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2023 American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) Guideline for the Screening and Monitoring of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases

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Objective. We provide evidence-based recommendations regarding screening for interstitial lung disease (ILD) and the monitoring for ILD progression in people with systemic autoimmune rheumatic diseases (SARDs), specifically rheumatoid arthritis, systemic sclerosis, idiopathic inflammatory myopathies, mixed connective tissue disease, and Sjögren disease.

Methods. We developed clinically relevant population, intervention, comparator, and outcomes questions related to screening and monitoring for ILD in patients with SARDs. A systematic literature review was performed, and the available evidence was rated using the Grading of Recommendations, Assessment, Development, and Evaluation methodology. A Voting Panel of interdisciplinary clinician experts and patients achieved consensus on the direction and strength of each recommendation.

Results. Fifteen recommendations were developed. For screening people with these SARDs at risk for ILD, we conditionally recommend pulmonary function tests (PFTs) and high-resolution computed tomography of the chest (HRCT chest); conditionally recommend against screening with 6-minute walk test distance (6MWD), chest radiography, ambulatory desaturation testing, or bronchoscopy; and strongly recommend *against* screening with surgical lung biopsy. We

conditionally recommend monitoring ILD with PFTs, HRCT chest, and ambulatory desaturation testing and conditionally recommend *against* monitoring with 6MWD, chest radiography, or bronchoscopy. We provide guidance on ILD risk factors and suggestions on frequency of testing to evaluate for the development of ILD in people with SARDs.

Conclusion. This clinical practice guideline presents the first recommendations endorsed by the American College of Rheumatology and American College of Chest Physicians for the screening and monitoring of ILD in people with SARDs.

INTRODUCTION

Interstitial lung disease (ILD) is characterized by inflammation and/or fibrosis of the lung parenchyma and is a significant cause of morbidity and mortality in people with systemic autoimmune rheumatic diseases (SARDs). Although people with SARDs are at risk for developing ILD in general, those with rheumatoid arthritis (RA), systemic sclerosis (SSc), idiopathic inflammatory myopathies (IIM; including polymyositis, dermatomyositis, immune-mediated necrotizing myopathy, and anti-synthetase syndrome), mixed connective tissue disease (MCTD), and Sjögren disease (SjD) are at particularly high risk.[1–4] For example, ILD affects >50% of adults with SSc and is the leading cause of death and hospitalization in this population.[5–8] ILD is also a major cause of death in adults with RA.[9–12] Furthermore, some patients with RA, SSc, IIM, MCTD, and SjD are at risk for rapidly progressive ILD. Risk factors for the development of ILD include demographics, disease manifestations, and antibody profile, as summarized in Table 1.

There are no existing guidelines for ILD screening for people with SARDs. This guideline was developed to provide recommendations for the screening of ILD in people with SARDs (RA, SSc, IIM, MCTD, and SjD) at greatest risk of ILD and for monitoring for ILD progression. These recommendations will facilitate rheumatologists' identification of people with SARDs who have ILD and assist in optimizing the co-management of people with SARD-associated ILD by rheumatologists and pulmonologists.[27] This guideline does not address the evaluation for SARDs among persons with newly diagnosed ILD who lack a formal SARD diagnosis.

METHODS

This guideline was developed following the American College of Rheumatology (ACR) guideline development process and ACR policy guiding management of conflicts of interest and disclosures (https://rheumatology.org/clinical-practice-guidelines), which includes Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology.[28–30] Supplementary Materials 1 includes a detailed description of the methods. Briefly, the Core Leadership Team composed of rheumatologists, pulmonologists, and a radiologist—all with expertise in SARD-ILD—drafted clinical population, intervention, comparator, and outcomes (PICO)

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Table 1. Risk factors for the development of ILD that may indicate the need for screening*

Disease	Risk factors
Systemic sclerosis	• Anti–Scl-70 positivity, antinuclear antibody with nucleolar pattern[13] • Diffuse cutaneous subtype, male sex, African American race[14,15] • Early disease (first 5–7 y after onset) • Elevated acute phase reactants[13,16]
Rheumatoid arthritis	• High-titer rheumatoid factor, high-titer anti-CCP[17–19] • Cigarette smoking,[20,21] older age at rheumatoid arthritis onset,[22,23] high disease activity • Male sex,[22] higher body mass index
Idiopathic inflammatory myopathies	• Anti-synthetase (Jo-1, PL7, PL12, EJ, OJ, KS, Ha, Zo), anti–MDA-5, anti-Ku, anti-Pm/Scl, anti-Ro52 antibody positivity • Mechanic's hands, arthritis/arthralgia, ulcerating lesions[24]
Mixed connective tissue disease	• Dysphagia, Raynaud phenomenon • Other systemic sclerosis clinical or laboratory features
Sjögren disease	• Anti-Ro52 antibody, antinuclear antibody[25,26] • Raynaud phenomenon • Older age • Lymphopenia • Severe dental caries

* These disease features have been identified as placing a person at increased risk for developing ILD; however, the absence of these risk factors does not preclude the development of ILD in patients with these SARDs. Screening for ILD should be performed in shared decision-making with the rheumatologist and patient. As such, screening for ILD should not necessarily be limited only to those with these risk factors. CCP, cyclic citrullinated peptide; ILD, interstitial lung disease; MDA-5, MDA-5 melanoma differentiation-associated protein 5; SARD, systemic autoimmune rheumatic disease.

questions (Supplementary Materials 2). A medical librarian searched MEDLINE and Embase via Ovid on August 1, 2022 (last surveillance on January 6, 2023). Database searches were supplemented by suggestions from the Core Leadership Team and Voting Panel and by reviewing reference lists of conference proceedings and other guidelines.[27,31–33] The Literature Review Team conducted systematic literature reviews for the PICO questions and, with input from the Core Leadership Team, rated the certainty of evidence (high, moderate, low, very low) and produced an evidence report (Supplementary Materials 3).

