# Management and burden of disease of SSc-ILD in eight European countries: Results of the BUILDup project

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## INTRODUCTION

Between 30% and 70% of systemic sclerosis (SSc) patients suffer from interstitial lung disease (SSc-ILD)[1]. ILD is the leading cause of death in SSc patients, accounting for up to 35% of SSc-related mortality[2], and with a three times higher mortality risk in SSc-ILD patients compared to SSc patients without ILD[3].

Little is known about the treatment path, and the related economic and social burden of SSc-ILD. The aim of the BUILDup study (BUrden of Interstitial Lung Disease Consensus Panel) was to reach consensus on the current management of the disease and to estimate the healthcare resources used (HCRU), cost and social burden of SSc-ILD patients across eight European countries.

## METHODS

A modified DELPHI methodology was used to understand the management, resources used and economic burden of: Patient's diagnosis, monitoring (including treatment), exacerbations and end of life care. The study involved 8 European countries: Belgium, Denmark, Finland, Greece, Netherlands, Norway, Portugal and Sweden. Two types of SSc-ILD were differentiated according to Goh, et al. classification[4]: 1) limited (SSc-L-ILD), and 2) extensive (SSc-E-ILD). An online questionnaire was sent in two waves to pulmonologists and rheumatologists during February and June 2019. All questions where consensus was not reached in the first round were repeated in a second wave. Resources' costs were obtained through national database and literature search.

## RESULTS

Forty healthcare providers, including 32 pulmonologists and 8 rheumatologists, participated in the study and treated on average 20 SSc-ILD patients yearly; of these, 39.1% were classified as having limited disease and 60.9% as extensive disease.

**Diagnosis:** Mean time from ILD symptoms onset to definite SSc ILD diagnosis was 2.1 years. By order of relevance, the most important professionals involved in definite diagnosis of SSc-ILD were rheumatologists, pulmonologists, and internal medicine physicians.

When considering the resources routinely used in their clinical practice to obtain diagnosis of SSc-ILD, panellists indicated a mean of 4.2 outpatient visits, 9.2 laboratory tests, and 9.5 other tests in total (Table 1).

**Table 1. HCRU for the diagnosis of SSc-ILD**

| | Mean HCRU [Q1-Q3] |
|---|---|
| **Number of outpatient visits** | **4.2 [3-5]** |
| Rheumatologists | 2.2 [2-3] |
| Pulmonologists | 1.8 [2-2] |
| Dermatologists | 0.4 [0-1] |
| **Number of lab tests** | **9.2 [7-9]** |
| Complete blood count | 1.4 [1-2] |
| Antinuclear antibodies | 1.2 [1-4] |
| Hepatic profile | 1.2 [1-1] |
| CPK | 1.1 [1-1] |
| Rheumatoid factor | 1.1 [1-1] |
| Sedimentation rate | 1.1 [1-1] |
| Others | 2.6 [1-3] |

| | Mean HCRU [Q1-Q3] |
|---|---|
| **Number of imaging & other tests** | **9.5 [6-12]** |
| Diffusing capacity for carbon monoxide | 1.5 [1-2] |
| Spirometry | 1.3 [1-2] |
| HRCT | 1.2 [1-2] |
| Body plethysmography | 1.1 [1-1] |
| Chest X-Ray | 1.0 [1-1] |
| 6-minute walk test | 1.0 [1-1] |
| Blood gases | 0.7 [0-1] |
| Bronchoscopy | 0.5 [0-1] |
| Bronchoalveolar lavage | 0.5 [0-1] |
| Others | 1.1 [0-2] |

**Monitoring and treatment:** Rheumatologists, pulmonologists and cardiologists were specified as the most involved professionals in SSc-ILD follow-up for both extensive and limited SSc-ILD. The proportion of panellists indicating treatment initiation of SSc-ILD at diagnosis was 32.8%. 42.3% waited until signs of deterioration/progression and 24.7% until the disease became extensive.

