Home monitoring in patients with idiopathic pulmonary fibrosis a randomized controlled trial

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ORIGINAL ARTICLE

Home Monitoring in Patients with Idiopathic Pulmonary Fibrosis
A Randomized Controlled Trial

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Abstract

Rationale: Idiopathic pulmonary fibrosis (IPF) is a deadly disease with increasingly impaired health-related quality of life (HRQOL). eHealth technologies facilitate collection of physiological outcomes and patient-reported outcomes at home, but randomized controlled trials (RCTs) on the effects of eHealth are scarce.

Objectives: To investigate whether a home monitoring program improves HRQOL and medication use for patients with IPF.

Methods: We performed a multicenter RCT in newly treated patients with IPF. Patients were randomly assigned to standard care or a home monitoring program on top of standard care for 24 weeks. The home monitoring program included home spirometry, reporting of symptoms and side effects, patient-reported outcomes, information, a medication coach, and eConsultations. The primary endpoint was between-group difference in change in King's Brief Interstitial Lung Disease Questionnaire (K-BILD) score at 24 weeks.

Measurements and Main Results: A total of 90 patients were randomized (46 assigned to the home monitoring group and 44 to the standard care group). After 24 weeks, no statistically significant difference was found in K-BILD total score, with a 2.70-point increase in the home monitoring group (SD = 9.5) and a 0.03-point increase in the standard care group (SD = 10.4); between-group difference was 2.67 points (95% confidence interval [CI], −1.85 to 7.17; $P = 0.24$). Between-group difference in psychological domain score was 5.6 points (95% CI, −1.13 to 12.3; $P = 0.10$), with an increase of 5.12 points in the home monitoring group (SD = 15.8) and a decline of 0.48 points in the standard care group (SD = 13.3). In the home monitoring group, medication was more often adjusted (1 vs. 0.3 adjustments per patient; 95% CI, 0.2 to 1.3; $P = 0.027$). Patient satisfaction with the home monitoring program was high. Home-based spirometry was highly correlated with hospital-based spirometry over time.

Conclusions: The results of this first-ever eHealth RCT in IPF showed that a comprehensive home monitoring program did not improve overall HRQOL measured with K-BILD but tended to improve psychological well-being. Home monitoring was greatly appreciated by patients and allowed for individually tailored medication adjustments.

Clinical trial registered with www.clinicaltrials.gov (NCT03420235).

Keywords: idiopathic pulmonary fibrosis; quality of life; eHealth; home spirometry; interstitial lung disease

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At a Glance Commentary

Scientific Knowledge on the Subject: Previous studies on home spirometry in idiopathic pulmonary fibrosis (IPF) yielded mixed results regarding reliability and adherence. However, these studies did not allow for real-time data sharing with the hospital nor with the patient, which limits quality and compliance control and the possibility to react to changes. eHealth tools have been increasingly investigated in chronic diseases, but studies in IPF are scarce. Until now, no randomized controlled trials evaluating the effect of eHealth interventions in IPF have been published.

What This Study Adds to the Field: This is the first-ever randomized controlled trial of an eHealth intervention in IPF. A comprehensive online home monitoring program, including home spirometry, did not improve health-related quality of life in IPF but tended to improve psychological well-being. Home monitoring was highly appreciated by patients and allowed for individually tailored treatment adjustments. Moreover, home spirometry correlated well with hospital spirometry over time. Thus, home monitoring could be a reliable tool for close monitoring and follow-up of patients, both for research and in daily practice.

Idiopathic pulmonary fibrosis (IPF) is a progressive, deadly disease resulting in an increasingly impaired health-related quality of life (HRQOL) (1). Currently, two antifibrotic drugs are available that slow down disease decline and improve survival (2–4). Patients with IPF are regularly followed up at the outpatient clinic with pulmonary function testing. At each visit, potential effects of antifibrotic drugs versus potential side effects are balanced together with the patient. Furthermore, intercurrent events, such as infections or acute exacerbations, may require extra hospital visits. For optimal, individually tailored treatment of patients, frequent hospital visits would be desirable. However, hospital visits can be burdensome for patients because of dyspnea, extra oxygen needs, and often considerable travel distances. Consequently, home monitoring could hold great benefits in this patient population.

New eHealth technologies can facilitate collection of physiological outcomes and patient-reported outcomes (PROMs) at home. Earlier studies in other lung diseases showed that eHealth interventions can improve health outcomes (5, 6). Furthermore, eHealth tools focusing on symptoms and side effects could stimulate self-management, reduce symptom burden, and enhance medication use (7, 8). To date, a few studies have investigated the feasibility of home monitoring in IPF, in particular home spirometry (9–11). These studies demonstrated that home spirometry was feasible, reliable, and informative in this elderly patient population. However, none of these studies allowed for direct data sharing with the hospital.

Together with patients with IPF, we have developed a home monitoring program that integrates real-time home spirometry with collection of PROMs, symptom scores, side effects, an information library, and eConsultations. Pilot studies showed that this home monitoring program was feasible and highly appreciated by patients (12, 13). We hypothesized that a comprehensive home monitoring program could optimize HRQOL for patients with IPF by supporting self-management, better tailoring of medication, and allowing for low-threshold communication. To our knowledge, no randomized controlled trials evaluating the effect of eHealth interventions in IPF have been published.