Of note is the rating of evidence for surrogate outcomes. Consistent with GRADE guidance, we defined surrogate outcomes as those that would not lead patients to accept a test that was also associated with burdens or harms if they were the only outcomes to improve.[34] For instance, if the surrogate outcome of forced vital capacity (FVC) improves without improvement in symptoms or reduction in death (the outcomes most valued by patients), then patients may avoid the test. In such situations, the team rated certainty in the patient-important outcome (eg, symptoms or death) as inferred from the surrogate and rated down once or twice for indirectness.[35]

A Patient Panel was convened that included 21 people with SARDs of interest (at risk for ILD [n = 4, 19%] or diagnosed with ILD [n = 17, 81%]), median 53 years of age (range 33–73 years); it was composed of n = 16 women (71%), n = 14 White individuals (67%), n = 7 Black or multiracial individuals (33%), and n = 2 Hispanic individuals (10%). They met virtually with three members of the Core Team (MBB, MDG, and RDM) and two ACR staff members. The Patient Panel provided perspectives on values and preferences related to ILD screening and monitoring.[36] An expert Voting Panel composed of rheumatologists (n = 19), pulmonologists (n = 4), a radiologist (n = 1), and representatives from the Patient Panel (n = 3) reviewed the evidence report and voted on the recommendations at virtual Voting Panel meetings (February–March 2023). Supplementary Materials 4 includes rosters of the Core Leadership Team, Literature Review Team, Voting Panel, and Patient Panel.

As per ACR policy, consensus required ≥70% agreement on both the direction (for or against) and strength (strong or conditional) of each recommendation. A recommendation could be either in favor of or against the proposed intervention and either strong or conditional. According to GRADE, a recommendation is categorized as strong if the panel is very confident that the benefits of an intervention clearly outweigh the harms (or vice versa); a conditional recommendation denotes uncertainty regarding the balance of benefits and harms, such as when the evidence certainty is low or very low, or when the decision is sensitive to individual patient preferences, or when costs are expected to impact the decision. Thus, conditional recommendations refer to decisions in which incorporation of patient preferences is a particularly essential element of decision-making.

Scope

Patients. This guideline applies to people with SARDs with high risk of ILD, specifically RA, SSc, IIM, MCTD, and SjD. This guideline does not include recommendations for pediatric SARDs (juvenile SSc, juvenile dermatomyositis, systemic juvenile idiopathic arthritis) or people with sarcoidosis, interstitial pneumonia with autoimmune features (IPAF), undifferentiated connective tissue disease, ankylosing spondylitis, antineutrophil cytoplasmic antibody–associated vasculitis, systemic lupus erythematosus (SLE), or unclassifiable ILD. There was a need to limit the guideline scope, so the five diseases in which ILD occurs most frequently were prioritized. IPAF was not included because it is a research classification rather than a clinical diagnosis. Also, this guideline was not developed to guide evaluation for SARDs in patients with newly diagnosed ILD without a prior recognized SARD.

Interventions. The panel considered the following diagnostic and screening interventions: history and physical examination alone (including assessment of dyspnea, functional class,

cough, and fatigue on history; tachypnea, cyanosis, and percussion for altered lung resonance and auscultation for crackles on physical examination), pulmonary function tests (PFTs; including spirometry, lung volumes, and diffusion capacity for carbon monoxide [DLco]), high-resolution computed tomography of the chest (HRCT chest), 6-minute walk test distance (6MWD), chest radiography, ambulatory desaturation testing, bronchoscopy (bronchoalveolar lavage, transbronchial biopsy, and/or cryobiopsy), and surgical lung biopsy. This guideline does not make recommendations on education, self-monitoring of oxygen saturation, testing for supplemental oxygen requirement, or patient-reported outcomes, including questionnaires, eg, Chronic Respiratory Questionnaire, St. George's Respiratory Questionnaire, Mahler Dyspnea Index, University of California, San Diego Shortness of Breath Questionnaire, Leicester Cough Questionnaire, Functional Assessment of Chronic Illness Therapy-Dyspnea, Modified Medical Research Council, and King's Brief Interstitial Lung Disease.

Outcomes. For screening recommendations, critical outcomes included disease-related outcomes (eg, progression of ILD), diagnostic accuracy as a surrogate for disease-related outcomes, and diagnostic testing-related adverse events. For monitoring recommendations, critical outcomes were disease-related outcomes, responsiveness/sensitivity to change of the test as a surrogate for disease-related outcomes, and testing-related adverse events.

RESULTS/RECOMMENDATIONS

Based on 24 PICO questions, the panel developed 15 screening and monitoring recommendations (Tables 2–5). The literature search identified 5,235 records for the full set of PICO questions covering screening, monitoring, and treatment (the latter reported in separate treatment guidelines).[37] After excluding 4,038 titles and abstracts, 1,197 full-text articles were reviewed, of which 1,083 were excluded. Thus, the overall evidence included 114 studies, of which 10 studies addressed the screening questions and 13 studies (in 17 publications) addressed the monitoring questions (Supplementary Materials 3, 5, 6). No publications were found to address 4 screening questions (PICOs 3, 4, 5, and 7) and 10 of the monitoring questions (PICOs 12, 14–18, 20–22, and 24). The number of recommendations resulting from PICO questions was reduced by combining recommendations when appropriate.