HCRU for patients' monitoring were reported to be higher for the extensive form of the disease (Table 2).

Regarding the maintenance treatment, 40% of the panelists followed a "watch and wait" approach for SSc-L-ILD vs. 20% for SSc-E-ILD.

Regarding the pharmacological drug used, mycophenolate mofetil was stated as the main option for treating these patients, followed by systemic corticosteroids and cyclophosphamide (Table 2)

**Table 2. HCRU for the monitoring of SSc-ILD**

| | Mean [Q1-Q3] Limited | Mean [Q1-Q3] Extensive |
|---|---|---|
| **Number of outpatient visits** | **5.3 [4-6]** | **7.5 [5-9]** |
| **Number of lab tests** | **9.2 [6-12]** | **13.2 [10-18]** |
| **Number of imaging & other tests** | **8.9 [6-12]** | **14.3 [10-18]** |
| **Number of hospital admissions** | **0.5 [0-1]** | **2.6 [1-4]** |
| Duration of admissions ( total of days) | 5.1 [4-6] | 13.6 [8-18] |
| **Lung transplant rate** (% of patients) | **0.1% [0-1]** | **1.5% [0-1]** |
| **Long term oxygen** (% of patients) | **3.5% [4-4]** | **11.7% [8-14]** |
| **Number of rehabilitation sessions** | **0.5 [0-1]** | **5.5 [0-10]** |
| **Maintenance treatment** (% of patients) | | |
| No treatment. Watch and wait | 26.1% | 5.5% |
| Mycophenolate mofetil | 35.4% | 64.5% |
| Systemic corticosteroid | 10.6% | 30.5% |
| Cyclophosphamide | 9.1% | 27.7% |
| Methotrexate | 5.0% | 2.8% |
| Hydroxychloroquine | 4.7% | 2.0% |
| Rituximab | 3.8% | 13.1% |
| Azathioprine | 3.4% | 10.3% |
| Other | 2.2% | 1.8% |

**Exacerbations:** These events were more common in patients with extensive than limited disease (12.5% Vs. 2.5%). After an exacerbation, 31% of patients stabilized and recovered under previous health status. HCRU for the management of an exacerbation and its 6-month follow-up management included hospitalisations (mean=1.7), outpatient visits (mean=4.4), laboratory tests (mean=8.9), and imaging and other tests (mean=10.6).

**Table 3. HCRU for exacerbation management**

| | Mean [Q1-Q3] |
|---|---|
| **Number of outpatient visits** | 4.4 [2-6] |
| **Number of lab tests** | 8.9 [6-12] |
| **Number of imaging & other tests** | 10.6 [6-16] |
| **Number of hospital admissions** | 1.7 [1-2] |
| Duration of admissions ( total of days) | 15.3 [9-22] |
| **Exacerbation treatment** (% of patients) | |
| Prednisone | 34.8% |
| Methylprednisolone | 17.9% |
| Prednisone + Methylprednisolone sequentially | 1.7% |
| Other | 8.8% |

**End of life care:** Panellists reported that the mean duration of palliative care was 5.8 months, taking part mostly at home (37.8%) or in hospitals (36.2%), but also in nursing homes (11.1%), at intensive care units (6.6%), and other places (4.5%).

**Economic burden of disease:** The total yearly cost of SSc-ILD was calculated by summing diagnosis, monitoring, and exacerbation events. The average total yearly cost of the disease was estimated at €13,495 (Figure 1). Additionally, end of life care amounted to €2.769.

