Detection of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease using home monitoring in the Netherlands (DecreaSSc) a prospective, observational study

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Summary

Background In patients with systemic sclerosis, interstitial lung disease (ILD) is the leading cause of mortality. Early detection of progressive ILD associated with systemic sclerosis is warranted for timely adjustment of management strategies and improved prognosis. We aimed to investigate the validity of home spirometry to detect a decline in pulmonary function in patients with systemic sclerosis-associated ILD.

Methods DecreaSSc was a prospective, observational study done in two tertiary referral centres in the Netherlands. Eligible patients were aged 18 years or older, fulfilled the American College of Rheumatology–European Alliance of Associations for Rheumatology criteria for systemic sclerosis, had a disease duration from first non-Raynaud phenomenon symptom of 5 years or less, had high-resolution CT-confirmed diagnosis of ILD, and had a maximum immunosuppressive treatment duration of 8 weeks at baseline. Patients took weekly home spirometry measurements using a handheld spirometer for 1 year. At baseline and at semi-annual study visits, patients pulmonary function testing was done in the hospital and patients completed questionnaires on patient-reported outcome measurements. The primary outcome was the κ agreement between home and hospital measurements after 1 year to detect a decline in force vital capacity (FVC) of 5% or more, estimated using separate linear regression analyses for home-based and hospital-based FVC% predicted in individual patients. The sensitivity and specificity of home spirometry to detect an absolute decline in FVC% predicted of 5% or more was assessed using the hospital pulmonary function test as the gold standard. The longitudinal correlation between hospital and home measurements was assessed with regression analysis, whereas the cross-sectional correlation was assessed with the intraclass coefficient. People with lived experience were involved at several stages of the study.

Findings Between Jan 26, 2021, and Feb 27, 2023, 43 patients were enrolled, 35 of whom completed 6 months of follow-up and 31 of whom completed 12 months of follow-up. The last follow-up visit took place on March 28, 2024. 20 (57%) of patients were women and 15 (43%) were men; 32 (91%) were White. Mean age was 57·7 years (SD 10·7). The agreement between hospital and home measurements had a κ value of 0·40 (95% CI 0·01–0·79). The sensitivity of home spirometry to detect a decline in FVC% predicted of 5% or more was 60% (95% CI 44–76) and specificity was 87% (75–98). Regression analysis showed that the course of pulmonary function was not different between hospital and home assessment as the interaction term was not significant (–0·0003 [95% CI –0·0006 to 0·000008]; p=0·057) with a longitudinal correlation of 0·55 (95% CI 0·26–0·74; p=0·0070). The intraclass coefficient between both measurements was 0·85 (95% CI 0·73–0·92; p<0·0001) at baseline, 0·84 (0·71–0·92; p<0·0001) at 6 months, and 0·72 (0·50–0·86; p<0·0001) at 12 months.

Interpretation Home spirometry has the potential to detect a decline in pulmonary function in patients with systemic sclerosis-associated ILD earlier when used in addition to regular health care management. Future research could reveal whether home spirometry can contribute to improved outcomes of patients with systemic sclerosis-associated ILD.

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Introduction

Systemic sclerosis is a heterogeneous autoimmune disease characterised by a triad of inflammation, vascular damage, and fibrosis.[1] Different organ systems might be affected to a varying degree, causing increased morbidity and mortality.[1] Interstitial lung disease (ILD) associated with systemic sclerosis is an important complication that leads to reduced quality of life and represents the most frequent cause of disease-related mortality in patients with systemic sclerosis.[2]

Research in context

Evidence before this study

Interstitial lung disease (ILD) is the leading cause of mortality in people with systemic sclerosis and for the majority of patients there is no curative treatment available. A high-resolution CT scan is the gold standard to diagnose ILD. In clinical practice, regular monitoring of pulmonary function is often used to detect progressive ILD, which is suboptimal given that hospital pulmonary function tests are hampered by measurement variability and patients are required to visit the hospital often. Telemonitoring might be a viable alternative; therefore, we searched PubMed from Jan 1, 2010, to Jan 1, 2021, for publications in English using the following search terms "home spirometry" OR "home monitoring" AND "interstitial lung disease" OR "Idiopathic pulmonary fibrosis" and filtered the results by clinical trials. An increasing number of prospective observational studies, as well as randomised controlled trials, using daily handheld spirometry have been performed in patients with pulmonary fibrosis to evaluate disease course. These studies showed that home spirometry is feasible in patients with idiopathic pulmonary fibrosis, and might allow better disease prediction and decrease sample size for future trials. The cross-sectional correlation between home and hospital measurements was very high in patients with idiopathic pulmonary fibrosis and sarcoidosis (r=0·90–0·97). With respect to the longitudinal correlation, some studies reported a weak correlation, while other studies reported a moderate correlation. No previous studies examined the validity of home spirometry to detect progressive ILD in patients with systemic sclerosis. Given that patients with systemic sclerosis might have difficulties with home spirometry due to skin fibrosis and limited hand function, we first performed a pilot study in which we established that home spirometry is feasible in patients with systemic sclerosis.

