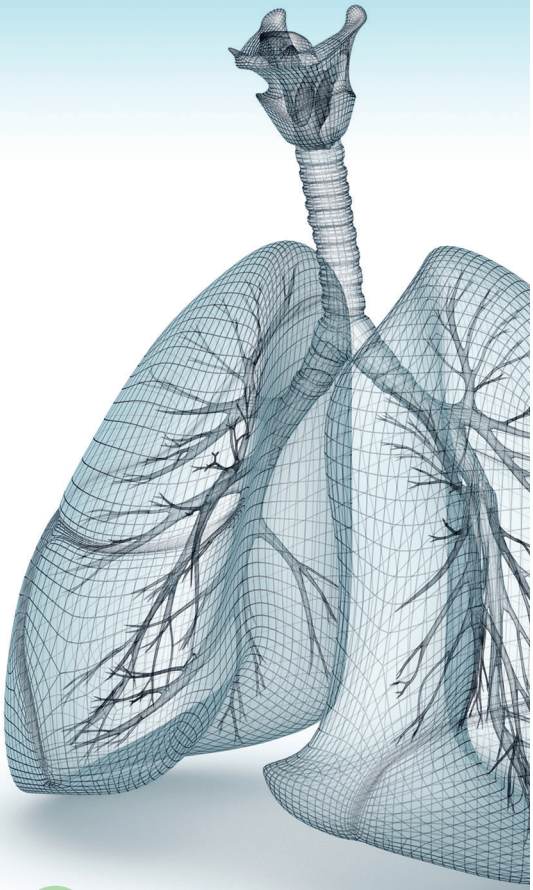
Sjögren's Foundation Clinical Practice Guidelines



Sjögren's FOUNDATION

Pulmonary Manifestations in Sjögren's

Pulmonary complications occur much more frequently in Sjögren's than is often recognized by healthcare providers and are a potentially serious complication of Sjögren's. Clinical practice guidelines for pulmonary manifestations in Sjögren's were developed under the leadership of the Sjögren's Foundation to improve early identification, evaluation and consistency of care by primary care physicians, rheumatologists and pulmonologists. Of note:

- Approximately 16% of Sjögren's patients demonstrate pulmonary complications with increased mortality and lower quality of life. This figure may be low due to gaps in awareness and education.
- In all, 52 recommendations are provided for patient evaluation (by rheumatologists and primary care physicians for pulmonary symptoms and by pulmonologists for potential Sjögren's), airways disorders, interstitial lung disease (ILD) and lymphoproliferative disease.
- As many as 65% of asymptomatic Sjögren's patients will have abnormal pulmonary imaging, highlighting the need for awareness of pulmonary manifestations in Sjögren's.
- A baseline chest x-ray should be considered for all Sjögren's patients, and if concern is high for lung involvement, a high-resolution computerized tomography (HRCT) scan may be preferred.
- Airway disorders in Sjögren's are associated with a wide range of symptoms, including a dry nonproductive cough, dry trachea, reflux, vocal cord lesions, bronchiectasis (characterized by narrowed airways) and respiratory inflammation.
- Nearly 40% of Sjögren's patients will have a chronic cough, which should be investigated and the cause identified.
- ILD symptoms can include shortness of breath, cough, sputum production or chest pain. Onset of ILD in Sjögren's may increase with time following diagnosis of Sjögren's.
- Approximately 6% of Sjögren's-associated lymphomas may directly involve the lungs.
- A multidisciplinary approach for pulmonary complications is encouraged and should include a rheumatologist, primary care physician, pulmonologist, pathologist, radiologist, and, when appropriate, an oncologist.