Screening for SARD-ILD

Who should be screened. It was recognized that RA, SSc, IIM, MCTD, and SjD all confer an increased risk of ILD development compared to the general population. However, it was also recognized that the risks of ILD development and progression vary among and within these diseases. For example, people with RA have low frequency (ie, 3%–5% of people with RA) of progressive ILD, and a larger proportion have asymptomatic or stable disease. SSc confers a higher risk of ILD compared with other SARDs, but a subset of people with long-standing limited cutaneous SSc can have mild, stable ILD. Patients with RA-ILD with high-titer anti-cyclic citrullinated peptide (CCP) or rheumatoid factor positivity, patients with SSc-ILD with early diffuse cutaneous disease and/or Scl-70 positivity, and patients with IIM-ILD with anti-melanoma differentiation-associated protein 5 (anti-MDA-5), anti-synthetase, or overlap antibodies (eg, PM-Scl, Ku, Ro52) are at increased risk for ILD progression. Thus, screening must be tailored to an individual patient, recognizing the need for shared decision-making. Although most people with SSc and many people with IIM warrant screening, it is not necessary to screen all people with RA or SjD. The Voting Panel voted on recommendations for people at higher risk of ILD within each disease. Although defining the magnitude of risk within diseases was beyond the scope of this guideline, Table 1 summarizes risk factors for ILD across diseases, identified by review of the literature, to inform clinicians of people who may warrant heightened screening and monitoring for ILD. Screening for ILD should not be limited to those with just these risk factors. The Patient Panel expressed a preference for identifying ILD early, even if there was a risk for identifying either subclinical disease that might not progress or incidental findings requiring additional testing. If there is uncertainty regarding whom to screen, clinicians should proceed with screening for ILD. Figure 1 summarizes tests

Table 2. Summary of recommendations for screening of SARD-ILD*

Summary of recommendations
For people with SARDs at increased risk of developing ILD, we **conditionally** recommend screening with PFTs over history and physical examination or ambulatory desaturation testing alone.
For people with SARDs at increased risk of developing ILD, we **conditionally** recommend screening with HRCT chest over history and physical examination or PFTs alone.
For people with SARDs at increased risk of developing ILD, we **conditionally** recommend screening with HRCT chest and PFTs over PFTs alone.
For people with SARDs at increased risk of developing ILD, we **conditionally** recommend *against* screening with chest radiography.
For people with SARDs at increased risk of developing ILD, we **conditionally** recommend *against* screening with 6MWD.
For people with SARDs at increased risk of developing ILD, we **conditionally** recommend *against* screening with ambulatory desaturation testing.
For people with SARDs at increased risk of developing ILD, we **conditionally** recommend *against* screening with bronchoscopy.
For people with SARDs at increased risk of developing ILD, we **strongly** recommend *against* screening with surgical lung biopsy.

* SARDs at increased risk of developing ILD are rheumatoid arthritis, systemic sclerosis, idiopathic inflammatory arthritis, mixed connective tissue disease, and Sjögren syndrome. PFTs included spirometry, lung volumes, and DLco. DLco, diffusion capacity for carbon monoxide; HRCT chest, high-resolution computed tomography of the chest; ILD, interstitial lung disease; PFT, pulmonary function test; SARD, systemic autoimmune rheumatic disease; 6MWD, 6-minute walk test distance.

Table 3. Summary of recommendations for monitoring for ILD progression*

Summary of recommendations
For people with SARD-ILD, we **conditionally** recommend monitoring with PFTs.
For people with SARD-ILD, we **conditionally** recommend monitoring with HRCT chest.
For people with SARD-ILD, we **conditionally** recommend monitoring with PFTs and HRCT chest over PFTs alone.
For people with SARD-ILD, we **conditionally** recommend monitoring with ambulatory desaturation testing.
For people with SARD-ILD, we **conditionally** recommend *against* monitoring with chest radiography.
For people with SARD-ILD, we **conditionally** recommend *against* monitoring with 6MWD.
For people with SARD-ILD, we **conditionally** recommend *against* monitoring with bronchoscopy.
For people with IIM-ILD and SSc-ILD, we suggest PFTs for monitoring every 3–6 months rather than either shorter or longer intervals for the first year, then less frequently once stable.
For people with RA-ILD, SjD-ILD, and MCTD-ILD, we suggest PFTs for monitoring every 3–12 months rather than shorter or longer intervals for the first year, then less frequently once stable.
For people with SARD-ILD, we do not provide guidance about frequency of routine HRCT chest for monitoring ILD but suggest HRCT chest when clinically indicated.
For people with SARD-ILD, we suggest assessment for ambulatory desaturation every 3–12 months rather than at shorter or longer intervals.

* PFTs included spirometry, lung volumes, and DLco. DLco, diffusion capacity for carbon monoxide; HRCT chest, high-resolution computed tomography of the chest; IIM, idiopathic inflammatory myopathies; ILD, interstitial lung disease; MCTD, mixed connective tissue disease; PFT, pulmonary function test; RA, rheumatoid arthritis; SARD, systemic autoimmune rheumatic disease; SjD, Sjögren disease; SSc, systemic sclerosis; 6MWD, 6-minute walk test distance.

suggested for screening at presentation. Figure 2 summarizes tests that are not recommended, along with examples of situations in which these tests may be useful.

For people with SARDs at increased risk of developing ILD, we conditionally recommend screening with PFTs over history and physical examination or ambulatory desaturation testing alone.

Given the poor diagnostic accuracy of history (dry cough: 15% sensitive, 89% specific) and examination (dry "velcro" crackles: 69% sensitive, 66% specific), despite very low certainty of evidence (one observational study),[38] PFTs are preferred over history and physical examination alone for screening of ILD. PFTs should include spirometry, lung volumes, and DLco. Seeking history for ILD symptoms and performing lung auscultation should remain part of the routine assessment of a patient with an SARD, and rheumatologists should note even mild pulmonary symptoms, including subtle reductions in physical activity.

