combination therapies may become an option in the future but are not yet established.
- In patients with IPF with disease progression on therapy, stopping antifibrotic therapy may be appropriate in the setting of significant side effects and/or when the primary goal is palliation of symptoms.
- Because there is a lack of robust data to guide the timing of initiation and choice of medications to treat non-IPF fibrotic ILD, we suggest that clinicians make pharmacotherapy decisions on an individual basis, considering disease severity and/or risk factors for progressive disease.
- In patients with CTD-ILD, we suggest that clinicians pursue a multidisciplinary approach involving rheumatology, when making treatment decisions.

## *Comorbidity screening*

**Q6. Should patients with fibrotic ILD be screened for pulmonary vascular disease in order to improve outcomes and assist with prognostication?**

According to data from a large United States medical claims database, patients with IPF are at a 7- and 16-fold increased risk of pulmonary embolism (PE) and PH, respectively, as compared to age and gender matched controls.[23] PE remains an important consideration in patients with an acute or subacute change in their respiratory status. The overall prevalence of PH among patients with advanced IPF primarily assessed in the tertiary care setting varies between 32% and 55%[59–63] in retrospective cohort data. Recognition of PH may be pertinent for prognostication of patients being considered for lung transplant given its association with increased mortality; however, we do not recommend routine screening echocardiography outside of these select populations.[64] Treatment of PH with targeted pulmonary arterial hypertension (PAH) therapies has not been proven effective or safe for patients with IPF. However, Canadian and international PH clinical practice guidelines recommend that selected patients with moderate-severe PH and/or right-ventricular failure in the setting of only mild-moderate fibrotic lung disease without significant hypoxemia should be referred to specialized PH clinics for further assessment of the cause of PH and potential therapeutic options.[65,66] Patients with certain CTDs, particularly systemic sclerosis, are at increased risk of PAH and annual screening with echocardiography is typically recommended for those with a DLCO <80%.[67]

**Comorbidity screening**

**Q6. Should patients with fibrotic ILD be screened for pulmonary vascular disease in order to improve outcomes and assist with prognostication?**

**Key messages:**

- Pulmonary embolism and pulmonary hypertension are recognized comorbidities in patients with fibrotic ILD and important considerations in the setting of acute or subacute respiratory deterioration in these patients.
- We suggest that clinicians refer patients with more than mild pulmonary hypertension and/or right ventricular failure with only mild-moderate fibrotic ILD to pulmonary hypertension clinics, particularly in the setting of CTD or other conditions associated with pulmonary arterial hypertension or chronic thromboembolic disease.
- Pulmonary hypertension is an important prognostic factor and may be relevant for patients being considered for lung transplant.

**Q7. Should lung cancer screening be routine in patients with fibrotic ILD?**

The cumulative incidence of lung cancer amongst patients with IPF is 3.3%, 15.4% and 52.7% after 1, 5 and 10 years follow-up.[68] Patients with IPF independently have a 4- to 5-fold increased risk of developing lung cancer compared to patients with emphysema[69] and matched controls in the general population.[70] Lung cancer risk appears to be highest in patients with combined pulmonary fibrosis and emphysema.[71] Lung cancer rates may also be increased in other fibrotic ILDs, although the evidence is less robust compared to IPF.[72–75] CTD patients on chronic immunosuppressive medications and recipients of solid organ transplant have a modestly increased

risk of malignancy[76,77] compared to the general population, and patients with fibrotic ILD on long term immunosuppressive agents likely have a similarly increased risk.