Recommendations for Patient Evaluation

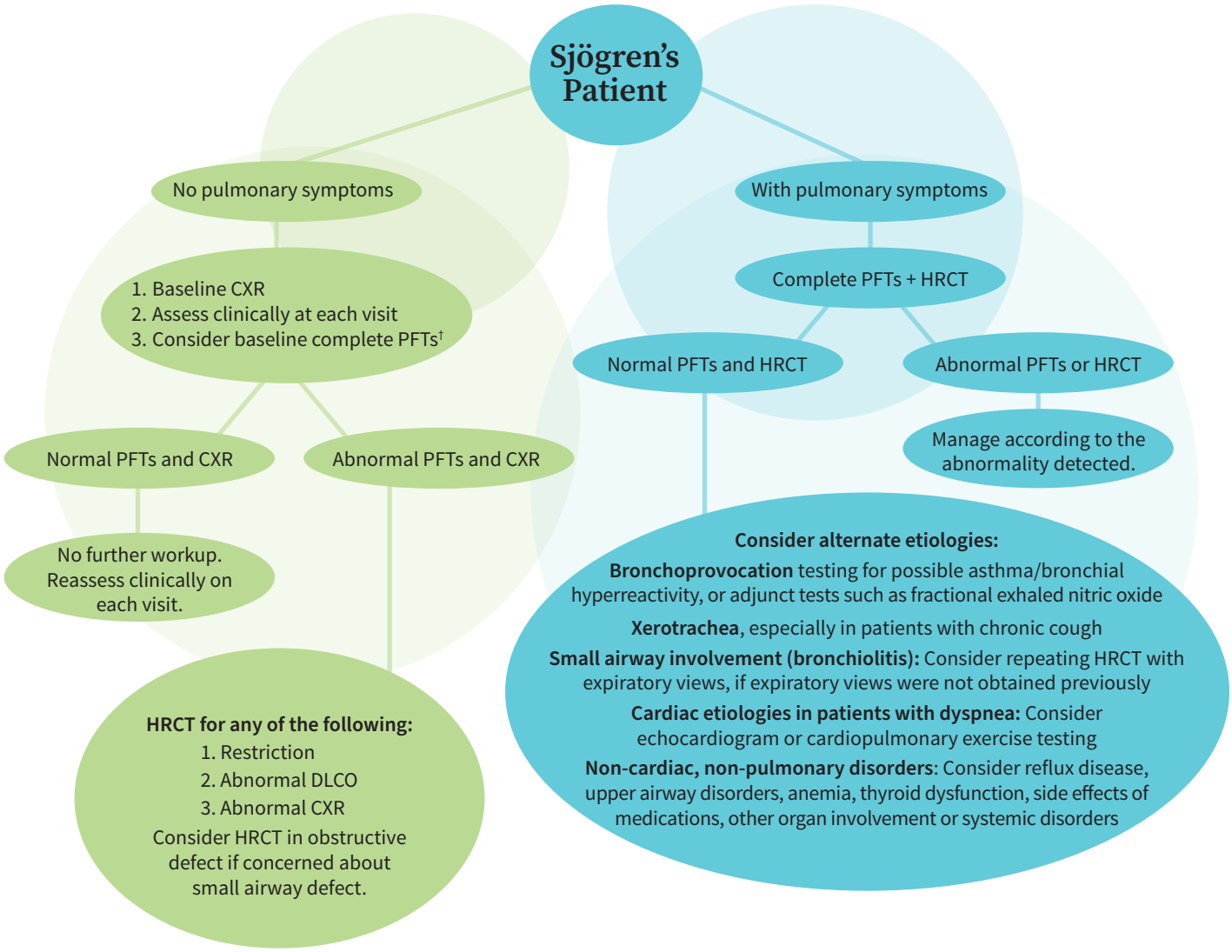
Evaluating Asymptomatic Sjögren's Patients for Pulmonary Complications	Strength of Evidence	Strength of Recommendation
1. Serologic biomarkers must not be employed to evaluate for pulmonary involvement in patients with established Sjögren's disease.	INTERMEDIATE	STRONG
2. Due to the prevalence of respiratory involvement in Sjögren's, clinicians must obtain a detailed medical history inquiring about respiratory symptoms in all Sjögren's patients at the initial and every subsequent visit.	HIGH	STRONG
3. In Sjögren's patients without respiratory symptoms, a baseline two-view chest x-ray (CXR) may be performed. The baseline chest radiograph can 1) help identify pulmonary involvement despite the absence of symptoms, 2) identify alternate etiologies of sicca symptoms such as sarcoidosis, vasculitis and lymphoma, and 3) serve as a baseline for future comparisons.	INTERMEDIATE	WEAK
4. In Sjögren's patients who have no respiratory symptoms, baseline complete pulmonary function tests (PFTs) may be considered to evaluate for the presence of underlying pulmonary manifestations. PFTs should include pre- and post-bronchodilator spirometry, lung volumes, and diffusing capacity of the lung for carbon monoxide (DLCO). Abnormalities identified may require further corroboration with advanced testing.	INTERMEDIATE	WEAK
5. In asymptomatic Sjögren's patients, routine echocardiogram is not recommended.	INTERMEDIATE	STRONG

Evaluating Sjögren's Patients with Pulmonary Symptoms	Strength of Evidence	Strength of Recommendation
1A. In Sjögren's patients with chronic cough and/or dyspnea, complete PFTs and HRCT should be done to evaluate for pulmonary involvement.	INTERMEDIATE	MODERATE
1B. In a Sjögren's patient with respiratory symptoms, the interval for repeat HRCT and PFTs must be determined on a case-by-case basis and individualized according to the nature and severity of the underlying pulmonary abnormality and the degree of symptoms and functional impairment.	INSUFFICIENT	STRONG
2. In a Sjögren's patient with dyspnea, an echocardiogram is recommended in the following circumstances: • In patients with suspected pulmonary hypertension (PH) • In patients with unexplained dyspnea after pulmonary etiologies (asthma, small airways disease, bronchiectasis, ILD) have been excluded • In patients with suspected cardiac involvement	HIGH	STRONG
3. In a Sjögren's patient with respiratory symptoms, a computed tomography pulmonary angiogram (CTPA) to look for pulmonary embolism must not be performed routinely in all patients but rather dictated by clinical suspicion for pulmonary embolism in individual circumstances. If clinically concerned about a pulmonary embolism, CTPA is the confirmatory test of choice. Ventilation-perfusion (VQ) scan should only be considered in the following circumstances: • To rule out chronic thromboembolic pulmonary hypertension (CTEPH) in patients with PH • When clinical concern for pulmonary embolism exists, and a physician is unable to do a CTPA because of patient allergy to contrast or renal insufficiency	LOW	STRONG

Evaluating for Sjögren's in Patients with Lung Disease	Strength of Evidence	Strength of Recommendation
1. In patients who have an uncharacterized ILD, diffuse cystic lung disease (DCLD) or pulmonary lymphoma, clinical and serologic evaluation for Sjögren's is recommended.	HIGH	STRONG

