Optimizing access to care for patients with systemic sclerosis & interstitial lung disease-related complications.

Backgrounder for preliminary consensus meeting

October, 2019

IHE INSTITUTE OF HEALTH ECONOMICS ALBERTA CANADA

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OVERVIEW OF AUTOIMMUNE DISORDERS ASSOCIATED WITH LUNG DISEASE

Interstitial lung disease is an all-encompassing term for diseases that lead to scarring (fibrosis) of the lungs. There are numerous causes, including injury from exposure to hazardous chemicals, dusts or molds; or alternatively due to inflammation from acute or chronic disease. Scarred lung tissue reduces the ability of the lungs to exchange gas, and leads to reduced lung function. While some ILD results in a limited amount of worsening, others are associated with ongoing worsening, or progressive loss of lung function. Progressive ILD is associated with both significant morbidity and premature mortality.

The most common and well-studied form of progressive ILD is idiopathic pulmonary fibrosis (IPF), occurring mainly in adults over 60 years[1]. Some patients with IPF experience rapid loss of function while others much slower functional loss. Current data suggests that 50% of patients die, usually from lung failure, between two and five years from the time of diagnosis, with younger patients typically surviving longer.[2]

Another significant cause of ILD, and leading to progressive disease quite similar to IPF, are those associated with autoimmune and inflammatory disorders. These autoimmune disorders lead to connective tissue disease, and include systemic lupus erythematosus, Sjögrens syndrome, mixed connective tissue disease, Wegener's granulomatosis, Churg-Strauss syndrome, polymyositis/dermatomyositis, rheumatoid arthritis, Goodpasture's syndrome, ankylosing spondylitis, sarcoidosis, rheumatoid arthritis and scleroderma (systemic sclerosis, SSc).[3] Some patients may also exhibit features of autoimmune disorders without a definitive diagnosis.

Current analysis from the US pulmonary fibrosis registry suggests ~15% of patients have ILDs associated with the diagnosis of autoimmune diseases.[4] Of the many autoimmune diseases associated with ILD, systemic sclerosis, and rheumatoid arthritis are more common and much more likely to lead to progressive lung disease.[5] However, both autoimmune disorders have unique features, which can lend to different clinical management and may lend to different health policy approaches..

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[1] Martin Kolb and Martina Vašáková, "The Natural History of Progressive Fibrosing Interstitial Lung Diseases," *Respiratory Research* 20, no. 1 (March 14, 2019): 57, https://doi.org/10.1186/s12931-019-1022-1.

[2] Brett Ley and Harold R. Collard, "Epidemiology of Idiopathic Pulmonary Fibrosis," *Clinical Epidemiology* 5 (November 25, 2013): 483–92, doi:10.2147/CLEP.S54815; American Thoracic Society et al., "Idiopathic Pulmonary Fibrosis: Diagnosis and Treatment. International Consensus Statement," 2000, *http://dspace.iss.it/srdspace/handle/2198/930*.

[3] Manole COJOCARU et al., "Pulmonary Manifestations of Systemic Autoimmune Diseases," *Mædica* 6, no. 3 (July 2011): 224–29.

[4] "PFF Patient Registry | Pulmonary Fibrosis Foundation," accessed October 16, 2019, https://www.pulmonaryfibrosis.org/medical-community/pff-patient-registry.

[5] Vincent Cottin et al., "Presentation, Diagnosis and Clinical Course of the Spectrum of Progressive-Fibrosing Interstitial Lung Diseases," *European Respiratory Review* 27, no. 150 (December 31, 2018): 180076, https://doi.org/10.1183/16000617.0076-2018.

Systemic sclerosis-related progressive interstitial lung disease

Systemic sclerosis (SSc) is an autoimmune rheumatic disease characterized by high mortality, loss of quality-of-life and high unmet need.[6] It is thought to affect 1 in 10,000 people worldwide. The disease is characterized by immune system involvement, similar to other rheumatic diseases (such as rheumatoid arthritis), but more detrimental in terms of premature mortality and worsening of quality of life. Genetic factors similar to other auto-immune conditions along with environmental factors are believed to play a key role in how the disease is acquired.[7]

People with this disease experience inflammation and scarring of connective tissue throughout the body leading to a variety of complications. They may also experience pain, a loss of function, and a feeling of helplessness.[8] A particular challenge in disease management is that signs and symptoms of disease can vary widely, making diagnosis or characterizing disease progression difficult.[9] Because organ involvement usually occurs early in the course of the disease, a wide variety of investigations across several clinical specialty areas may occur. This includes further exploration of gastric symptoms, or the potential for serious cardiac, renal, arterial, or pulmonary disease. (See **Error! Reference source not found.**). Treatments for major complications then vary according to which organs or systems are affected.

An early and important potential complication in patients with SSc is progressive ILD. While lung fibrosis or interstitial lung disease is present in 80% of patients with SSc, fewer - 25-30% of (i.e., 25-30 per 100,000) - patients are thought to develop progressive lung disease (i.e., SSc-ILD).[10] Database studies of patients suggest SSc-ILD is the most frequent cause of SSc-related premature death, causing between 33-35% of all deaths from SSc.[11] While lung function testing can help us understand rates of progression in the long-term, they may not be useful for clinical decision making over the short term. [12]

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[6] Yannick Allanore et al., "Systemic Sclerosis," *Nature Reviews. Disease Primers* 1 (23 2015): 15002, https://doi.org/10.1038/nrdp.2015.2; Christopher P. Denton and Dinesh Khanna, "Systemic Sclerosis," *Lancet (London, England)* 390, no. 10103 (October 7, 2017): 1685–99, https://doi.org/10.1016/S0140-6736(17)30933-9.