Lung cancer is associated with a particularly poor prognosis in fibrotic ILD. Patients with ILD and lung cancer have decreased survival compared to those with lung cancer alone, after adjusting for various factors, including age, sex, performance status, cancer type and smoking status.[78,79] In addition, the treatment of lung cancer in patients with fibrotic ILD is associated with increased risk of radiation pneumonitis, chemotherapy related toxicity and surgical complications,[72] although select early stage cancers may benefit from surgical management.[80] In theory, screening fibrotic ILD patients for lung cancer could identify early-stage malignancy that has more therapeutic options, such as minimally invasive surgical procedures or stereotactic body radiotherapy, given the challenges in managing these patients. More data are needed to test this possibility and to identify which patients might be most appropriate to screen. International IPF guidelines state the role of lung cancer screening in the setting of IPF remains unknown.[81]

**Comorbidity screening**

**Q7. Should lung cancer screening be routine in patients with fibrotic ILD?**

**Key message:**

- In patients with fibrotic ILD, we do not currently recommend annual lung cancer screening. Evidence regarding lung cancer screening in fibrotic ILD is urgently needed.

**Q8. Should obstructive sleep apnea screening be routine in patients with fibrotic ILD?**

Small retrospective studies have suggested that OSA is common in patients with ILD, although the majority of data available is for IPF and prevalence estimates have varied widely (from 5.9% to 88%) depending on the population and number of years studied.[23,82–86] IPF patients with OSA typically do not endorse excessive daytime sleepiness making widely available screening tools such as the Epworth Sleepiness Scale and STOP-BANG score less helpful in this subgroup.[87–90] Fibrotic ILD patients experience poor sleep quality with abnormal sleep architecture and nocturnal hypoxemia,[85,91,92] that is associated with fatigue, reduced quality of life, new or worsening PH and increased mortality.[85,90,93] The presence of OSA with nocturnal hypoxia has also been associated with IPF related morbidity and mortality, although the direction of association is unknown and requires further study.[83]

Limited evidence in highly selected populations suggests that initiation of continuous positive airway pressure (CPAP) therapy for IPF patients with moderate to severe OSA may improve quality of life, although patients may require additional support to ensure adherence to therapy.[87,94,95] Screening fibrotic ILD patients for OSA would conceivably allow for earlier identification of a potentially treatable comorbidity; however, more data are required to demonstrate any utility of such an approach. Maintaining a high index of suspicion for OSA in this population is reasonable, giving that patients with fibrotic ILD may not report the typical symptoms of excessive daytime sleepiness.

**Comorbidity screening**

**Q8. Should obstructive sleep apnea screening be routine in patients with fibrotic ILD?**

**Key message:**

- Common screening tools for obstructive sleep apnea have limited utility in patients with fibrotic ILD.
- Maintaining a high index of suspicion for obstructive sleep apnea in patients with fibrotic ILD is reasonable and we suggest that clinicians order additional testing with overnight oximetry and/or polysomnography in patients in whom obstructive sleep apnea is suspected.

## Conclusions

Longitudinal monitoring of patients with fibrotic ILD is essential for identifying disease progression and guiding management decisions. Key components of monitoring include assessment of symptoms, functional capacity, physiology, radiology and disease- and treatment-related comorbidities. We advocate for a multidisciplinary and collaborative approach to patient care when feasible that may include ILD clinicians, community respirologists or internists, primary care physicians and other relevant subspecialties. Additional studies are needed to generate ILD-specific data that will inform the ideal screening approach for common comorbidities of ILD.

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## Editorial independence

The CTS ILD Assembly is accountable to the CTS CRGC and the CTS Board of Directors. The CTS ILD Assembly is functionally and editorially independent from any funding sources of the CTS and does not receive any direct funding from external sources. The CTS receives unrestricted grants that are combined into a central operating account to facilitate the knowledge translation activities of the CTS Assemblies. No funders played a role in the collection, review, analysis or interpretation of the scientific literature or in any decisions regarding the key messages presented in this document.

## Disclosure statement

Members of the CTS ILD Assembly declared potential conflicts of interest at the time of appointment and these were updated throughout the process in accordance with the CTS Conflict of Interest Disclosure Policy. Individual member conflict of interest statements are posted at https://cts-sct.ca/guideline-library/.

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