Added value of this study

This study was a two-centre, prospective cohort study assessing the validity of home spirometry to detect a decline in pulmonary function in patients with systemic sclerosis-associated ILD. In line with previous studies, we showed a moderate to high cross-sectional correlation between home and hospital measurements. However, the longitudinal agreement between home and hospital measurements was lower. Moreover, the sensitivity of home spirometry to detect a decline in pulmonary function was relatively low. Nonetheless, visual inspection of the data suggests that home spirometry might provide a more granular overview of pulmonary function than hospital measurements. Future research is warranted to establish the validity of this statement.

Implications of all the available evidence

Although these results do not support replacing hospital pulmonary function tests with home spirometry, they do support further evaluation of the implementation of home spirometry in addition to usual health care. This type of tight monitoring might help to detect progressive disease earlier and improve treatment strategies. Future studies with improved study designs are warranted to optimise the added value of home spirometry.

Systemic sclerosis-associated ILD typically occurs in the initial 3–5 years after disease onset, with reported incidence varying between 30% and 50%.[3,4] The course of systemic sclerosis-associated ILD is heterogeneous. Some patients will have stable disease without any treatment, whereas other patients might have rapid or slow progressive ILD.[5] The annual incidence of progressive ILD associated with systemic sclerosis is 30%, with a major decline in forced vital capacity (FVC) occurring in approximately half of patients within 3 years after diagnosis.[6,7]

It is recommended to treat patients with severe or progressive ILD associated with systemic sclerosis with immunosuppressive treatment, with the aim of halting further progression, as well as antifibrotic drugs in individuals with progression despite immunosuppression.[8,9] A high-resolution CT scan at diagnosis of systemic sclerosis is recommended for screening of ILD. Regular pulmonary function tests are also often used to monitor progression of ILD. Although FVC is an accepted surrogate marker for decline in pulmonary function, it is hampered by variability in measurements.[3,10] Furthermore, the decline might occur between hospital visits as the disease course is unpredictable and can be easily missed.

In the past decade, research has shown that home spirometry is feasible and reliable for most patients with ILD.[11] The first clinical trial using home spirometry in patients with idiopathic pulmonary fibrosis (IPF) showed a good agreement between hospital and home measured FVC, and reported that FVC change at 3 months as measured by home spirometry was predictive of progressive disease.[12] Several other single-centre studies in patients with IPF reported a high cross-sectional correlation between hospital and home spirometry measurements (r=0·90–0·97).[13–15] For the longitudinal correlation, the INMARK trial reported a weak correlation between home and hospital rates of change in FVC (r=0·26 for decline in FVC during 52 weeks) in patients with IPF.[16] However, a randomised controlled trial in patients with IPF showed that the rates of change in FVC over time between hospital and home measurements were similar during a follow-up period of 24 weeks (r=0·96, p<0·001).[17] In patients with fibrotic ILD, two studies reported a strong cross-sectional correlation between hospital and home spirometry measurements,[18,19] although a moderate correlation was reported for the change in FVC (r=0·44).[18] In patients with sarcoidosis and asbestosis, home spirometry has

been reported to provide reliable results.[20–22] Three clinical trials including home spirometry as the primary outcome measure faced problems with their analysis due to technical and analytical issues.[23–25]

Based on learnings from previous studies—technical and analytical improvements, as well as the assumption that home monitoring enables the collection of a greater number of datapoints, potentially providing a comprehensive perspective of disease progression to inform treatment decisions—it was hypothesised that in patients with systemic sclerosis-associated ILD, home spirometry could serve as an effective method for timely identification of progressive disease.[11] Moreover, home monitoring allows the online collection of patient-reported outcomes, providing valuable insight into patients' experience of disease, which is essential for clinical practice and clinical trials.[26,27] Findings from our pilot study showed that home spirometry is feasible in patients with systemic sclerosis-associated ILD.[28] Here, we aimed to investigate the validity of home spirometry to detect progressive systemic sclerosis-associated ILD, defined as an absolute decline in FVC% predicted of 5% or more. We also aimed to evaluate the association between decline in both hospital-based and home-based FVC and symptoms and health status assessed with patient-reported outcome measures and 6-min walking tests (6MWTs).