[7] Denton and Khanna, "Systemic Sclerosis."

[8] Dinesh Khanna et al., "Health Values of Patients with Systemic Sclerosis," *Arthritis & Rheumatism* 57, no. 1 (February 15, 2007): 86–93, https://doi.org/10.1002/art.22465.

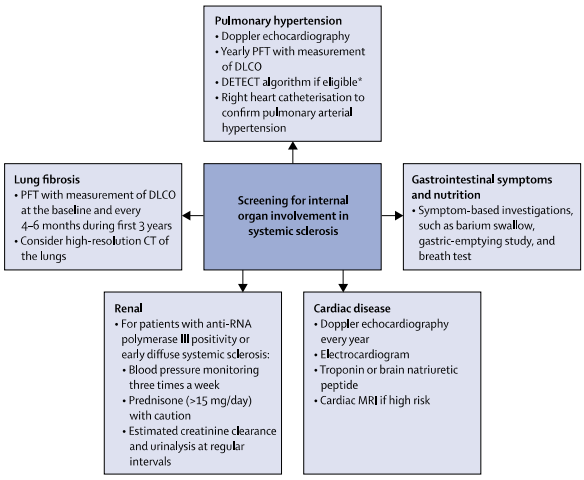
[9] Denton and Khanna, "Systemic Sclerosis."

[10] Denton and Khanna.

[11] Vincent Cottin and Kevin K. Brown, "Interstitial Lung Disease Associated with Systemic Sclerosis (SSc-ILD)," *Respiratory Research* 20, no. 1 (December 2019): 13, https://doi.org/10.1186/s12931-019-0980-7.

[12] Denton and Khanna, "Systemic Sclerosis"; Sabina A. Guler et al., "Does Systemic Sclerosis–Associated Interstitial Lung Disease Burn Out? Specific Phenotypes of Disease Progression," *Annals of the American Thoracic Society; New York* 15, no. 12 (December 2018): 1427–33, http://dx.doi.org.proxy.bib.uottawa.ca/10.1513/AnnalsATS.201806-362OC; Cottin and Brown, "Interstitial Lung Disease Associated with Systemic Sclerosis (SSc-ILD)," December 2019.

Figure 1 Investigations for systemic sclerosis (adapted from Denton and Khanna[13])



Systematic investigation of newly diagnosed cases of systemic sclerosis and during regular follow-up is important to identify complications that might require management. This systematic approach allows proactive management and has been associated with improved overall survival in cohorts of patients with systemic sclerosis.1 *The DETECT algorithm incorporates clinical and laboratory tests, PFTs, and transthoracic echocardiography for early detection of pulmonary arterial hypertension. PFT=pulmonary function test. DLCO=diffusing capacity for carbon monoxide.

Like other complications associated with SSc, the presence of lung disease opens up a wide variety of clinical management strategies. There are no widespread or widely accepted evidence-based clinical practice guidelines for the management of SSc-ILD.[14] However, in a survey of the experts from the Scleroderma Clinical Trials Consortium and the Canadian Scleroderma Research group (n = 170), a majority of Canadian experts see the use of disease-modifying regimens as appropriate with referrals to lung transplantation hematopoietic stem cell transplantation in select (unresponsive and fit) individuals.[15]

Owing to the evolving nature of clinical evidence, guidance in the choice of what drugs should be used first-line to modify the disease course of SSc-ILD has changed. Publication of pivotal clinical trials in 2017[16] has shifted Canadian expert preferences for first line therapy from cyclophosphamide to mycophenolate mofetil, a drug also used for preventing organ rejection after transplant. However, these trials have also left some unanswered questions which will require further study.[17] There may still be widespread disagreement regarding the use of other drugs, such as corticosteroids, and many drug therapies are currently still investigational.[18]

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[13] Denton and Khanna, "Systemic Sclerosis."

[14] Vanessa Smith et al., "Systemic Sclerosis: State of the Art on Clinical Practice Guidelines," *RMD Open* 4, no. Suppl 1 (October 2018): e000782, https://doi.org/10.1136/rmdopen-2018-000782.

[15] Andreu Fernández-Codina et al., "Treatment Algorithms for Systemic Sclerosis According to Experts," *Arthritis & Rheumatology (Hoboken, N.J.)* 70, no. 11 (2018): 1820–28, https://doi.org/10.1002/art.40560.

[16] Elizabeth R. Volkmann et al., "Mycophenolate Mofetil Versus Placebo for Systemic Sclerosis-Related Interstitial Lung Disease: An Analysis of Scleroderma Lung Studies I and II," *Arthritis & Rheumatology (Hoboken, N.J.)* 69, no. 7 (2017): 1451–60, https://doi.org/10.1002/art.40114.