Use of Bronchoscopy	Strength of Evidence	Strength of Recommendation
1. In a Sjögren's patient with respiratory symptoms, bronchoscopy with bronchoalveolar lavage (BAL) must not be performed routinely but determined on a case-by-case basis and limited to special circumstances, such as the need to: 1) Rule out infectious etiologies, especially in patients on immune suppression 2) Rule out endobronchial abnormalities such as amyloidosis in patients with chronic cough not otherwise responsive to treatment 3) Distinguish between other etiologies of sicca symptoms such as sarcoidosis	**LOW**	**STRONG**
2. In a Sjögren's patient with respiratory symptoms, use of bronchoscopy with endobronchial biopsies and transbronchial lung biopsy are not recommended for routine use.	**INSUFFICIENT**	**STRONG**

Figure 1:
Respiratory Evaluation for Sjögren's Patients



† The benefit of obtaining baseline PFTs in asymptomatic Sjögren's patients with regards to long-term outcomes is not clear. This paucity of evidence and potential costs of the test should be taken into account and discussed with individual patients prior to proceeding with PFTs.

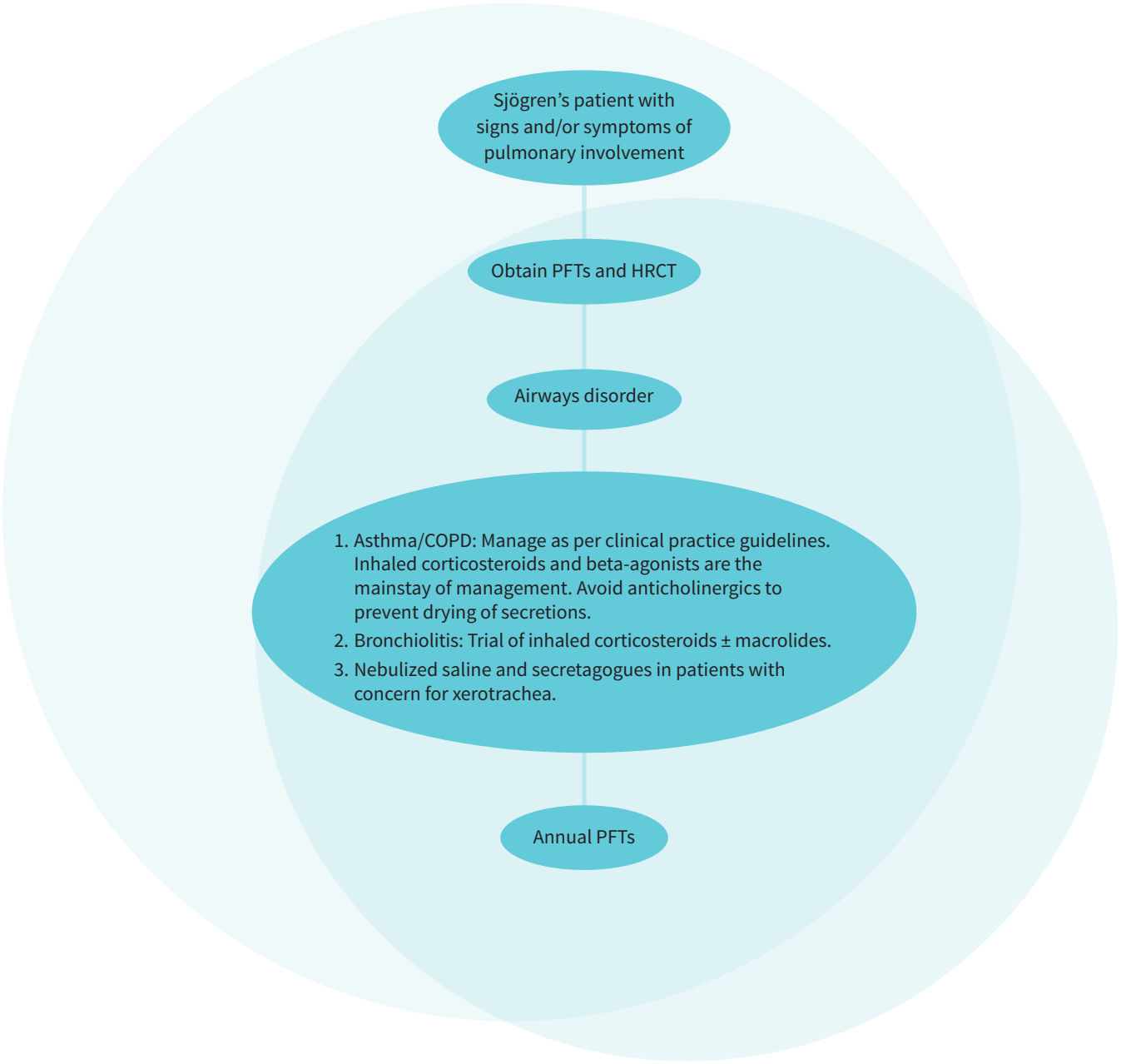
Complete PFTs includes spirometry, DLCO, lung volumes, ideally measured by body plethysmography

Abbreviations: CXR = chest x-ray; HRCT = high-resolution computed tomography; PFTs = pulmonary function tests; DLCO = diffusing capacity of lung for carbon monoxide