Methods

Study design and patients

DecreaSSc was a prospective, observational study done at the Department of Rheumatology of Radboud University Medical Center in Nijmegen and the Department of Rheumatology of Leiden University Medical Center in Leiden, both tertiary referral centres for systemic sclerosis in the Netherlands. All patients visiting these two rheumatology departments between Jan 26, 2021, and Feb 27, 2023, were screened for eligibility, and were enrolled in the study if they met the eligibility criteria. Eligible patients were aged 18 years or older, fulfilled the American College of Rheumatology–European Alliance of Associations for Rheumatology criteria for systemic sclerosis,[29] had a disease duration from first non-Raynaud phenomenon symptom of 5 years or less, had high-resolution CT-confirmed diagnosis of ILD, and had a maximum immunosuppressive treatment duration of 8 weeks at baseline. A treatment duration of 8 weeks was allowed because there is no major effect of immunosuppressive treatment expected in this period. Patients not able to speak, read, or write in Dutch, who did not have access to a compatible device, or with no internet or mobile phone network access were excluded.

The study was conducted in accordance with the Declaration of Helsinki, and the Institutional Review Board of the Radboud University Medical Centre, Nijmegen, determined that the study was not subject to the Dutch Medical Research Involving Human Subjects Act (file number 2020-7066). All participants gave written informed consent.

We involved two individuals with systemic sclerosis-associated ILD in the development of the study design, selection of outcome measures, and planning of patient recruitment. One of these individuals also had experience conducting pulmonary function tests at home using the application implemented in this study.

Procedures

We used the CE-marked home monitoring application ILD-online (Curavista, Geertruidenberg, Netherlands), which is a secured online application integrated with home spirometry using a Bluetooth-enabled handheld spirometer (MIR, Spirobank Smart, Rome, Italy). The application records patient-reported outcomes and provides an overview of home measurements. The spirometer does not require periodic calibrations to ensure diagnostic accuracy and reproducibility of measurements. During the baseline visit, patients received training of approximately 45 min about the use of the application and the spirometer. An additional mouthpiece with a different size was provided if needed, to increase user convenience. Patients were considered sufficiently trained if they were able to perform three reproducible FVC measurements with less than 150 mL difference in the two highest FVCs. Patients were instructed to perform three consecutive home measurements once a week for the study period of 1 year. Patients were asked to perform the home measurements at fixed timepoints to reduce variability in the measurements.[30] The results were directly visible for both the patient and research team, and were evaluated weekly by a trained physician. When an unexplainable decline in pulmonary function was observed (ie, ≥5% during three consecutive measurements) in the home measurement, an extra outpatient visit with pulmonary function test was scheduled.

At baseline and the semi-annual visits, patients did pulmonary function tests in the hospital under the guidance of trained personnel who were blinded to the home measurements. Patients also completed patient-reported outcome measurements, including the King's Brief Interstitial Lung Disease (KBILD) health status, the Hospital Anxiety and Depression Scale (HADS), the EQ-5D-5L, and the Scleroderma Health Assessment Questionnaire (SHAQ). The KBILD health status questionnaire is a 15-item, validated, self-completed questionnaire. It has three domains: breathlessness and activities, psychological symptoms, and chest symptoms. The KBILD domain and total score ranges are 0–100, with higher scores corresponding with better health-related quality of life.[31] The HADS consists of two domains, anxiety and depression, with each domain containing seven questions with scores ranging from 0 to 21. A score of more than 8 indicates the presence of anxiety or depressive symptoms.[32] The EQ-5D-5L is a self-reported health status measure that relates to the respondent's

situation at the time of completion. It comprises five questions on the domains of mobility, self-care, daily activities, pain, and mood, and a visual analogue scale on general health status.[33] The output of the questionnaire was transformed into an index value using the Dutch valuation set.[34] The EQ-5D-5L index ranges between 0 and 1, whereby 1 represents the best health status. The SHAQ assesses disability and has eight subdomains (score range 0–3) about functioning in daily life and seven separate visual analogue scale scores (score range 0–3) about pain and perceived hindrances due to systemic sclerosis-specific symptoms.[35] At baseline and 12 months, patients completed a 6MWT to evaluate submaximal exercise capacity. Demographic data were extracted from the electronic patient files. Sex data were collected from patient medical records.

Statistical analysis

We aimed to include 43 patients based on a power calculation to show a κ of 0·90 with 0·15 precision (95% CI), assuming that both home and hospital spirometry detect a decline in FVC of 5% or more in 30% of patients and accounting for a drop-out of 10%. Data for the home-based and hospital-based measurements were used until the last available follow-up hospital visit (ie, 6 months or 12 months).