[17] Christopher P. Denton, "Scleroderma Lung Study II-Clarity or Obfuscation?," *The Lancet. Respiratory Medicine* 4, no. 9 (2016): 678–79, https://doi.org/10.1016/S2213-2600(16)30191-6.

[18] Vincent Cottin and Kevin K. Brown, "Interstitial Lung Disease Associated with Systemic Sclerosis (SSc-ILD)," *Respiratory Research* 20, no. 1 (January 18, 2019): 13, https://doi.org/10.1186/s12931-019-0980-7.

Along with these numerous therapeutic interventions, patients with SSc-ILD will also require supportive measures,[19] that might include patient and caregiver education, as well as pulmonary rehabilitation programs- i.e., exercise training, strengthening, nutritional counselling and other measures to improve lung function and promote quality of life and well-being.

Rheumatoid arthritis-related progressive ILD

Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects approximately 300,000 Canadians. It causes pain, swelling, and stiffness in joints as well irreversible damage and scarring to joints and connective tissue. RA can lead to severe disability, loss of independence and have a significant impact on quality of life. While total disease remission before significant damage occurs is a goal of treatment, it is not always achievable, leading some patients to seek enough control over their disease to allow them to live independently and pain-free.

Like SSc, lung disease is a leading cause of death in RA, second only to infection.[20] However this includes other types of lung disease outside of ILD, with ILD being the most common. Evidence of ILD is thought to occur in approximately 10% of RA patients, with an average survival of three years from the time of diagnosis of RA-ILD. For this reason, routine screening for ILD has been recommended during the clinical management of the disease.

An interesting aspect of the management of disease is that the drugs used to modify the disease course can, themselves, lead to drug-induced lung injury. These drugs include both traditional disease modifying anti-rheumatic drugs, such as methotrexate, as well as newer biologic disease modifying anti-rheumatic drugs, such as infliximab.

Unlike systemic sclerosis, treatment for RA-ILD is not well studied, with no randomized controlled trials from which to base clinical decisions about the effectiveness of interventions. This, in turn, makes clinical consensus about the management of illness more challenging.

Patient-centered care and the patient journey

Studies that have explored the experience of diagnosis, treatment and living with RA-ILD and SSc-ILD have identified several emerging themes regarding how they negatively impacts quality of life and health-related quality of life, what unmet needs exist and what outcomes are important to patients.

Impact on quality of life

Rheumatoid arthritis has a significant impact on quality of life due to fatigue, pain, stiffness and impaired physical functioning.[21]It also disproportionately affects certain marginalized groups, including women and those with lower income.

A 2011 Canadian survey of people with SSc identified fatigue, Raynaud's phenomenon, stiff hands, joint pain and sleeping disorders were symptoms experienced at the highest frequency and the most likely to have at

[19] Cottin and Brown, "Interstitial Lung Disease Associated with Systemic Sclerosis (SSc-ILD)," December 2019.

[20] COJOCARU et al., "Pulmonary Manifestations of Systemic Autoimmune Diseases."

[21] Faith Matcham et al., "The Impact of Rheumatoid Arthritis on Quality-of-Life Assessed Using the SF-36: A Systematic Review and Meta-Analysis," *Seminars in Arthritis and Rheumatism* 44, no. 2 (October 2014): 123–30, https://doi.org/10.1016/j.semarthrit.2014.05.001.

least moderate impact on daily activities.[22] Challenges with sleep, and sexual function are also widely observed.[23] Up to half of SSc patients have been observed to experience mild to severe psychological distress, which includes depressive symptoms including anxiety.[24] Impaired hand function (due to Raynaud's, stiffness, ulcers, joint contractures and pain) plays an important role in disability for people with SSc.[25] A recently published study of a European population with SSc also identified difficulty with breathing, muscle weakness and gastrointestinal symptoms as key subjective factors in disability.[26]

In addition to a higher rate of premature mortality compared to other rheumatic diseases[27], health-related quality of life has also been shown to at least as poor, and possibly more poor compared to other autoimmune conditions.[28] Comparisons with systemic lupus erythematosus, Sjogren's syndrome and rheumatoid arthritis in a newly diagnosed Asian population using validated measures and appropriate statistical tests showed a worse perception of HRQL in SSc patients versus other conditions (**Error! Reference source not found.**) A comparison in Canadian patients that also included patients with idiopathic inflammatory myopathies (IIM) corroborated these findings, although also revealed even poorer perceptions of HRQL in people with IIM.[29] A higher proportion of those with newly-diagnosed IIM also have interstitial lung disease, when compared to those with SSc.

[22] Marielle Bassel et al., "Frequency and Impact of Symptoms Experienced by Patients with Systemic Sclerosis: Results from a Canadian National Survey," *Rheumatology* 50, no. 4 (April 1, 2011): 762–67, https://doi.org/10.1093/rheumatology/keq310.

[23] Cristiana Almeida, Isabel Almeida, and Carlos Vasconcelos, "Quality of Life in Systemic Sclerosis," *Autoimmunity Reviews* 14, no. 12 (December 2015): 1087–96, https://doi.org/10.1016/j.autrev.2015.07.012.