Recommendations for Assessment and Management of Upper and Lower Airway Disease in Sjögren's Patients

Assessment and Management of Upper and Lower Airway Disease in Sjögren's Patients	Strength of Evidence	Strength of Recommendation
1. In Sjögren's patients with symptomatic vocal cord cystic lesions ('bamboo nodules'), less aggressive interventions including voice therapy, inhaled corticosteroids or intralesional corticosteroid injection, should be tried first. Surgical resection should be considered if initial measures fail, with consultation by a laryngologist with experience in Sjögren's.	LOW	MODERATE
2. Sjögren's patients with dry bothersome cough and documented absence of lower airway or parenchymal lung disease must be assessed for treatable or preventable etiologies other than xerotrachea, including gastroesophageal reflux, post-nasal drip and asthma.	INTERMEDIATE	STRONG
3. In a Sjögren's patient with dry, nonproductive cough, humidification, secretagogues and guaifenesin may be empirically initiated after exclusion of other causes.	INSUFFICIENT	WEAK
4. The use of humidification for improving positive airway pressure (PAP) tolerance and compliance may be recommended in Sjögren's patients.	INSUFFICIENT	WEAK
5. Smoking cessation is recommended in all Sjögren's patients.	INTERMEDIATE	STRONG
6A. In Sjögren's patients with symptomatic small airway disease, bronchoscopic biopsy is not recommended as part of routine assessment or evaluation.	INSUFFICIENT	STRONG
6B. In Sjögren's patients with symptomatic small airway disease, complete pulmonary function testing must be performed to assess severity of small airways disease, and HRCT imaging with additional expiratory views can be helpful in suggesting its presence.	INSUFFICIENT	STRONG
7. In Sjögren's patients with small airways disease, time-limited empiric therapy in newly diagnosed and previously untreated disease may include: • A short course of systemic steroids for 2-4 weeks with a repeat spirometry to determine reversibility, especially if uncontrolled asthma is suspected • Nebulized or inhaled short or long-acting bronchodilators and/or inhaled corticosteroids if there is physiologic obstruction • Short course (i.e. 2-3 months) of empiric macrolide antibiotics (most commonly azithromycin 250mg three days a week) for persistent, non-reversible, symptomatic bronchiolitis	LOW	WEAK
8. It is recommended that Sjögren's patients with clinically relevant bronchiectasis be treated similarly to those with primary or secondary bronchiectasis of other etiologies and may include any of the following: • Mucolytic agents/expectorants • Nebulized saline or hypertonic saline • Oscillatory positive expiratory pressure (PEP) • Postural drainage • Mechanical high frequency chest wall oscillation (HFCWO) therapies • Chronic macrolides in those without non-tuberculous mycobacterium (NTM) colonization or infection	LOW	STRONG

Figure 2:
Evaluation and Management of Sjögren's Patients Who Exhibit Symptoms and/or Physical Examination Signs of Airway Disorders



Abbreviations: CXR = chest x-ray; HRCT = high resolution computed tomography; PFTs = pulmonary function tests; DLCO = diffusing capacity of lung for carbon monoxide; COPD = chronic obstructive pulmonary disease

References

1. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): Guidelines for the diagnosis and management of asthma summary report 2007. *J Allergy Clin Immunol*. 2007 Nov;120(5 Suppl):594-138.
2. Quaseem A et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society, *Ann Intern Med*. 2011 Aug 2;155(3):179-91. doi: 10.7326/003-4819-155-3-201 108020-00008.

Recommendations for Interstitial Lung Disease (ILD) in Sjögren's

ILD: Diagnosis, Evaluation and Management	Strength of Evidence	Strength of Recommendation
1. In a Sjögren's patient with suspected ILD, an HRCT with expiratory views is recommended.	HIGH	STRONG
2. In a Sjögren's patient with suspected ILD, oximetry testing is recommended as part of a patient's initial evaluation.	HIGH	STRONG
3. Baseline pulmonary function tests (PFTs) must be performed in all Sjögren's patients with suspected or established ILD and followed initially at 3-6 month intervals for at least 1 year. Subsequent testing requires consideration of the type of ILD, the clinical course and the pace of change noted on the serial PFTs. The baseline PFTs should include lung volumes by body plethysmography, spirometry, diffusing capacity and oxygen saturations at rest and exercise.	LOW	STRONG
4. In a Sjögren's patient with ILD, a surgical lung biopsy is not routinely recommended. A lung biopsy may be considered following a multidisciplinary review where a biopsy may have significant management implications, such as in: • Neoplastic and non-neoplastic lymphoproliferative disorder • Other cancers • Amyloid • Progressive deterioration and a suspected infection failing empiric therapies where less invasive testing proved nondiagnostic	INTERMEDIATE	STRONG
5. If a Sjögren's-ILD patient is asymptomatic for lung disease or demonstrates minimal impairment on PFTs or HRCT, serial monitoring by PFTs is recommended every 3-6 months to establish disease trajectory and initiation of pharmacotherapy only if serial studies document a significant decline in lung function.	INTERMEDIATE	STRONG