For people with SARDs at increased risk of developing ILD, we conditionally recommend screening with HRCT chest over history and physical examination or PFTs alone.

Very low-certainty evidence suggests that the HRCT chest has a sensitivity of 95.7% and specificity of 63.8% for the detection of ILD (≥20% extent of lung involvement).[38,39] Traditionally, the difference between HRCT chest and a standard CT chest has been the slice reconstruction or acquisition thickness (<1.5 mm for HRCT and 3–5 mm for standard chest CT), although this distinction at many modern centers has now blurred because even standard chest CT scans are often reconstructed using thin slices. HRCT chest typically includes inspiratory prone images (to differentiate mild dependent lung atelectasis from early fibrosis) and supine end-expiratory imaging (to assess for air-trapping). Nearly all cases of significant ILD can be detected on high-quality low-dose chest CT or even on standard chest CT imaging, all without contrast. However, one must be cautious with CT angiogram studies; they are often inadequate for ILD assessment because these studies are typically performed in incomplete inspiration, which may produce marked atelectasis that can obscure, accentuate, or mimic ILD.[40–42]

For people with SARDs at increased risk of developing ILD, we conditionally recommend screening with HRCT chest and PFTs over PFTs alone.

Low-certainty evidence from five observational studies suggests that PFTs alone may be insufficient to detect ILD among patients with newly diagnosed SARDs.[7,38,43–45] For example, an FVC <80% has a sensitivity of 47.5% and specificity of 78.7%, whereas HRCT chest has a sensitivity of 100% and specificity of 55.3%.[44] Patients with ILD can have normal PFTs or have difficulty performing PFTs because of cough or microstomia. The Patient Panel expressed a preference for more comprehensive screening even when considering the potential risks of radiation exposure or incidental findings leading to additional testing. In fact, although some may be concerned about HRCT radiation exposure,[46] the amount of exposure is low, and the risk of radiation-induced malignancy on a per-scan basis is extremely low. Moreover, this low-risk estimate is based on extrapolations from atomic bomb survivors using the linear no-threshold model, which some have criticized for being overly conservative.[47,48] There is no direct evidence of increased risk of radiation-induced malignancy in adults from chest CT exposure. HRCT chest and PFTs provide complementary information about presence and pattern of ILD (HRCT) and physiologic impact (PFTs); thus, the combination is preferred over PFTs alone. PFTs and HRCT chest are helpful for diagnosis of other lung and thoracic diseases occurring in people with SARDs (eg, pulmonary hypertension, airway diseases, infection, and cancer).

For people with SARDs at increased risk of developing ILD, we conditionally recommend *against* screening with chest radiography.

Three studies indicated a low sensitivity of chest radiography (58%–64%), limiting utility as a screening test for ILD.[39,44,49] The

Table 4. Summary of Voting Panel decisions, PICO questions, and evidence for screening of people with SARDs at risk of developing ILD that led to recommendations*

Voting Panel decision	Certainty of evidence	Based on the evidence reports of the following PICO questions	Evidence table in Supplementary Materials 3, page number
Conditionally recommend PFTs over history and physical examination alone	Very low	1	1
Conditionally recommend HRCT chest over history and physical examination alone	Very low	2	5
Conditionally recommend *against* 6MWD over history and physical examination alone	Very low	3	12
Conditionally recommend *against* chest radiography over history and physical examination alone	Very low	4	13
Conditionally recommend *against* ambulatory desaturation testing over history and physical examination alone	Very low	5	15
Conditionally recommend HRCT chest over chest radiography	Very low	6	16
Conditionally recommend PFTs over ambulatory desaturation testing	Very low	7	23
Conditionally recommend HRCT chest over PFTs	Low	8	24
Conditionally recommend HRCT chest and PFTs over PFTs alone	Very low	9	34
Conditionally recommend *against* bronchoscopy	Very low	10	40
Strongly recommend *against* surgical lung biopsy	Very low	11	46

* This table summarizes the Voting Panel decisions for each intervention and comparator, the certainty of evidence, the associated PICO questions, and the pages in the evidence report where detailed synopsis of the data can be found. After voting, many of the PICO questions were clustered into recommendation statements. We provide this table to be transparent about the process of moving from evidence to recommendation statement. HRCT chest; high-resolution computed tomography of the chest; ILD, interstitial lung disease; PICO, population, intervention, comparison, and outcomes; PFT, pulmonary function test; SARD, systemic autoimmune rheumatic disease; 6MWD, 6-minute walk test distance.

Patient Panel reported that, because an HRCT chest is required in the presence of normal or abnormal chest radiography, they would prefer an HRCT chest as the only imaging modality for screening alone.

For people with SARDs at increased risk of developing ILD, we conditionally recommend *against* screening with 6MWD.

The Literature Review Team found no published evidence regarding 6MWD as a screening test for ILD. Rather, it is used for evaluation for lung transplantation and for monitoring in those with pulmonary hypertension. In people with SARDs, the 6MWD can be impacted by other SARD manifestations that affect mobility including arthritis and cardiac disease. The Patient Panel felt the 6MWD frequently did not reflect symptoms and may not reflect functional status or ability to perform activities of daily living.

For people with SARDs at increased risk of developing ILD, we conditionally recommend *against* screening with ambulatory desaturation testing.