The aim of the current study was to investigate whether a comprehensive home monitoring program improved HRQOL and medication use for patients with IPF. Furthermore, we aimed to assess patient satisfaction with home monitoring and compare home-based with hospital-based spirometry.

Methods

Study Design and Participants

This was a nonblinded, multicenter randomized controlled trial conducted at four sites in the Netherlands. Ethics approval was obtained from the Erasmus Medical Center (MEC-2017-501) and local ethics committees. This trial is registered with www.clinicaltrials.gov (NCT03420235). All patients provided written informed consent before study entry. Eligible patients were adults (≥18 yr) with a diagnosis of IPF according to the American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association 2018 guideline, and about to start on antifibrotic treatment (nintedanib or pirfenidone) (14). Patients were excluded if they were not able to speak, read, or write Dutch or if they received prior treatment for IPF.

Study Procedures

Allocation of each subject was done with a centralized electronic system using varying block sizes. Participants were randomly assigned in a 1:1 ratio to a home monitoring program as add-on to standard care or standard care alone for 24 weeks. Randomization was stratified per site and for use of nintedanib or pirfenidone.

The intervention consisted of the home monitoring program, IPF Online, which includes daily home spirometry, weekly reporting of symptoms and side effects, and PROMs at baseline and 12 and 24 weeks. The program contains information about IPF, a medication coach, and eConsultation possibility. A flowchart about study procedures and more information about the content of the program are provided in the online supplement. IPF Online is a secured personal platform, compliant with the General Data Protection Regulation (Curavista). At baseline, patients received a password-protected tablet with a preinstalled application, and a Bluetooth-enabled handheld spirometer (Spirobank Smart; MIR). Standardized instructions were provided for use of the application, including home spirometry. Patients were considered adequately trained if they performed three reproducible FVC measurements, with <150 ml difference in the highest FVCs and <10% difference with hospital FVC. Patients were instructed to perform one spirometry each day at approximately the same time. All results were directly transferred via an encrypted connection and were available in real time to the research team. An automated e-mail reminder was sent to patients when spirometry was not performed for two consecutive days. Patients were able to see their own daily spirometry values, an

overview of FVC over time, a flow–volume loop, and a quality assessment (*see* Figures E3 and E4 in the online supplement). The research team received an e-mail alert when no FVC results were sent or FVC declined more than 10% on three consecutive days and when patients reported bothersome side effects. In case of a reported side effect, a pop-up with advice to handle the side effect was automatically generated. A flowchart of the alert system is provided in Figure E5.

Standard care comprised of three monthly outpatient clinic visits with pulmonary function testing. Participants completed PROMs online on a tablet at baseline and 12 weeks and 24 weeks but did not have access to the home monitoring program (Figure E1).

Outcome Measures

The primary outcome measure was between-group difference in change of the King's Brief Interstitial Lung Disease health status questionnaire (K-BILD). K-BILD has been developed and validated in interstitial lung diseases (ILDs) and consists of 15 items in three domains: breathlessness and activities, chest symptoms, and a psychological domain (15). The minimal clinically important difference (MCID) is 3.9 points for the total score (16). A higher score represents a better HRQOL, with scores ranging from 0 to 100.

Secondary endpoints included between-group differences in the Patient Experiences and Satisfaction with Medication questionnaire (PESaM), the EQ-5D-5L questionnaire, the Hospital Anxiety and Depression Scale (HADS), the visual analog scale (VAS), and the Global Rating of Change (GRC) scores at 12 and 24 weeks, number of adjustments in medication, and hospitalizations. Adjustments in medication were defined as a dose change, medication switch, or (temporarily) treatment discontinuation. The PESaM questionnaire has recently been validated in IPF, and it assesses patient expectations, experiences, and satisfaction with antifibrotic medication (17). Expectations regarding effectiveness, side effects, and ease of use before start of treatment were recorded on a Likert scale from 0 to 4, with higher scores representing more positive expectations. Satisfaction with medication was scored on a scale from −5 (very unsatisfied) to 5 (very satisfied). Side effects of medication were scored on a Likert scale from 1 (not bothersome at all) to 5 (very bothersome). The EQ-5D-5L is a generic instrument to assess HRQOL; a higher score corresponds with a better HRQOL. General health status is evaluated using the EQ-VAS score ranging between 0 and 100, with a higher score representing a better general health status (18). The HADS is a validated questionnaire with a subscale for anxiety and depression: a score of 8 or greater is used as the cut-off for anxiety or depressive symptoms (19). Symptoms (general well-being, dyspnea, fatigue, cough, and urge to cough) were reported on a VAS from 0 to 10. On the GRC scale, patients indicate whether their quality of life improved or deteriorated over time, on a scale from −7 to 7. In the intervention group, satisfaction with home monitoring was evaluated with a nonvalidated 10-item questionnaire with VAS scores from 0 to 10.

Other secondary outcomes were FVC change (ml) over 24 weeks, correlation between home-based FVC and hospital-based FVC over time, and within-patient variability in home-based FVC.