Non-Pharmacological and Other Management	Strength of Evidence	Strength of Recommendation
1. **Vaccination:** All Sjögren's patients must be immunized against influenza and pneumococcal infection (Prevnar and Pneumovax) in accordance with U.S. Centers for Disease Control and Prevention (CDC) guidelines.	HIGH	STRONG
2. **Pneumothorax and Cystic Lung Disease:** Because a Sjögren's patient with cystic lung disease might have an increased risk of pneumothorax, patients and caregivers/family must be educated about signs and symptoms of pneumothorax and instructed to seek immediate medical attention if they experience signs or symptoms.	INTERMEDIATE	STRONG
3. **Pulmonary Rehab and ILD:** In a symptomatic Sjögren's patient with ILD and impaired pulmonary function, referral for pulmonary rehabilitation is recommended.	INTERMEDIATE	STRONG
4. **Oxygen and ILD:** In a Sjögren's patient with suspected ILD and clinically significant resting hypoxemia (defined by resting O_2 sat <88%, PaO_2 <55mm Hg or <60mm Hg with complication of chronic hypoxemia such as cor pulmonale), long-term oxygen therapy is recommended.	INTERMEDIATE	STRONG
5A. **Air Travel and ILD:** In a Sjögren's-ILD patient considering air travel, the need for supplemental oxygen should be evaluated by a physician.	INTERMEDIATE	MODERATE
5B. **Air Travel and ILD:** In a Sjögren's patient with ILD, discouraging air travel is not recommended unless the patient develops signs and symptoms of pneumothorax or new onset/unexplained chest pain or dyspnea prior to boarding.	INTERMEDIATE	STRONG
6. **Lung Transplant and ILD:** In a Sjögren's patient with ILD whose condition is advanced with resting hypoxia or whose lung function is rapidly deteriorating, lung transplant evaluation is recommended.	INTERMEDIATE	STRONG

ILD: Pharmacological Interventions	Strength of Evidence	Strength of Recommendation
1A. **Symptomatic/Moderate-Severe ILD – Systemic Corticosteroids:** In Sjögren's patients with symptomatic ILD with moderate-to-severe impairment on lung function, imaging or in gas-exchange and especially in organizing pneumonia (OP), systemic steroids should be considered as a first-line treatment at a dosage based on the clinical context and disease severity, with standard dosage being 0.5-1.0 mg/kg.	**INTERMEDIATE**	**MODERATE**
1B. **Cautions for Systemic Corticosteroids:** In a Sjögren's patient with ILD or related disorder and considering use of systemic steroids, patients and healthcare providers must be aware of the following risks/potential harms: **Potential short-term side effects:**† • Glucose intolerance • Avascular necrosis • Mineralocorticoid effect, leading to potential fluid retention and/or hypertension • Myopathy • Psychological, including hyperactivity, insomnia, psychosis • Pancreatitis • Hypertension • Truncal obesity • Acne • Hematopoietic, including leukocytosis • Ecchymosis • Acanthosis nigricans **Potential long-term side effects:** • Osteoporosis • Diabetes • Adrenal insufficiency • Gastrointestinal symptoms, including peptic ulcer, hepatic steatosis • Ophthalmological, including glaucoma, cataract • Hyperlipidemia • Congenital malformation in utero exposure (very rare) • Growth suppression (only in pediatrics)	**HIGH**	**STRONG**
2A. **Symptomatic/ Moderate-Severe ILD – Mycophenolate mofetil (MMF) or Azathioprine (AZA):** In a Sjögren's patient with symptomatic ILD with moderate to severe impairment as determined by lung function testing, imaging, or gas-exchange, mycophenolate mofetil (MMF) or azathioprine (AZA) should be considered when long-term steroid use is contemplated, and steroid-sparing immunosuppressive therapy is required.	**INTERMEDIATE**	**MODERATE**
2B. **Cautions for Azathioprine:** In a Sjögren's patient with ILD or related disorder and considering use of azathioprine (AZA), patients and healthcare providers must be aware of potential risks for drug-induced pneumonitis, gastrointestinal upset, hepatotoxicity, bone marrow suppression, rash and hypersensitivity syndrome. Testing for Thiopurine methyltransferase (TPMT) activity or genotype before initiating AZA is recommended to reduce the risk of severe, life-threatening leucopenia due to complete lack of TPMT activity.†	**HIGH**	**STRONG**
2C. **Cautions for Mycophenolate Mofetil (MMF):** In a Sjögren's patient with ILD or related disorder and considering use of mycophenolate mofetil (MMF), patients and healthcare providers must be aware of potential side effects, including nausea, diarrhea, hepatotoxicity and bone marrow suppression.†	**HIGH**	**STRONG**
3. **Symptomatic/ Moderate-Severe ILD – Maintenance therapies:** Following initial treatment for Sjögren's patients with ILD who are symptomatic and in whom PFTs or HRCT demonstrated moderate-severe impairment, first-line maintenance drugs should be either mycophenolate mofetil (MMF) or azathioprine (AZA).	**LOW**	**MODERATE**
4A. **Symptomatic/ Moderate-Severe ILD – Second-Line Therapies:** If initial treatment with mycophenolate mofetil (MMF) or azathioprine (AZA) is insufficient or not tolerated in Sjögren's patients with ILD who are symptomatic and in whom PFTs or HRCT demonstrated moderate-severe impairment, subsequent second line maintenance drugs may include rituximab (RTX) and calcineurin inhibitors, cyclosporine or tacrolimus.	**LOW**	**WEAK**