The Literature Review Team found no published evidence regarding the use of ambulatory desaturation testing as a screening test for ILD in SARDs. Given feasibility concerns in rheumatology outpatient practices, routine ambulatory desaturation testing was not recommended as a screening test. Within pulmonary outpatient practices and/or interdisciplinary models of shared care, ambulatory desaturation testing is more feasible and can be more easily offered in selected patients such as those with inadequate PFT quality, those who are unable to perform PFTs, or those with associated pulmonary hypertension.

For people with SARDs at increased risk of developing ILD, we conditionally recommend *against* screening with bronchoscopy.

Based on very low-certainty evidence from two observational studies,[50,51] we suggest against any bronchoscopic procedures (including bronchoalveolar lavage, transbronchial biopsy, endobronchial ultrasound, and cryobiopsy) for the routine screening of ILD. Bronchoscopy may be considered in selected circumstances—for example, to rule out infection or to evaluate for conditions such as sarcoidosis, alveolar hemorrhage, or hypersensitivity pneumonitis.

Table 5. Summary of Voting Panel decisions, PICO questions, and evidence for monitoring of people with SARD-associated ILD that led to recommendations*

Voting Panel decisions	Certainty of evidence	Based on the evidence reports of the following PICO questions	Evidence table in Supplementary Materials 3, page number
Conditionally recommend PFTs over history and physical examination alone	Very low	12	50
Conditionally recommend HRCT chest over history and physical examination alone	Very low	13	55
Conditionally recommend *against* 6MWD over history and physical examination alone	Very low	14	66
Conditionally recommend *against* chest radiography over history and physical examination alone	Very low	15	67
Conditionally recommend ambulatory desaturation testing over history and physical examination alone	Very low	16	68
Conditionally recommend *against* chest radiography over HRCT chest	Very low	17	69
Conditionally recommend *against* bronchoscopy	Very low	18	70
Conditionally recommend HRCT chest over bronchoscopy	Very low	19	72
Conditionally recommend PFTs over 6MWD	Very low	20	79
Conditionally recommend PFTs and HRCT chest over PFTs alone	Very low	23	86

* This table summarizes the Voting Panel decisions for each intervention and comparator, the certainty of evidence, the associated PICO questions, and the pages in the evidence report where detailed synopsis of the data can be found. After voting, many of the PICO questions were clustered into recommendation statements. We provide this table to be transparent about the process of moving from evidence to recommendation statement. HRCT chest, high-resolution computed tomography of the chest; ILD, interstitial lung disease; PICO, population, intervention, comparison and outcome; PFT, pulmonary function test; SARD, systemic autoimmune rheumatic disease; 6MWD, 6-minute walk test distance.

For people with SARDs at increased risk of developing ILD, we strongly recommend *against* screening with surgical lung biopsy.

One retrospective observational (very low-certainty evidence) study provided indirect evidence for this recommendation.[52] Surgical lung biopsy carries a 1% mortality risk, requires hospital admission and general anesthesia, and is associated with the need for chest tube thoracostomy, a small but not insignificant risk of ILD flare, and recovery time. Because the evidence of harm associated with lung biopsy is high quality and the evidence of any benefit is very low quality, this is one of the circumstances that GRADE has identified in which a strong recommendation in the presence of low-quality evidence may be appropriate.[28] Surgical lung biopsy may be warranted, however, in certain circumstances, such as to rule out malignancy. Patient Panelists preferred, given the associated risks, to avoid surgical lung biopsy unless medically necessary.

Suggestions for frequency of screening

Evidence to support the frequency of testing was limited,[53,54] but suggestions for frequency were deemed to be important. Therefore, this guidance is provided to inform implementation of the recommendations. There is substantial clinical variation from patient to patient that may affect frequency, so these should be seen as general guidance rather than firm recommendations.

The Core Team and Voting Panel preferred a risk-based approach. We suggest that most people with SSc, IIM, and MCTD with SSc features should have ILD screening tests at presentation. We also suggest that people with IIM have myositis-specific antibody testing to screen for the presence of high-risk ILD-associated antibodies (anti-synthetase and anti–MDA-5 antibodies). Although we do not suggest that all patients with RA and SjD be screened for ILD, we suggest screening at presentation in those with ILD risk factors such as those specified in, but not limited to, Table 1. We suggest that people with SARDs and associated greater risk of ILD be considered for rescreening with PFTs annually based on the presence of risk factors, and consideration for more frequent screening early in the patient's disease course should be based on specific high-risk autoantibody presence (eg, anti–Scl-70, anti–MDA-5, and anti-synthetase antibodies) or the development of ILD symptoms.