[24] Thomas N. Hyphantis et al., "The Impact of Psychological Functioning upon Systemic Sclerosis Patients' Quality of Life," *Seminars in Arthritis and Rheumatism* 37, no. 2 (October 2007): 81–92, https://doi.org/10.1016/j.semarthrit.2007.03.008; Christelle Nguyen et al., "Clinical, Functional and Health-Related Quality of Life Correlates of Clinically Significant Symptoms of Anxiety and Depression in Patients with Systemic Sclerosis: A Cross-Sectional Survey," *PloS One* 9, no. 2 (2014): e90484, https://doi.org/10.1371/journal.pone.0090484.

[25] Linda Kwakkenbos et al., "Reasons for Not Participating in Scleroderma Patient Support Groups: A Comparison of Results from the North American and European Scleroderma Support Group Surveys," *Disability and Rehabilitation*, September 14, 2019, 1–8, https://doi.org/10.1080/09638288.2019.1656292.

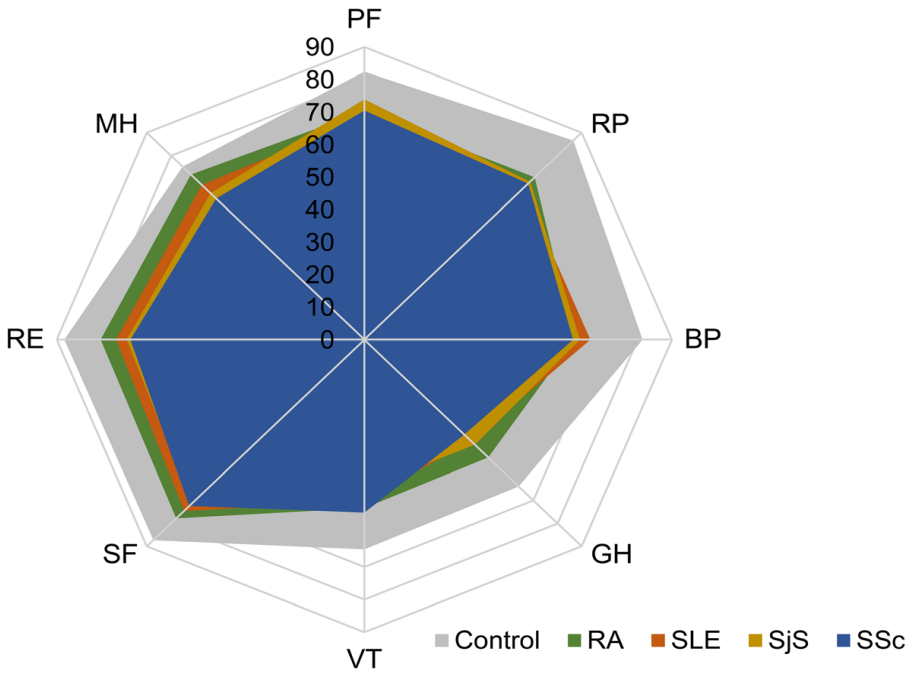
[26] Veronika K. Jaeger et al., "Functional Disability and Its Predictors in Systemic Sclerosis: A Study from the DeSScipher Project within the EUSTAR Group," *Rheumatology (Oxford, England)* 57, no. 3 (01 2018): 441–50, https://doi.org/10.1093/rheumatology/kex182.

[27] Denton and Khanna, "Systemic Sclerosis."

[28] Elisabetta Danieli et al., "Health-Related Quality of Life Measured by the Short Form 36 (SF-36) in Systemic Sclerosis: Correlations with Indexes of Disease Activity and Severity, Disability, and Depressive Symptoms," *Clinical Rheumatology* 24, no. 1 (February 2005): 48–54, https://doi.org/10.1007/s10067-004-0970-z; Sindhu R. Johnson et al., "Quality of Life and Functional Status in Systemic Sclerosis Compared to Other Rheumatic Diseases," *The Journal of Rheumatology* 33, no. 6 (June 2006): 1117–22; Julia Greenfield et al., "A Comparison of Health-Related Quality of Life (HRQoL) across Four Systemic Autoimmune Rheumatic Diseases (SARDs)," *PLoS ONE* 12, no. 12 (December 19, 2017), https://doi.org/10.1371/journal.pone.0189840; Eun Hye Park et al., "Health-Related Quality of Life in Systemic Sclerosis Compared with Other Rheumatic Diseases: A Cross-Sectional Study," *Arthritis Research & Therapy* 21, no. 1 (February 15, 2019): 61, https://doi.org/10.1186/s13075-019-1842-x.

[29] Greenfield et al., "A Comparison of Health-Related Quality of Life (HRQoL) across Four Systemic Autoimmune Rheumatic Diseases (SARDs)."

Figure 2 Comparison across domains of health-related quality of life in newly diagnosed autoimmune conditions from Park[ref]



Legend: Comparison of the SF-36 subscales adjusted by age and sex. SF-36, Short Form (36) health survey; SSc, systemic sclerosis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SjS, Sjogren's syndrome; PF, physical function; RP, role–physical; BP, bodily pain; GH, general health perception; VT, vitality; SF, social function; RE, role–emotional; MH, mental health. Higher scores indicate better health-related quality of life.