ILD: Pharmacological Interventions *(continued)*	Strength of Evidence	Strength of Recommendation

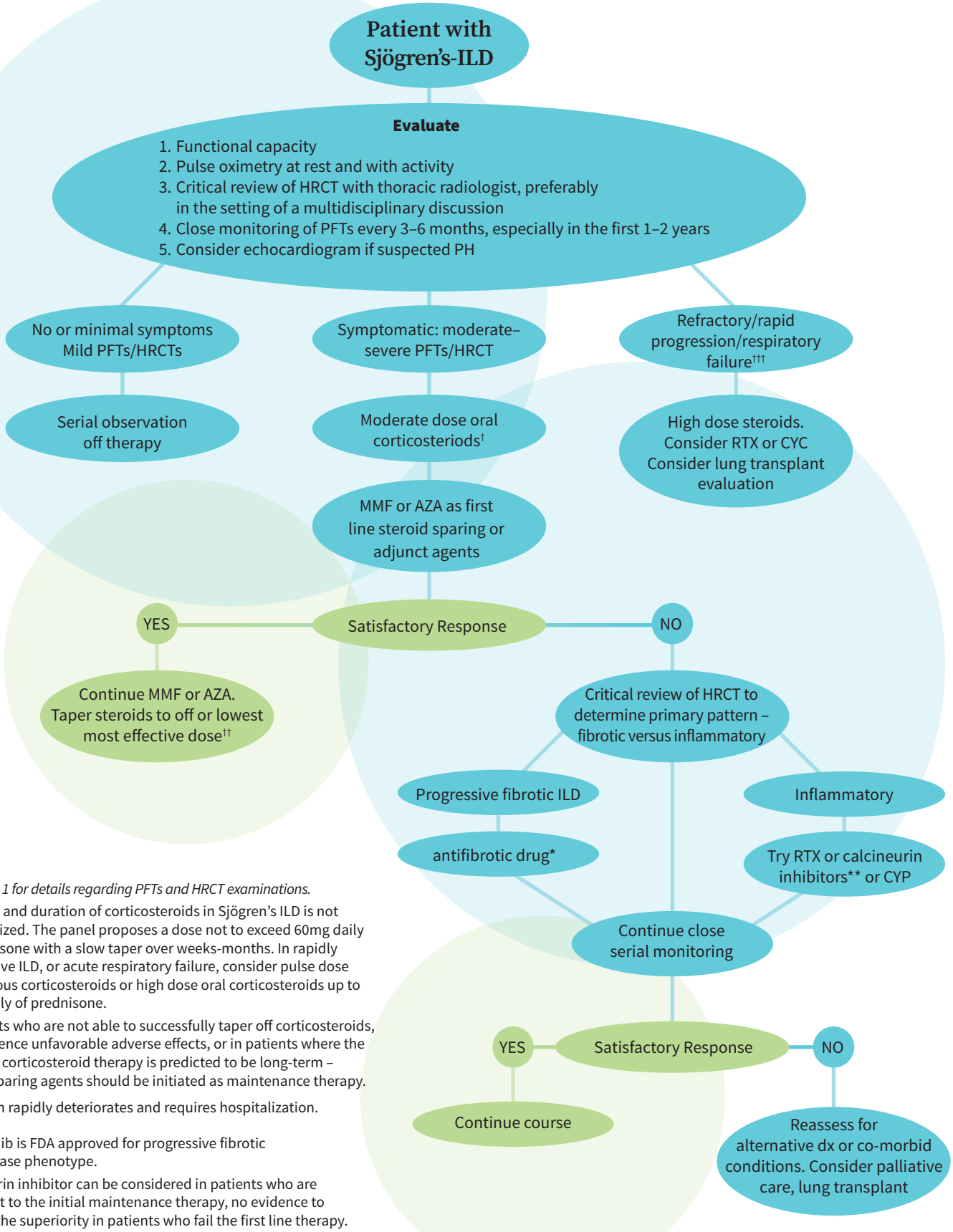
4B. **Cautions for Rituximab (RTX):** In a Sjögren's patient with ILD considering use of rituximab (RTX), patients and healthcare providers must be aware of the following potential risks/harms, although rare:†
• Pneumonitis
• Worsening of ILD
• Infusion reactions
• Tumor lysis syndrome in those with NHL
• Bacterial, viral or fungal infections including:
  • Hepatitis B reactivation with possible fulminant hepatitis
  • Progressive multifocal leukoencephalopathy (PML)
• Hypogammaglobulinemia
• Cytopenias
• Severe mucocutaneous reactions
• Bowel obstruction and perforation
• Cardiac arrhythmias and angina
• In pregnancy and nursing, risk vs benefit must be carefully considered
• Avoid live vaccines with rituximab
	HIGH	**STRONG**