The built-in quality assessment of the home monitoring application according to the American Thoracic Society–European Respiratory Society guidelines was used to evaluate the quality of the measurements.[36] Measurements that were graded as physiologically impossible (grade F according to the American Thoracic Society–European Respiratory Society criteria) were filtered out before the analysis. This resulted in a maximum variability of 250 mL between measurements. The primary outcome was the κ agreement between home and hospital measurements after 1 year to detect a decline in FVC of 5% or more, estimated by means of separate linear regression analyses for home-based and hospital-based FVC% predicted without any other covariates in individual patients. A threshold of 5% was used in line with the guidelines for progressive pulmonary fibrosis, which defines progressive fibrosis as a decline in FVC% predicted of at least 5% combined with either symptoms or progression of ILD on a CT scan.[9] Change in FVC at the end of follow-up was predicted using regression analysis with FVC% predicted as the dependent variable and time (in days) as the independent variable. The sensitivity, specificity, and likelihood ratios to detect a decline in FVC of 5% or more were also assessed. To evaluate the agreement over the course of pulmonary function between home and hospital measurements, we did a mixed linear regression analysis with an indicator for home versus hospital measurement and an interaction term between the indicator and time. Through visual inspection of the data, it was established that the assumptions underlying a linear mixed-effects model, including normality and homogeneity of variance of residuals and linearity for quantitative predictors, were met (appendix pp 2–6). In addition, the within-person reproducibility of FVC% predicted was assessed with the coefficient of variation. Intraclass correlation coefficient using a two-way mixed model and Bland–Altman plots were used to compare home spirometry with hospital-based pulmonary function tests at baseline, 6 months, and 12 months. Furthermore, adherence to home spirometry was assessed by dividing the actual number of home spirometry measurements performed by the expected number of home spirometry measurements during the study period and presented as a proportion. Differences in patient-reported outcome measures and the 6MWT were compared between patients with and without progressive ILD associated with systemic sclerosis based on hospital pulmonary function tests using an unpaired *t* test or Wilcoxon signed rank test as appropriate. All statistical analyses were performed two-sided in Stata version 18.

See Online for appendix

Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Jan 26, 2021, and Feb 27, 2023, 76 patients were screened for eligibility. 49 eligible patients were identified, of whom 43 were willing to participate in the study and gave informed consent. One patient was excluded from the analysis because they were unable to perform adequate home pulmonary function tests due to concomitant myositis. Seven patients dropped out before the 6-month follow-up and four patients dropped out of the study after 6 months, resulting in 35 patients completing 6 months of follow-up and 31 patients completing the entire study (figure 1). 20 (57%) of 35 patients were women and 15 (43%) were men; 32 (91%) were White (table 1). The mean age was 57·7 years (SD 10·7). Patients who dropped out of the study had a shorter disease duration at baseline (appendix p 7). The last follow-up visit took place on March 28, 2024. The mean follow-up duration was 364 days (SD 53).

1588 home measurements were made, 213 (13%) of which were marked as insufficient (ie, insufficient performance technique or blew <25% of expected volume) by the inbuilt quality check in the home spirometry application. These insufficient measurements were excluded from the analysis. The agreement between hospital and home measurements was a κ of 0·40 (95% CI 0·01–0·79). The sensitivity of home spirometry to detect a decline in FVC% predicted of 5% or more was 60% (95% CI 44–76) and the specificity was 87% (75–98) based on a prevalence of progressive ILD of 14% (five of 35 patients). The positive likelihood

ratio was 4·50 (95% CI 1·41–14·35) and the negative likelihood ratio was 0·46 (95% CI 0·16–1·36). The mixed regression analysis suggested that the course of pulmonary function was not different between hospital-based and home-based measurements, given that the interaction term was not significant (interaction term –0·0003 [95% CI –0·0006 to 0·000008]; p=0·057) with a moderate correlation between slopes (r=0·55 [95% CI 0·26–0·74]; p=0·0007). The median adherence for performing home spirometry throughout the study was 85% (IQR 69–95). The median coefficient of variation was 4·1% (IQR 3·3–6·4). The intraclass correlation coefficient for home and hospital FVC measurements at baseline was 0·85 (95% CI 0·73–0·92; p<0·0001), at 6 months was 0·84 (0·71–0·92; p<0·0001), and at 12 months was 0·72 (0·50–0·86; <0·0001). The Bland–Altman plot showed good agreement between hospital-based and home-based measurements (95% limits of agreement –17·1 to 23·6; figure 2). We did not observe any significant differences in patient-reported outcome measures or 6MWT between patients with and without progressive disease based on the hospital measurements (table 2). Compared with patients who showed no decline in pulmonary function in the home measurements, patients who did show a decline showed an improvement in depressive symptoms measured with the HADS scale (table 2). However, these results should be interpreted with caution as no corrections for multiple testing were