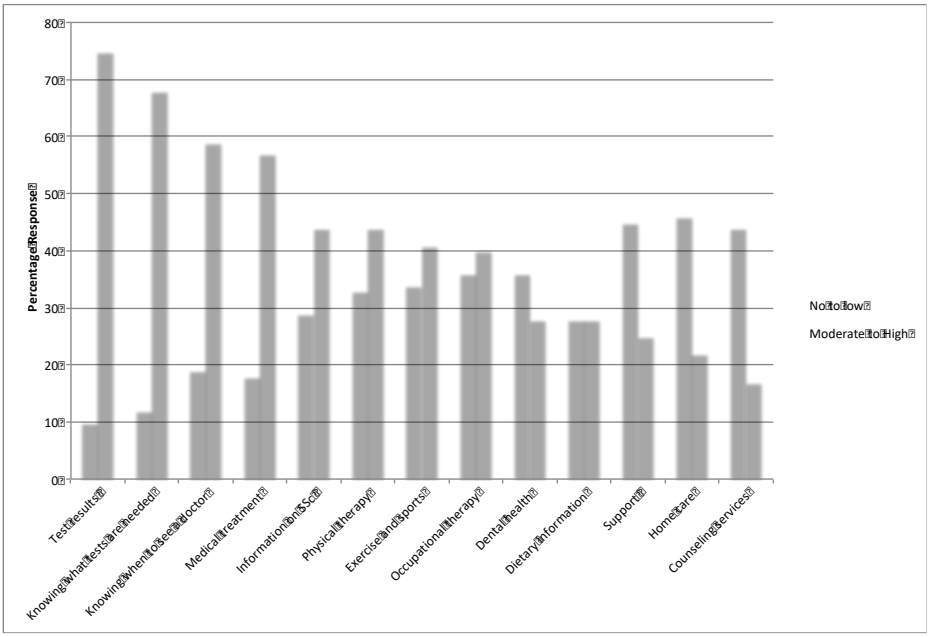
Unmet needs

The needs of people diagnosed with autoimmune conditions can be viewed as reflecting their diagnostic / patient care journey as well as underlying complications. This includes support via psychological and coping interventions to manage symptoms of psychological distress (and their underlying factors), as well as occupational and physical therapy for hand function and disability.[30] These needs have been reflected in previous surveys of European and US SSc patients, where better health service navigation and information,

[30] Almeida, Almeida, and Vasconcelos, "Quality of Life in Systemic Sclerosis."

followed by a high need for physical and occupational rehabilitation have also been identified[31] (Figure 3) The desire for disease-related information has also been reflected in a survey of Canadian patients.[32]

Figure 3 Type of information needs identified by 64 Dutch SSc patients



Patient Support and Information

Like other patients with severe or debilitating diseases, patients with autoimmune conditions require support for the physical, psychological, and emotional aspects of living with the disease.[33] For SSc, research has indicated that while patients see rheumatologists as the preferred provider of medical information, patients may face additional physical or psychological problems that are not sufficiently addressed by rheumatologists.[34]

[31] Anne Schouffoer et al., "The Educational Needs of People with Systemic Sclerosis: A Cross-Sectional Study Using the Dutch Version of the Educational Needs Assessment Tool (D-ENAT)," *Rheumatology International* 36, no. 2 (February 2016): 289–94, https://doi.org/10.1007/s00296-015-3352-8; Tamara T. Rubenzik and Chris T. Derk, "Unmet Patient Needs in Systemic Sclerosis," *Journal of Clinical Rheumatology: Practical Reports on Rheumatic & Musculoskeletal Diseases* 15, no. 3 (April 2009): 106–10, https://doi.org/10.1097/RHU.0b013e31819dbe83.

[32] Teresa Semalulu, Karen A. Beattie, and Maggie J. Larché, "Assessing the Educational Needs of Canadians with Systemic Sclerosis," *The Journal of Rheumatology* 46, no. 6 (June 2019): 658–59, https://doi.org/10.3899/jrheum.180554.

[33] Danielle B. Rice and Brett D. Thombs, "Support Groups in Scleroderma," *Current Rheumatology Reports* 21, no. 4 (February 21, 2019): 9, https://doi.org/10.1007/s11926-019-0808-y.

[34] Schouffoer et al., "The Educational Needs of People with Systemic Sclerosis."

This additional support can be derived from psychological counselling, close social relationships[35] or the use of patient support groups[36], which provide patients and care givers with information and educational resources to help them better manage these aspects of disease. Patients may also benefit from information and resources that help patients learn to "communicate and advocate more effectively."[37]

In addition to the need for information, navigation, psychological and physical rehabilitation required by newly diagnosed RA and SSc patients, patients diagnosed with progressive ILD will require further support through that includes pulmonary rehabilitation and palliative care measures. While there is a recognized need for these supportive measures, there is also very little evidence supporting their use (see section, Treatment options).[38] They may also be confronted with co-morbidities or complications of pharmacologic measures, or high-risk surgical and treatment interventions (i.e., lung transplant, hematopoietic stem cell transplant). [39]

The Patient Journey

Given the demands on the health care system that optimal care (diagnosis, treatment, support) represents, the patient journey requires substantial time and healthcare resources. In a global (US, Japan, Germany, France, Italy, Spain, and UK) survey of 486 physicians (243 respirologists, 203 rheumatologists, 40 internists), it was estimated that SSc-ILD is typically diagnosed 8.6 to 11.5 months after symptoms develop.[40] The patient journey requires multiple consultations across multiple specialty areas. Extended time to diagnosis may be of concern for patients or care providers who need to recognize and manage complications from SSc early. A patient pathway based on this research[40] is depicted in Figure 4.