5. **Symptomatic/ Moderate-Severe Sjögren's-ILD – Antifibrotic drugs:**†† The use of anti-fibrotic therapy such as nintedanib should be tried as a second-line maintenance therapy either alone or in combination with immunomodulatory agents in Sjögren's patients with progressive fibrotic ILD who are symptomatic and in whom PFTs or HRCT demonstrated moderate-severe impairment.	**LOW**	**MODERATE**
6. **Rapidly progressive or exacerbating ILD – IV Steroids:** In Sjögren's patients with ILD who are rapidly progressive or present with acute respiratory failure, a trial of high dose corticosteroids (such as intravenous methylprednisolone) is recommended. Alternative etiologies, such as infections or lymphoproliferative disorders, must be considered.	**INTERMEDIATE**	**STRONG**
7A. **Symptomatic/Refractory, rapidly progressive or exacerbating ILD – Cyclophosphamide (CYP):** In a Sjögren's patient with ILD who has acute or subacute hypoxic respiratory failure requiring hospitalization, despite initial therapies, rituximab (RTX) or cyclophosphamide (CYP) should be considered in addition to high dose corticosteroids.	**LOW**	**MODERATE**
7B. **Cautions for Cyclophosphamide (CYP):** In Sjögren's with ILD when cyclophosphamide is considered, the significant risks must be assessed†, and Pneumocystis jiroveci prophylaxis provided. Risk of bladder cancer can be greatly reduced with intravenous versus oral route.	**INTERMEDIATE**	**STRONG**
8. **Drug-induced lung disease:** Clinicians and patients must be aware of pulmonary complications associated with medications used in Sjögren's and related CTDs, particularly when patients are progressive or refractory to therapies. Complications may include infections, malignancies, bronchospasm and drug-induced ILD, and may require bronchoscopy, biopsy and/or withdrawal of the medication. In addition to medication withdrawal, corticosteroids may be used if significant symptoms and respiratory impairment are present. While the risk is low for most agents (~1%), healthcare providers should keep in mind that medications used to treat Sjögren's have been associated with drug-induced ILD, including: • TNF-alpha inhibitors • Sulfasalazine • Cyclophosphamide • Rituximab • Leflunomide • Methotrexate • Sulfonamides	**INTERMEDIATE**	**STRONG**

† Refer to the FDA label for additional information.

†† The antifibrotic, nintedanib, was FDA-approved for progressive fibrotic ILD just as these recommendations went to consensus. This factor, in addition to the authors' awareness of minimal experience with antifibrotics in autoimmune disease, precluded inclusion of a Recommendation listing cautions for antifibrotics. Please consult the Physician's Desk Reference (PDR) for potential risks and side effects.

Figure 3:
Evaluation and Management of Patients With Sjögren's Who Exhibit Symptoms and/or Physical Examination Signs of Interstitial Lung Disease



Legend:

Refer to Figure 1 for details regarding PFTs and HRCT examinations.

† The dose and duration of corticosteroids in Sjögren's ILD is not standardized. The panel proposes a dose not to exceed 60mg daily of prednisone with a slow taper over weeks-months. In rapidly progressive ILD, or acute respiratory failure, consider pulse dose intravenous corticosteroids or high dose oral corticosteroids up to 60mg daily of prednisone.

†† In patients who are not able to successfully taper off corticosteroids, or experience unfavorable adverse effects, or in patients where the length of corticosteroid therapy is predicted to be long-term – steroid sparing agents should be initiated as maintenance therapy.

††† Condition rapidly deteriorates and requires hospitalization.

* Nintedanib is FDA approved for progressive fibrotic lung disease phenotype.

** Calcineurin inhibitor can be considered in patients who are intolerant to the initial maintenance therapy, no evidence to support the superiority in patients who fail the first line therapy.

Abbreviations: *Same as Figure 1 plus*
MMF = mycophenolate mofetil; AZA = azathioprine; RTX = rituximab; CYP = cyclophosphamide; ILD = interstitial lung disease; PH = pulmonary hypertension

Drug Maintenance Therapy for Sjögren's-ILD

Drug	Mechanism of action	Common side effects	Level of recommendation
Mycophenolate Mofetil	Antimetabolite, inhibition of DNA synthesis	Nausea, diarrhea, hepatotoxicity, bone marrow suppression. Pregnancy risk category D	First line therapy for symptomatic ILD with moderate to severe impairment. Moderate strength of recommendation
Azathioprine	Antimetabolite, inhibition of DNA synthesis	Nausea, diarrhea, hepatotoxicity, bone marrow suppression, rash, hypersensitivity syndrome. Pregnancy risk category D	First line therapy for symptomatic ILD with moderate to severe impairment. Moderate strength of recommendation
Cyclosporin	Calcineurin inhibitor T cell target agent	Nephrotoxicity, neurotoxicity, hypertension, hyperglycemia, hirsutism, gingival hyperplasia. Pregnancy risk category C	Second line therapy for symptomatic ILD with moderate to severe impairment. Weak strength of recommendation
Tacrolimus	Calcineurin inhibitor T cell target agent	Nephrotoxicity, neurotoxicity, hypertension, hyperglycemia, alopecia. Pregnancy risk category C	Second line therapy for symptomatic ILD with moderate to severe impairment. Weak strength of recommendation
Cyclophosphamide	Cytotoxic alkylating agent	Infection, bone marrow suppression, gonadal toxicity, bladder toxicity, malignancy risk. Pregnancy risk category D	First line therapy for symptomatic ILD with refractory, rapidly progressive or exacerbating condition requiring hospitalization. Moderate strength of recommendation
Rituximab	Anti CD20 monoclonal antibody B cell target agent	Infusion reaction, cytopenias, infection, hypogammaglobulinemia, hepatitis B reactivation, progressive multifocal leukoencephalopathy. Pregnancy risk category C	First line therapy for symptomatic ILD with refractory, rapidly progressive or exacerbating condition requiring hospitalization. Moderate strength of recommendation Second line therapy for symptomatic ILD with moderate to severe impairment. Weak strength of recommendation
Nintedanib	Tyrosine kinase inhibitor	Nausea, vomiting, diarrhea, weight loss, hepatotoxicity. Pregnancy risk category D	Second line therapy for symptomatic ILD with moderate to severe impairment with progressive fibrotic lung disease phenotype. Moderate strength of recommendation