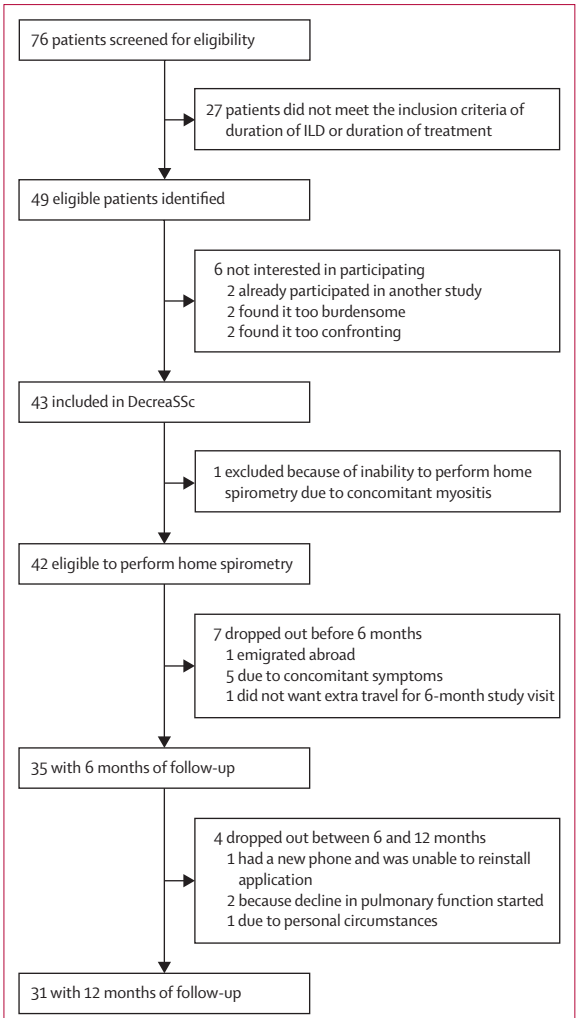

Figure 1: **Trial profile**
ILD=interstitial lung disease.

	Study population (n=35)
Age, years	57·7 (10·7)
Sex	
Female	20 (57%)
Male	15 (43%)
Ethnicity	
White	32 (91%)
Asian	1 (3%)
Arabic or Middle East	1 (3%)
Mix of White and Asian	1 (3%)
Current smoker	3 (9%)
Diffuse cutaneous systemic sclerosis	9 (26%)
Mean disease duration,* years	0·9 (1·0)
Mean modified Rodnan skin score (n=34)	6·9 (9·2)
Antibodies	
Antinuclear antibodies	29/31 (94%)
Antitopoisomerase-I antibodies	15/34 (44%)
Anticentromere antibodies	9/27 (33%)
Mean FVC, L	3·7 (0·9)
Mean FVC% predicted	93·5 (14·3)
Mean DLCO% predicted	73·8 (19·1)
Mean DLCO, mmol/L	8·6 (16·2)
Respiratory symptoms (n=28)	
Mean VAS cough severity, 0–10	2·1 (2·9)
Mean VAS urge-to-cough, 0–10	1·8 (2·5)
Mean VAS dyspnoea, 0–10	2·2 (2·7)
Gastro-oesophageal symptoms†	27 (77%)
Inflammatory arthritis	2 (6%)
Musculoskeletal pain	8 (23%)
Pulmonary comorbidities‡	0
Diastolic dysfunction	3/32 (9%)
Patients with treatment at baseline	6 (17%)
Median treatment duration at baseline, days	50·5 (25·0–56·0)
Immunosuppressive treatment at baseline	
Mycophenolate mofetil	5 (14%)
Azathioprine	1 (3%)

Data are mean (SD), n (%), n/N (%), or median (IQR). Data are shown for all patients included in the analysis (ie, who completed at least 6 months of follow-up). DLCO= diffusing capacity of the lungs for carbon monoxide. FVC=forced vital capacity. VAS=visual analogue scale. *Disease duration from first non-Raynaud phenomenon symptom. †Gastro-oesophageal symptoms included reflux symptoms or the use of proton-pump inhibitors. ‡Pulmonary comorbidities includes asthma, chronic obstructive pulmonary disease, and pleural effusion.

Table 1: **Baseline characteristics**

applied. All results disaggregated by sex are in the appendix (pp 8–9).