Patient journeys in rheumatoid arthritis follow a similar course, with frustration over disability, negative impacts on personal relationships, reduced productivity and the need for education featuring highly as unmet needs.[41] Similar lag times to diagnosis and treatment have also been reported in RA.[42] The need for followup, referral, tests and awaiting definitive diagnoses also feature prominently.

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[35] Katherine Milette et al., "Scleroderma Patient Perspectives on Social Support from Close Social Relationships," *Disability and Rehabilitation*, February 14, 2019, 1–11, https://doi.org/10.1080/09638288.2018.1531151.

[36] Rice and Thombs, "Support Groups in Scleroderma."

[37] Milette et al., "Scleroderma Patient Perspectives on Social Support from Close Social Relationships."

[38] Linda M. Willems et al., "Effectiveness of Nonpharmacologic Interventions in Systemic Sclerosis: A Systematic Review," *Arthritis Care & Research* 67, no. 10 (October 2015): 1426–39, https://doi.org/10.1002/acr.22595.

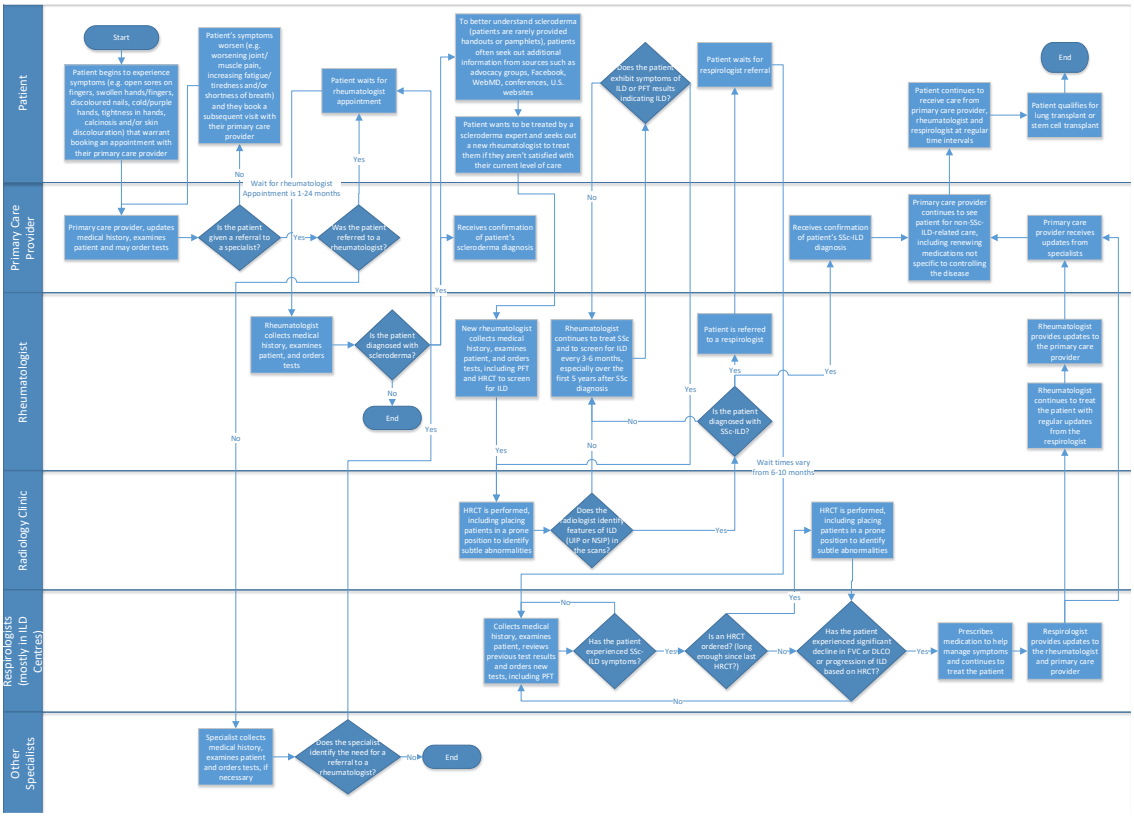
[39] Cottin and Brown, "Interstitial Lung Disease Associated with Systemic Sclerosis (SSc-ILD)," December 2019.

[40] "Canadian Rheumatology Association Meeting Fairmont The Queen Elizabeth Montreal, Quebec, Canada February 27 – March 2, 2019," *The Journal of Rheumatology* 46, no. 7 (July 1, 2019): 757–865, https://doi.org/10.3899/jrheum.190333.#33 Non-IPF Progressive Fibrosing Interstitial Lung Disease (PF-ILD): The Patient Journey

[41] "Living with Rheumatoid Arthritis | RA Matters," accessed October 16, 2019, https://ramatters.ca/.