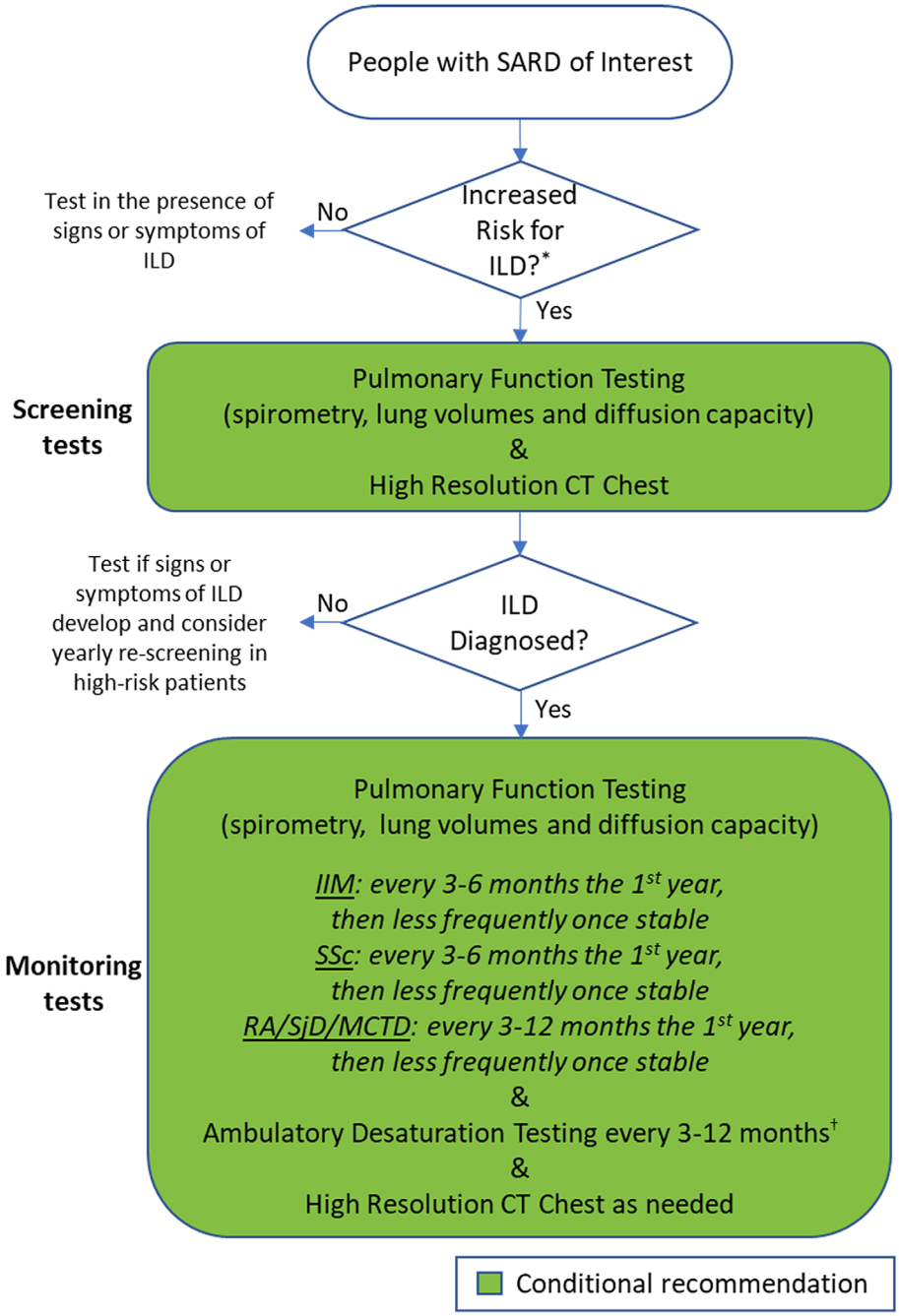

Figure 1. Recommendations for ILD screening and monitoring. Frequencies of monitoring in italics are suggestions to assist application of the recommendations. * See Table 1 for risk factors for ILD. † Ambulatory desaturation can be done during a routine office visit or as part of 6-minute walk testing. CT, computed tomography; IIM, idiopathic inflammatory myopathies; ILD, interstitial lung disease; MCTD, mixed connective tissue disease; RA, rheumatoid arthritis; SjD, Sjögren disease; SARD, systemic autoimmune rheumatic disease; SSc, systemic sclerosis.

Monitoring for ILD progression

Although screening for ILD in people with SARDs is largely the purview of rheumatologists, the monitoring of patients with identified SARD-associated ILD is expected to be a multidisciplinary collaboration between rheumatology and pulmonology. Thus, some recommendations will comment on potential variations in practice between these specialties.

For people with SARD-ILD, we conditionally recommend monitoring with PFTs.

PFTs (spirometry, volumes, and DL_{CO}) provide objective data that are helpful in following patients over time. Patients saw benefit in an objective test to help assess disease stability or progression. Although PFTs can reassure both patient and clinician when they are stable, patients commented that PFTs can also be stressful and difficult because of their symptoms of cough or

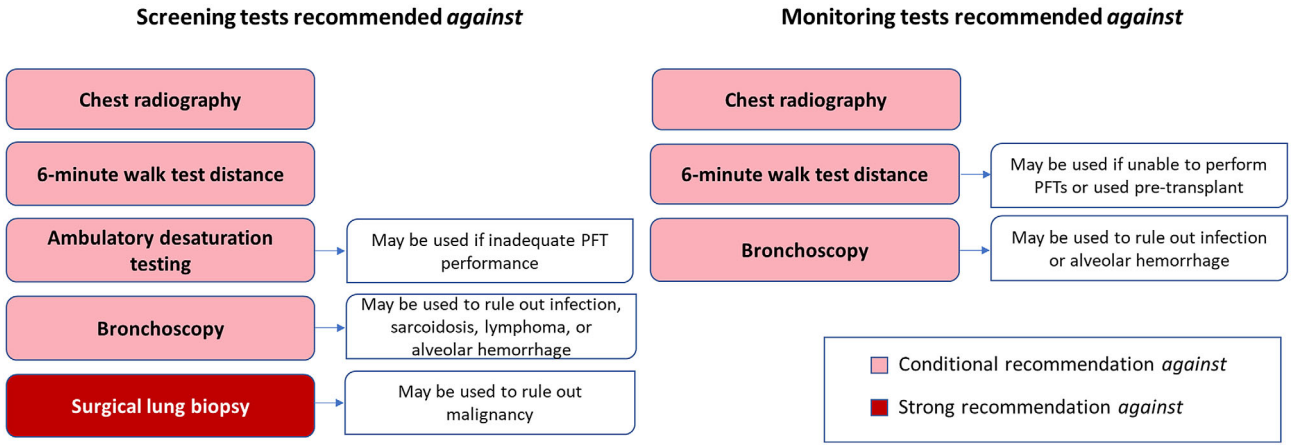

Figure 2. Interstitial lung disease screening and monitoring tests recommended *against*. Tests shown are recommended *against* for routine use, although examples are provided when these tests may have utility for assessing patients or ruling out other conditions. PFT, pulmonary function test. Color figure can be viewed in the online issue, which is available at http://onlinelibrary.wiley.com/doi/10.1002/art.42860/abstract.

dyspnea. Some people with SSc report difficulty achieving an adequate oral seal because of decreased oral aperture; these people may benefit from using a pediatric mouthpiece.