Discussion

To our knowledge, this is the first prospective study analysing the validity of home spirometry to detect a decline in pulmonary function (FVC) in patients with systemic sclerosis-associated ILD. We show a good cross-sectional and a moderate longitudinal correlation between home-based and hospital-based pulmonary function tests. Our findings showed no difference in the course of pulmonary function measured at home and in the hospital, with a sensitivity of home spirometry to detect progressive ILD associated with systemic sclerosis of 60% and a specificity of 87%.

Studies have reported strong cross-sectional correlations between hospital-based and home-based pulmonary function tests ranging between 0·72 and 0·98.[16–18] In our study, the correlation was similar but, as was also seen in other studies, we observed a decline in the correlation between home and hospital measurements at the end of the study (ie, 6 or 12 months), suggesting that follow-up training for patients is desirable. Another explanation for the lower correlation over time could be the reduction in adherence to home spirometry towards the end of the study. In patients with IPF and sarcoidosis, a within-person variation in home spirometry measurements similar to our study was observed.[17,20] Concerning the longitudinal association between home and hospital measurements, the results are variable. In patients with IPF, several studies have investigated this longitudinal correlation. Two studies reported a moderate correlation (r=0·44–0·58),[17,18] similar to our findings, and one study reported a weak correlation (r=0·26).[16] In patients with systemic sclerosis-associated ILD, the longitudinal correlation might be lower than in patients with IPF, given the natural variable disease course. Progressive ILD associated with systemic sclerosis is mainly characterised by more gradual progression than IPF, which typically lacks improvement and is characterised by progressive disease.[37] Home spirometry could also possibly be used to monitor improvements in pulmonary function in response to the start of therapy in patients with systemic sclerosis-associated ILD.

Our study might underestimate the efficacy of home spirometry to detect a decline in pulmonary function in patients with systemic sclerosis-associated ILD. Although home spirometry only showed a fair agreement with hospital pulmonary function tests (κ=0·40 [95% CI 0·01–0·79]), the broad CI does not exclude a reliable agreement between home and hospital measurements. We also found a relatively low sensitivity of home spirometry as a screening tool to detect a decline in FVC% predicted of 5% or more, with the risk of missing four of every ten patients with progressive ILD. It is unlikely that diurnal variations in FVC measurements have impacted the sensitivity of home spirometry, as patients were instructed to perform the tests at a fixed time each day.[30] However, we should interpret these results in light of the criteria proposed for progressive pulmonary fibrosis, in which two of three of the domains of symptoms, pulmonary function, and imaging are required to reach the definition of progression.[9] It is well known that pulmonary function assessed within a hospital setting can exhibit variability. Therefore, in case of minor changes in FVC (5–10%), support of a secondary parameter of progression is warranted. The use of home spirometry with more frequent measurements means that variability can be overcome by assessing trends in individual patients. In line with our previous findings, we instructed patients to perform home spirometry once a week, and our findings did not suggest reasons to alter this schedule. We observed that the trend in pulmonary function is different and more in line with home measurements when evaluating pulmonary function tests of a longer follow-up period. Previous studies have shown that in patients with systemic sclerosis-associated ILD, test–retest reliability within a month is acceptable.[38,39] However, in the pooled data of the Scleroderma Lung Studies I and II, the within-subject coefficient of variation was 4·8% between screening and the baseline visit, suggesting fluctuations in the hospital pulmonary function tests.[38] Taken together, considering fluctuations in pulmonary function tests and the heterogeneity in the course of pulmonary function in patients with systemic sclerosis-associated ILD, it is plausible that home spirometry provides a more accurate representation of the course of pulmonary function than hospital-based tests. Future studies using a combination of respiratory symptoms and home spirometry focusing on outcome measures such as mortality, respiratory hospitalisation, or lung transplantation with longer follow-up duration are needed to confirm the validity of this statement.