Clinical Practice Guidelines Development

The Sjögren's Foundation brought rheumatologists, pulmonologists and a hematologist-oncologist together to develop clinical practice guidelines to guide healthcare professionals in the diagnosis, management and treatment of pulmonary manifestations in Sjögren's.

A rigorous and transparent methodology was followed according to guidelines from the American College of Rheumatology (ACR) and other professional organizations. A Consensus Expert Panel (CEP), comprised of 68 members including healthcare professionals in rheumatology and pulmonology as well as Sjögren's patients and family members in healthcare, reviewed and provided input on the guidelines.

Citation

Lee AS, Scofield RH, Hammitt KM, Gupta N, Thomas DE, Moua T, Ussavarungsi K, St Clair EW, Meehan R, Dunleavy K, Makara M, Carsons SE, Carterson NL. Consensus guidelines for evaluation and management of pulmonary disease in Sjögren's. *Chest*. 2020 Oct 16:S0012-3692(20)34902-3. doi: 10.1016/*j.chest*.2020.10.011. Epub ahead of print. PMID: 33075377.

Recommendations for Lymphoproliferative Disease in Sjögren's

Diagnosis, Evaluation and Management for Lymphoproliferative Disease in Sjögren's Patients	Strength of Evidence	Strength of Recommendation
1. The possibility of lymphoma must be further investigated in a Sjögren's patient with symptoms such as unexplained weight loss, fevers, night sweats, and/or the presence of head and neck lymphadenopathy and/or parotitis.	HIGH	STRONG
2. All Sjögren's patients must be clinically monitored for signs and symptoms of pulmonary lymphoproliferative disorders including lymphoma and amyloid.	HIGH	STRONG
3. In Sjögren's patients suspected of having lymphoproliferative complications, an HRCT chest scan should be considered more appropriate than a baseline CXR at the time of initial diagnosis.	INTERMEDIATE	MODERATE
4. In a Sjögren's patient with pulmonary lesions (nodules >8mm, consolidations, or lymphadenopathy) in whom a neoplasm is suspected, a positron emission tomography (PET) should be considered.	INTERMEDIATE	MODERATE
5. In Sjögren's patients with lymphadenopathy, growing lung nodules, and/or progressive cystic lung disease, a biopsy should be recommended. Clinical and radiographic observation may be appropriate in select patients with incidental subcentimeter nodules, stable cysts and isolated PET negative subcentimeter lymphadenopathy.	INTERMEDIATE	MODERATE
6. In a Sjögren's patient in whom a neoplasm has been confirmed or suspected, multidisciplinary review involving rheumatologist/primary care physician, pulmonologist, pathologist, radiologist and hematologist/oncologist is recommended.	LOW	STRONG

Checklist to Screen for Pulmonary Involvement in Sjögren's

1. Does the patient experience shortness of breath upon exertion?
2. Does the patient experience chronic cough?
3. Does the patient have a history of wheezing?
4. Does the patient have a recent diagnosis of asthma/COPD?
5. What is the patient history regarding cigarette smoking, or other inhalation exposures, including marijuana and vaping?

Checklist to Screen for Sjögren's in Pulmonary Patients

Questions to Ask Patient

Oral Symptoms:

- Does your mouth feel dry?
- Do you need liquids to swallow dry foods?
- Do you frequently sip/drink water?
- Do you have a burning sensation in the mouth?
- Do you have painful sores or red patches at the corners of the mouth (angular cheilitis)?
- Do you get frequent dental cavities, particularly gumline cavities?
- Do your teeth tend to chip, crack and/or erode on the surfaces?
- Do you suffer from gum inflammation or receding gums (gingivitis?)

Ocular Symptoms:

- Do your eyes frequently feel dry, irritated, itchy or painful?
- Do you have a sensation that there might be a foreign body in your eye?
- Are your eyes light sensitive?
- Do you frequently use eye drops for irritation or dryness?
- Is your vision frequently blurry, or do you have unexplained vision changes?

Other Symptoms:

- Have you noticed gland swelling in your face or along the jaw line (swollen parotid and/or submandibular glands)?
- Do you suffer dryness of the vagina (is intercourse painful?) or skin (is your skin itchy or flaking?)?
- Do your feet, legs or hands ever feel numb, have a change in sensation or have burning pain (peripheral neuropathy)?
- Do you suffer from extreme fatigue?
- Do your joints or muscles ache when you are not sick (arthralgias, myalgias)?
- Do you ever notice your fingers turning pale or blue in the cold (Raynaud's)?

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Please visit www.sjogrens.org to view all published guidelines in Sjögren's and the most up-to-date information on the Sjögren's Foundation Clinical Practice Guidelines initiative.

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