For people with SARD-ILD, we conditionally recommend monitoring with HRCT chest.

Two observational studies and two post hoc analyses of the Scleroderma Lung Study (SLS) randomized controlled trial (RCT) contributed indirect evidence for this recommendation.[55–58] HRCT chest provides an assessment of the extent and pattern of parenchymal involvement, which is helpful for monitoring. The frequency of such monitoring should be determined by patient symptoms plus mindful consideration of radiation exposure. HRCT chest is useful when there is respiratory symptom progression with stable PFTs, a significant reduction in PFTs, screening for lung cancer,[59] or differentiating between tight skin or respiratory muscle weakness versus progressive ILD as the cause of a restrictive PFT pattern. However, HRCT chest requires an experienced radiologist or other qualified professional to compare to previous HRCT scans to assess for progression and has higher cost to society.

For people with SARD-ILD, we conditionally recommend monitoring with PFTs and HRCT chest over PFTs alone.

Thirteen studies (16 articles,[55–58,60–70] including five post hoc analyses of the SLS RCT) provided very low-certainty evidence suggesting that PFTs and HRCT chest may be more helpful in monitoring ILD progression compared with PFTs alone to permit monitoring ILD pattern and changes in extent of disease. Both the Patient and Voting Panels stated that HRCT chest should not be performed as often as PFTs for monitoring, especially in the setting of stable symptoms and PFTs.

For people with SARD-ILD, we conditionally recommend monitoring with ambulatory desaturation testing.

There was no published evidence in people with SARD-associated ILD, but, as is standard in other forms of ILD, recognition of ambulatory desaturation informs the need for oxygen use. Concerns were raised about accurate oxygen saturation measurement in patients with Raynaud phenomenon, particularly those with SSc, because of poor finger perfusion. Thus, an ear or forehead oxygen saturation monitor is preferable in these circumstances.

For people with SARD-ILD, we conditionally recommend *against* monitoring with chest radiography.

One case-control study demonstrated a low sensitivity (64.0%) and moderate specificity (73.6%) of chest radiography relative to HRCT chest for identifying ILD among patients with inflammatory rheumatic diseases.[44] Another cohort study demonstrated using lung auscultation and/or chest radiography for detecting extent of ILD had a low sensitivity (58.6%) and specificity (60.0%) compared with HRCT chest.[39] Chest radiography does not appear to have enough resolution to detect progression or improvement. However, chest radiography could be useful to evaluate for pneumonia in people with SARD-ILD who develop acute-onset respiratory symptoms.

For people with SARD-ILD, we conditionally recommend *against* monitoring with 6MWD.

There was no evidence to support or oppose using 6MWD in the monitoring of people with SARD-ILD. 6MWD can be impacted by other health factors, such as arthritis and cardiac disease. Patients reported that 6MWD often did not reflect activities of daily living or function in daily life. If patients without confounding health factors can perform the test, it can be a useful marker to follow disease progression. 6MWD is important in the monitoring of patients pre–lung transplantation, those with pulmonary hypertension, and those unable to perform PFTs.

For people with SARD-ILD, we conditionally recommend *against* monitoring with bronchoscopy.

There was no published evidence. The panel was not in favor of routine use of bronchoscopy for monitoring but recognized its utility in certain circumstances, such as in the evaluation of infection or alveolar hemorrhage.

Suggestions for frequency of monitoring

The Voting Panel decided not to provide firm recommendations for frequency of monitoring once an ILD diagnosis is made, but general guidance in the form of suggestions instead. Some patients may need more frequent monitoring, especially if symptoms change, and these suggestions should not be used to inform reimbursement decisions. There is substantial clinical variation from patient to patient that may affect testing frequency.

For people with IIM-ILD and SSc-ILD, we suggest PFTs for monitoring every 3 to 6 months for the first year, then less frequently once stable.

More frequent monitoring is needed early in the course of disease and in patients with active or progressive disease, and then every 6 to 12 months after the first year if the disease is stable. For people with long-standing SSc or IIM and prolonged stability of their ILD, we suggest less frequent monitoring. This range allows for flexibility.

For people with RA-ILD, SjD-ILD, and MCTD-ILD, we suggest PFTs for monitoring every 3 to 12 months for the first year, then less frequently once stable.

RA-ILD typically progresses more slowly than the other SARDs; however, a usual interstitial pneumonia (UIP) pattern confers a worse prognosis and may warrant more frequent monitoring. Monitoring those with RA-ILD with PFTs every 6 to 12 months is suggested, recognizing that specific situations may warrant more frequent monitoring (3–6 months). SjD-ILD tends to be milder than other types of SARD-associated ILD; however, those with the Ro52 antibody can progress quickly. SjD can occur as an overlap condition with anti-synthetase syndrome, SSc, and RA. More frequent monitoring, based on physician judgment, should be performed in patients with symptom worsening, a UIP pattern, presence of autoantibodies associated with rapidly progressive disease (eg, anti–MDA-5), and worsening PFTs. People with MCTD and prominent features of SSc or IIM may benefit from more frequent monitoring.