[42] Alaa S. Barhamain et al., "The Journey of Rheumatoid Arthritis Patients: A Review of Reported Lag Times from the Onset of Symptoms," *Open Access Rheumatology: Research and Reviews* 9 (2017): 139–50, https://doi.org/10.2147/OARRR.S138830; Javier E. Rosa et al., "Rheumatoid Arthritis Patient's Journey: Delay in Diagnosis and Treatment," *Journal of Clinical Rheumatology: Practical Reports on Rheumatic & Musculoskeletal Diseases*, October 11, 2019, https://doi.org/10.1097/RHU.0000000000001196.

Figure 4 The patient journey in SSc-ILD



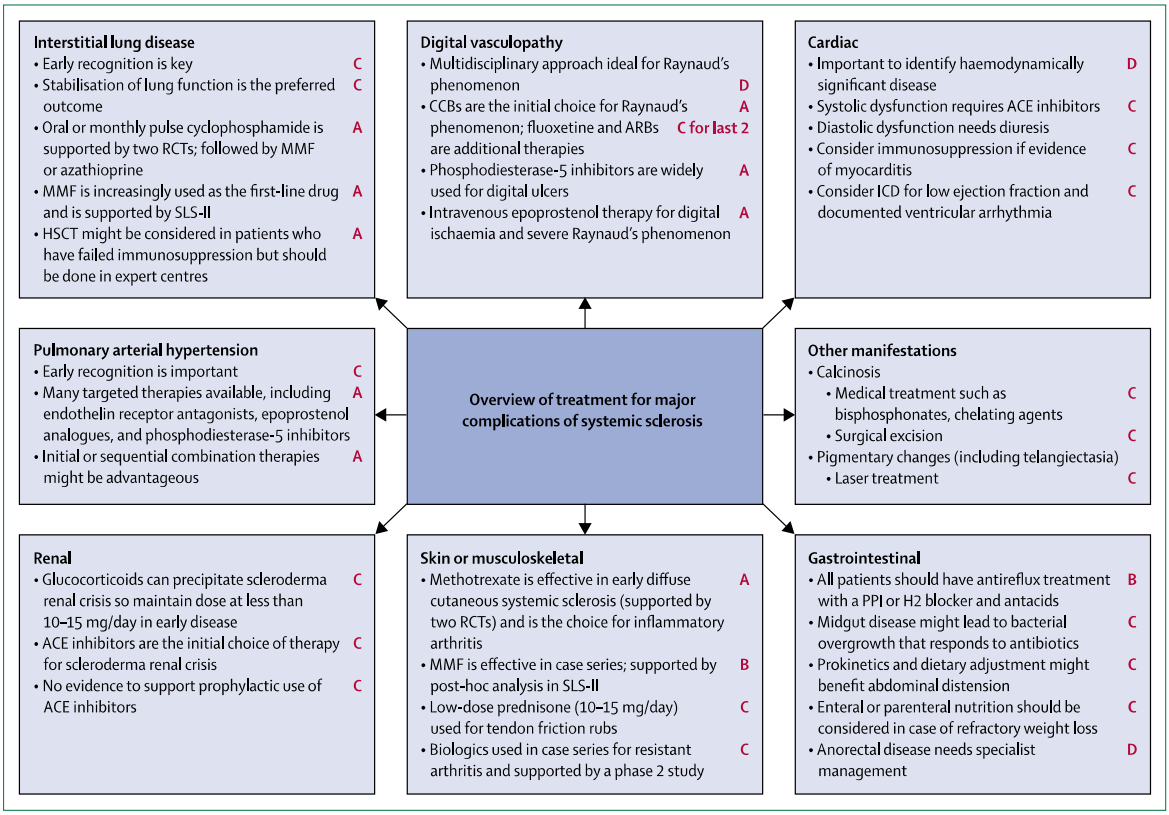
Treatment options and guidelines

Effectiveness

Treatments for SSc and SSc-ILD can be characterized as pharmacologic or non-pharmacologic and are typically designed to manage the various complications and manifestations of having SSc. (Figure 5) This includes therapies for the more obvious and debilitating manifestations of disease such as Raynaud's phenomenon and digital ulcers that include vasodilator therapy, lifestyle modification, smoking cessation, managing stress, and reducing exposure to medications or conditions that promote vasoconstriction. A challenge for clinicians is that many therapies are poorly tolerated, treatments may lack a SSc-specific indication or strong underlying evidence base, or have limited effectiveness even if they do.[43] Other possible challenges are an evolving evidence base, lack of Canadian consensus guidelines, and the use of investigational treatments, which requires further patient management.

[43] Kwakkenbos et al., "Reasons for Not Participating in Scleroderma Patient Support Groups."

Figure 5 Overview of treatments for major complications due to SSc



Summary of the key aspects of treatment for individual complications of systemic sclerosis, as informed by authors' opinions and the updated EULAR recommendations in 2017.[70] The strengths of recommendations (where A is the highest level of evidence and D is based on expert opinion) are provided based on the 2014 update of the EULAR standardised operating procedures for EULAR-endorsed recommendations.[74] EULAR=European League Against Rheumatism. RCT=randomised controlled trial. MMF=mycophenolate mofetil. sGC=soluble guanylate cyclase. CCBs=calcium channel blockers. ARB=angiotensin receptor blockers. ACE=angiotensin converting enzyme. SLS-II=Scleroderma Lung Study-II. HSCT=haemopoietic stem-cell transplantation. ICD=implantable cardioverter defibrillator. PPI=proton pump inhibitor.