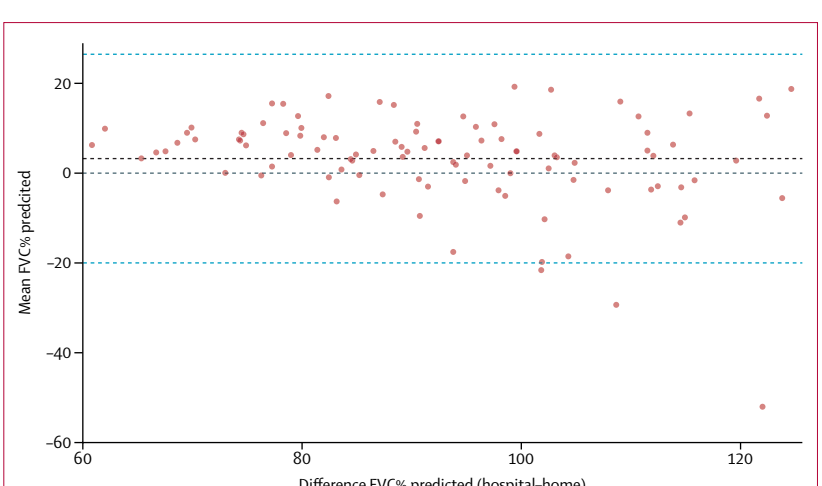

Figure 2: **Bland–Altman plot for agreement between home-based and hospital-based measurements of all patients at baseline, 6 months, and 12 months**
Blue dashed lines represent the 95% tolerance interval. The dashed grey line represents bias. FVC=forced vital capacity.

	Hospital measurements			Home measurements		
	No progression (n=30)	Progressive ILD (n=5)	p value	No decline (n=28)	Decline (n=7)	p value
Change in HADS anxiety	−0·1 (2·9)	−1·0 (0·8)	0·57	−0·2 (2·9)	−0·6 (1·7)	0·77
Change in HADS depression	−0·3 (2·4)	−0·8 (4·6)	0·78	0·0 (2·5)	−2·6 (2·3)	0·040
Change in EQ-5D-5L VAS	−2·2 (−10·4 to 1·0)	−3·6 (−34·8 to 16·3)	0·91*	−1·7 (−10·4 to 4·0)	−5·6 (−11·0 to 0·5)	0·63*
Median EQ-5D-5L index value	0·0 (−0·1 to 0·1)	0·0 (−0·2 to 0·2)	0·95*	0·0 (−0·1 to 0·1)	0·0 (−0·1 to 0·1)	0·67*
Change in KBILD health status total score	1·1 (−4·4 to 5·6)	−0·6 (−13·9 to 7·8)	0·70*	1·1 (−4·4 to 5·6)	−2·2 (−2·2 to −1·1)	0·24*
Change in SHAQ disability index	0·0 (0·3)	0·2 (0·2)	0·082	0·0 (0·3)	0·0 (0·5)	1·0
Change in SHAQ VAS						
Pain	0·0 (0·6)	0·1 (0·1)	0·68	0·1 (0·5)	−0·4 (1·0)	0·13
Bowel	0·0 (0·0 to 0·2)	0·3 (0·1 to 0·5)	0·12*	0·0 (0·0 to 0·4)	0·0 (0·0 to 0·0)	0·48*
Breathing	0·1 (0·4)	0·2 (0·6)	0·70	0·1 (0·4)	0·1 (0·6)	0·96
Ulcers	0·0 (−0·2 to 0·2)	0·3 (0·0 to 1·3)	0·10*	0·0 (0·0 to 0·2)	0·0 (0·0 to 0·0)	0·86*
Illness perception	−0·2 (0·6)	−0·2 (0·3)	0·93	−0·2 (0·6)	−0·3 (0·6)	0·67
Fatigue	−0·1 (0·7)	0·1 (0·3)	0·67	−0·1 (0·7)	0·1 (0·3)	0·68
Raynaud	0·0 (0·7)	0·1 (0·5)	0·74	0·1 (0·5)	−0·2 (1·4)	0·33
Change in 6MWT distance, m	3·0 (55·6)	−39·0 (5·6)	0·21	0·2 (56·8)	−12·5 (37·3)	0·67
Change in distance % predicted	0·1 (8·9)	−7·0 (1·0)	0·19	−0·7 (9·0)	−1·0 (8·1)	0·95
Change in oxygen saturation, %	−1·0 (−2·0 to 2·0)	−1·0 (−2·0 to 0·0)	0·63*	−0·5 (−2·0 to 2·0)	−1·0 (−1·5 to −0·5)	0·57*

Data are mean (SD) or median (IQR). For hospital measurements, progression of ILD is defined as an absolute decline in FVC% of 5% or more, whereas for the home measurements, decline is defined based on an absolute decline in FVC% of 5% or more. 6MWT=6-min walking test. FVC=forced vital capacity. HADS=Hospital Anxiety and Depression Scale. ILD=interstitial lung disease. KBILD=King's Brief Interstitial Lung Disease. SHAQ=Scleroderma Health Assessment Questionnaire. VAS=visual analogue scale. *Tested with Wilcoxon signed rank test; differences are tested with an unpaired *t* test unless otherwise stated.