For people with SARD-ILD, we do not provide guidance about frequency of routine HRCT chest for monitoring ILD but suggest HRCT chest when clinically indicated.

There was hesitancy to recommend how frequently HRCT chest should be performed. HRCT chest is a complementary test to PFTs for the monitoring of ILD progression and may be specifically useful in cases in which coughing or other factors might affect PFT performance or interpretation, when changes in symptoms or PFT results lead to uncertainty about whether there has been ILD progression, when there is concern for infection or malignancy, or when assessing treatment response.

For people with SARD-ILD, we suggest monitoring for ambulatory desaturation every 3 to 12 months.

There was a discrepancy between the application of this clinical assessment by rheumatologists and pulmonologists. Testing for ambulatory desaturation is inexpensive and informs a patient's need for supplemental oxygen. However, evaluation of ambulatory desaturation is not routine practice for many rheumatologists, and there may be operational challenges in performing ambulatory desaturation testing in some rheumatology offices. Pulmonologists on the panel routinely perform ambulatory desaturation testing in their offices. It is difficult to recommend a specific interval of ambulatory desaturation testing, and there is no evidence to support this guidance.

DISCUSSION

This guideline provides recommendations to clinicians for ILD screening and monitoring in people with RA, SSc, IIM, MCTD, and SjD. PFTs (including spirometry, lung volumes, and DL_{CO}) and HRCT chest are conditionally recommended for the screening of ILD in people with these SARDs, whereas PFTs, HRCT chest, and ambulatory desaturation testing are conditionally recommended for the monitoring of people with SARD-ILD. There are limited to no roles for chest radiography, 6MWD, bronchoscopy, or surgical lung biopsy for the routine screening or monitoring of people with SARD-ILD. We provide guidance on the risk factors and frequency of testing to evaluate for the development of ILD in people with SARDs.

The risk of ILD varies among people with an established diagnosis of an SARD. Screening tests should not be applied routinely to all people with SARDs. Rather, screening should be focused on people with an SARD of interest who have an increased risk of developing ILD. We summarize published risk factors as a guide, but clinicians are not limited to just these risk factors. We acknowledge that, in some cases, screening may identify mild, asymptomatic ILD that is not progressive. The high morbidity of ILD once symptomatic, emergence of more effective treatments, and general preference of the Patient Panel for screening to identify ILD early contributed to our recommendations. Screening may be initiated through shared discussion with the patient. Screening for ILD will typically be initiated by rheumatologists because people with SARDs usually do not see a pulmonologist until after a diagnosis of ILD.

Frequency of testing was also discussed. Guidance on the frequency of testing across diseases was provided to support guideline implementation. This guidance on testing frequency is

not based on evidence but rather expert opinion and patient preferences. Patients with a highly active underlying SARD warrant more frequent monitoring. Pulmonologists generally see more progressive than long-standing, stable disease and prefer more frequent monitoring. Similarly, the Patient Panel expressed that there is "nothing worse than being missed" and strongly preferred more frequent testing to be reassured that their disease is stable. Because the guideline's target population included people with SARDs who have stable ILD as well as those with progressive ILD, it was important to provide a wide and flexible range for frequency of testing that could be tailored to patients' needs. Because the guidance on frequency was based on expert opinion and patient preferences rather than evidence, we aimed for uniformity in our recommendations across diseases to ease implementation. We recognize that the frequency of monitoring will vary based on individual disease presentation and shared decision-making with each patient.

It was challenging for this group to reach consensus on the recommendation for ambulatory oxygen desaturation testing and the frequency of this testing. In people with Raynaud phenomenon, oxygen desaturation testing using a finger probe may not be accurate and, thus, may lead to the inappropriate prescription of supplemental oxygen. In such cases, ear or forehead probes offer potential for greater accuracy. Furthermore, although oxygen desaturation testing is routine practice for pulmonologists, implementation by rheumatologists may be challenging because of logistical considerations, highlighting one of many benefits of collaborative management between rheumatology and pulmonology for patients with SARD-ILD. It was clear that patients value and prefer collaboration and communication among their specialists.

These guidelines are limited by the low certainty of evidence available for review. Most of the questions addressed were supported by small-scale observational studies. In some cases, the evidence was indirect, indicating that the populations and/or interventions investigated in the included studies deviated from those intended for specific questions. Additionally, we did not have any available evidence to examine the relationship between frequency of screening or monitoring and subsequent outcomes. Furthermore, there was a lack of evidence regarding the effects of screening or monitoring on specific subpopulations, such as racial and ethnic minority groups. Finally, we were unable to include other important affected patient groups because the scope of the guideline focused on diseases associated with higher risk of developing ILD. Pediatric patient guidelines were not included given the existing Childhood Interstitial Lung Disease treatment guidance. SLE was not included in this guideline because the treatment of lung involvement most often aligns with treatment of the underlying SLE.[16]

Important questions related to screening and monitoring for ILD warrant further research. First, the frequency of screening and monitoring requires further investigation to ascertain the most cost-effective strategy. Second, on HRCT chest, it is uncertain whether monitoring should differ by histologically based patterns (eg, nonspecific interstitial pneumonia, UIP). Similarly, an improved understanding of risk factors, including expanded autoantibody profiling, to inform ILD screening and monitoring is needed. Together, radiographic patterns, autoantibody profiles, and/or other features may allow for the development of specific screening and monitoring recommendations for subsets of patients with SARD-ILD. In summary, we provide guidelines for tests that are recommended and not recommended for the screening of people with SARDs who are at risk for developing ILD and disease-specific guidelines for tests that are recommended and not recommended for the monitoring of SARD-associated ILD.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published.

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