Nonetheless, there appears to be some moderate consensus by Canadian clinical experts in regards to what therapeutic algorithms should be used. A survey of experts from the Scleroderma Clinical Trials Consortium (SCTC) and/or in the Canadian Scleroderma Research Group (CSRG) showed increased agreement from 2012, when international consensus guidelines were first developed.[44] Consensus opinion for SSC-ILD includes initial (induction) therapy with mycophenolate mofetil (MMF) first line (69% agreement), intravenous cyclophosphamide second line (69%), rituximab third-line (42%) and lung or hematopoetic stem cell transplant in qualified patients as a fourth line measure. This is then followed by a longer term (maintenance) regimen of either MMF 1st line (92%), azathioprine second-line, or oral cyclophosphamide 3rd line (62%).[45]

[44] Fernández-Codina et al., "Treatment Algorithms for Systemic Sclerosis According to Experts."

[45] Fernández-Codina et al.

Current consensus treatment guidelines in rheumatoid arthritis largely focus on reducing disease activity through the use of disease-modifying drugs and do not address lung manifestations or screening for ILD directly. The guidelines do suggest chest radiography needs to be avoided in those taking methotrexate due to an interaction between methotrexate and ionizing radiation. This may present a challenge in assessing risk of ILD or disease progression by respiratory specialists. Unlike SSc, RA has fewer internal organ manifestations and a longer average time to ILD manifestations.

What current initiatives exist for patients in Canada?

People with systemic sclerosis in Canada has benefitted from numerous research and policy initiatives including:

Scleroderma Canada: A registered charity established in 1999, Scleroderma Canada is Canada's National patient organization working closely with international organizations and six regional Canadian affiliates to provide support, research, education and other services to those with systemic sclerosis.

The Scleroderma Patient-centered Intervention Network (SPIN): "An organization of researchers, health care providers, and people living with scleroderma from around the world." SPIN brings patients together with care providers and researchers to conduct patient-centered research with a large network of international collaborators. Established in 2012 with the goal , " to develop, test, and disseminate a set of accessible interventions designed to complement standard care in order to improve health-related quality of life outcomes in SSc."[46]

Canadian Scleroderma Research Group : Founded in 2003, a consortium of multispecialty researchers who have created a detailed longitudinal database of 1500 patients as well as a biobank initiative.

Arthritis Society: Founded in 1948, the Arthritis Society of Canada (ASC) stated mission is to invest invests in arthritis research, advocate and provide innovative solutions in order to deliver better health outcomes and quality of life for people affected by arthritis. Arthritis Society of Canada runs support and education programs for people affected by arthritis.

Canadian Rheumatology Association: The stated mission of the CRA is "to represent Canadian rheumatologists and promote the pursuit of excellence in arthritis and rheumatic disease care, education and research." The CRA serves "as a national voice for practicing rheumatologists and researchers with an interest in rheumatic disease."

Canadian Arthritis Patient Alliance: The stared mission of CAPA is to "Improve access to medications, health care professionals, and services, increase patient involvement in arthritis research and policy agendas, and understand and influence research and treatments."

[46] Brett D. Thombs et al., "New Directions for Patient-Centred Care in Scleroderma: The Scleroderma Patient-Centred Intervention Network (SPIN)," *Clinical and Experimental Rheumatology* 30, no. 2 Suppl 71 (April 2012): S23-29.

Arthritis Consumer Experts: ACE is a "Arthritis Consumer Experts (ACE) is a national, patient-led organization that provides free, science-based information and education programs in both official languages to people with arthritis."

Issues and potential solutions to optimize care

Given the evolving understanding of autoimmune-associated ILD, including the development of new treatments for progressive disease, there may be several opportunities to develop policy-relevant tools that can contribute to the optimal care and management of patients. These might include:

- **Scope of practice and referral standards** – these diseases highlight the need for efficient care navigation between therapeutic specialty areas. There may be opportunities to promote better practices that optimize the time to diagnosis and treatment of patients

- **Consensus guidelines**– while there appears to be some consensus in SSc-ILD based on a recent survey, there are no formal, comprehensive Canadian consensus-based guidelines in this area. There are also no consensus-based guidelines for RA-ILD.

- **Patient charter** – While a Charter, outlining recommendations for provincial governments, institutions and healthcare organizations to improve patients' overall quality of life, and support efforts for targeted research to develop better long-term treatments, has been developed for IPF[47], no such Charter has been developed or adapted for autoimmune-associated ILD.

- **Patient journey maps** – A global patient journey has been described for SSc-ILD but no Canadian-specific map exists. Similarly, an RA map has been developed but does not illustrate the journey of the patient with RA-ILD.

- **Educational tools –** As education has been identified as a priority unmet need for patients with autoimmune disease, specific tools for patients with progressive ILD may be of use.

Planning a forum in 2021 means some work could be done towards the preliminary development of these tools., The forum can then be an opportunity to discuss these priorities or determine further ones.

[47] "CPFF Patient Charter – Canadian Pulmonary Fibrosis Foundation," accessed October 16, 2019, https://cpff.ca/get-involved/advocate/cpff-patient-charter/.