Table 2: **Difference in patient-reported outcomes and 6MWT between patients with and without progressive ILD associated with systemic sclerosis**

The results of this study support further evaluation of the implementation of home spirometry in addition to regular health-care management, but do not endorse relying solely on home monitoring to detect a decline in pulmonary function. Home spirometry alongside usual health care could facilitate earlier detection of progressive disease in patients with early disease. We focused on patients with systemic sclerosis-associated ILD who were almost treatment-naive and had early disease, but in our opinion, home spirometry is not only suitable for this subgroup of patients. In patients with a later disease stage, incidence of progressive ILD similar to the early disease stage has been reported.[40] In this patient group, with typically longer intervals between regular check-ups, tight monitoring might facilitate the timely detection of progressive ILD associated with systemic sclerosis. Of note, we have shown that adherence to home testing is high. Qualitative research in a subgroup of our study participants showed that patients with systemic sclerosis are generally willing to perform home spirometry. However, it also highlighted the importance of having an upfront consultation with the patient about the intensity of guidance, feedback about measurements, and frequency of face-to-face consultations, as they also require reassurance during home monitoring.[41]

A strength of our study is that we included an almost treatment-naive subgroup of patients with systemic sclerosis-associated ILD with a short disease duration. Furthermore, we included a substantial number of male patients, with nearly half of the study population being male. This is reflective of the patient demographics at our tertiary centre, where a large portion of patients with systemic sclerosis are male.[42] In addition, this study confirmed our previous findings that home spirometry is feasible for patients with systemic sclerosis-associated ILD, given that most participants completed the study and did not report major barriers. In particular, patients did not report any difficulty holding the home spirometry device due to hand dysfunction. A limitation is that our study is probably underpowered due to inaccuracies in our initial assumptions. Specifically, the prevalence of progressive ILD associated with systemic sclerosis was lower than anticipated, while the dropout rate was higher. We anticipated that 30% of the patients would have a decline in FVC of more than 5% predicted but found this in 14%. Furthermore, our dropout rate was anticipated to be 10% (ie, four patients) but seven patients dropped out of the study. Furthermore, data on American College of Rheumatology Composite Response Index in Systemic Sclerosis was not presented as initially intended, given that only eight patients with diffuse cutaneous systemic sclerosis completed a follow-up duration of 12 months. Finally, the patients assessed in this study are Dutch, which might affect the external validity for other settings with lower availability of internet access or literacy rate, such as in low-income countries. In conclusion, this study shows that home spirometry holds the potential to detect progressive ILD associated with systemic sclerosis.

Contributors

Substantial contributions to study conception and design: CCM, MSW-L, CHMvdE, and MCV. Substantial contributions to acquisition of data: all authors. Substantial contributions to analysis and interpretation of data: all authors. Drafting the article or revising it critically for important intellectual content: all authors. Final approval of the version of the article to be published: all authors. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. AV and CHMvdE directly accessed and verified the underlying data reported in the manuscript.

Declaration of interests

CCM declares grants and consultancy fees from Boehringer Ingelheim, AstraZeneca, and Daiichi Sankyo, outside of the submitted work, paid to the institution. JKdV-B received consulting fees from AbbVie, Janssen, and Boehringer Ingelheim, and received research grants from Roche, Galapagos Janssen, National Association for People with Lupus, APA, Scleroderma, and MCTD, and ReumaNederland; all payments were made to her institution. MSW-L received consulting or speakers fees from AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, CSL Behring, Galapagos, Galecto, Hoffmann-La Roche, Horizon Therapeutics, Kinevant Sciences, Molecure, NeRRe, Novartis, PureTech, Thyron, Trevi, and Vicore; and grants from The Dutch Pulmonary Fibrosis Patients Association, The Dutch Lung Foundation, The Netherlands Organisation for Health Research and Development, The Thorax Foundation, Sarcoidosis.nl, AstraZeneca/DaiichiSankyo, Boehringer Ingelheim, and Hoffmann-La Roche; all fees and grants were paid to her institution. MCV received consulting fees or speakers fees from Boehringer Ingelheim, GSK, Janssen, MSD, Novartis, Boehringer Ingelheim, and Janssen; and unrestricted research grants from Boehringer Ingelheim, Ferrer, and Galapagos; all fees and grants were paid to her institution. All other authors declare no competing interests.

Data sharing

Individual participant data will be made available for approved data sharing requests. Individual participant data that underlie the results reported in this article will be shared after de-identification and normalisation of information (text, tables, figures, and appendices). Anonymised data will be available up to 5 years after publication of this article to researchers who provide a completed Data Sharing Agreement that describes a methodologically sound proposal for the purpose of the approved proposal. Proposals should be directed to madelon.vonk@radboudumc.nl. Data will be shared once all relevant parties approve and sign the Data Sharing Agreement.

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