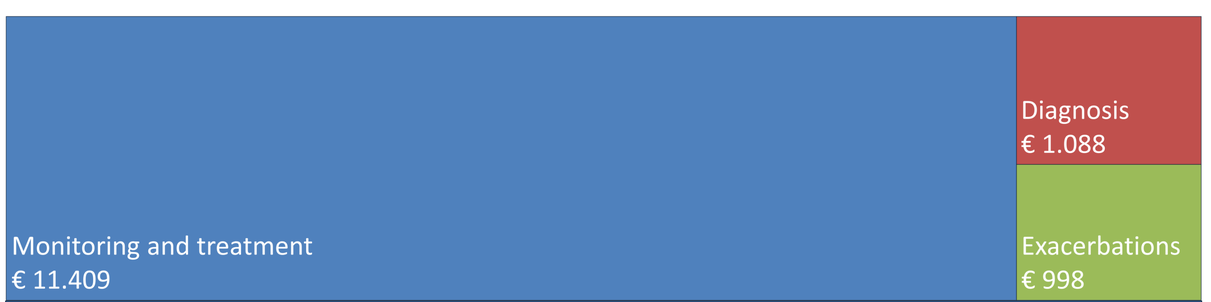


**Figure 1. Breakdown of the average yearly cost of SSc-ILD**

**Impact on quality of life:** SSc-ILD patients experience fatigue and depression, as well as significant impacts on their well-being and productivity. The latter includes retirement, sick leaves and job loss. SSc-ILD patients usually require support from a caregiver, being mostly a family member. These caregivers also experience an impact on quality of life (sleep & health, emotional impact, social impact, impact on daily activities and financial impact) (Figure 2).

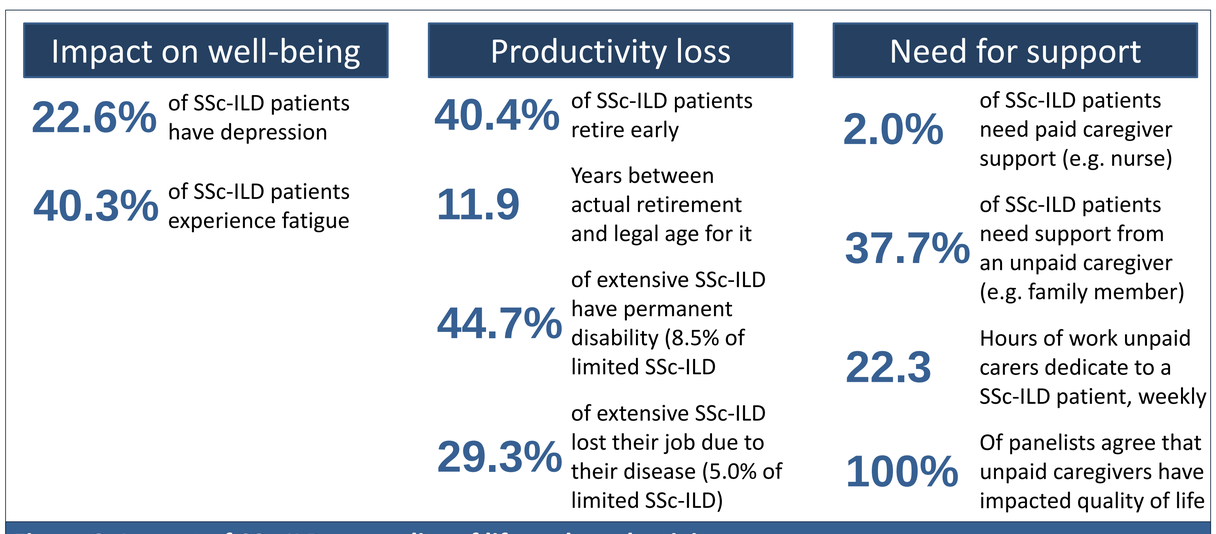


**Figure 2. Impact of SSc-ILD on quality of life and productivity**

## CONCLUSIONS

SSc ILD represents a clinical and economic burden for patients. Not limited to this, caregivers, healthcare systems and society are also impacted by the disease. In our study, the burden of disease increases with the severity of ILD.

## FUNDING & CONFLICTS OF INTEREST

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