Statistical Analysis

Between-group differences in PROMs were analyzed with independent Students' *t* tests in the intention-to-treat population. We performed complete case analyses, as missing data were considered to be independent of the primary outcome (e.g., missing questionnaires due to technical errors). Descriptive statistics were used to evaluate study variables at baseline. FVC change (ml) was analyzed using a linear mixed model accounting for within-patient correlations and allowing for random missing data. As fixed effects, we used a linear slope of time (d), and an indicator for whether the measurement was taken at home or in the hospital. In addition, an interaction term between the indicator and time was used. For random effects, random intercepts and slopes were used. The interaction term indicates whether the slopes for home-based FVC differ from hospital-based FVC slopes. Correlation between home and hospital spirometry was analyzed with Pearson correlation coefficient. Measurements of hospital-based FVC at all time points were

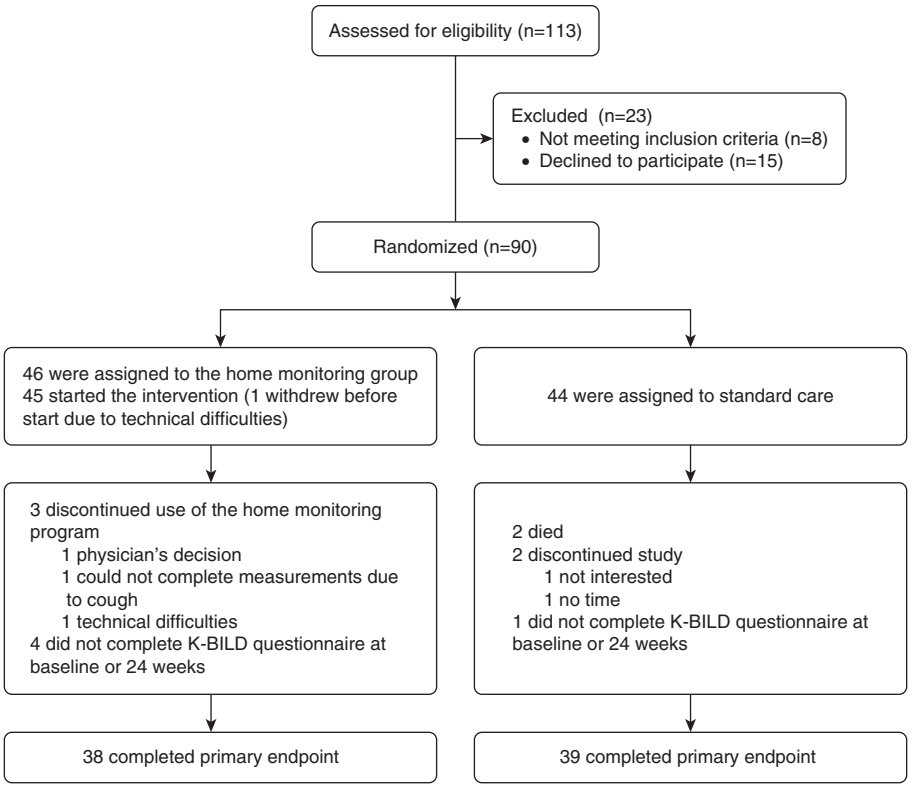

Figure 1. Flow chart of patient inclusion. K-BILD = King's Brief Interstitial Lung Disease questionnaire.

compared with the mean of seven home-based FVCs from that week. Within-patient variability was evaluated with the coefficient of variation, using "detrended" data points. These were obtained by fitting a linear regression model on each patient and subtracting the residuals of each spirometry measurement. A P value < 0.05 on a two-tailed test was considered statistically significant. Data were analyzed using *R* version 3.6.1 (www.r-project.org) and SPSS version 25 (IBM).

We determined that, with a sample size of 72 patients, the study would have 80% power to detect a significant between-group difference in change in total K-BILD score. The expected SD of change in K-BILD score after 24 weeks was 6 points, based on a group of untreated patients with IPF from our own cohort (M.S. Wijsenbeek, unpublished results). Sample size was calculated using a MCID of 4 points (16). To allow for 20% dropout, based on a previous home monitoring study, we aimed to include 90 patients in total (9).

Table 1. Baseline Characteristics of Study Patients ($n = 90$)

Characteristics	Home Monitoring ($n = 46$)	Standard Care ($n = 44$)
Age, yr, median (range)	70 (53–83)	72 (58–84)
Sex, M, *n* (%)	39 (85)	43 (98)
Antifibrotic medication, *n* (%)		
Nintedanib	20 (44)	19 (43)
Pirfenidone	26 (57)	25 (57)
Pulmonary function		
FVC % predicted	82 ± 17.7	78 ± 16.0
FVC, L	3.1 ± 0.8	3.1 ± 0.7
D_{LCO}c % predicted	48 ± 13.8	49 ± 13.0
K-BILD score		
Total	57.2 ± 10.9	56.2 ± 7.7
Breathlessness and activities	48.8 ± 19.3	41.3 ± 15
Chest symptoms	74.3 ± 18.8	73 ± 18.9
Psychological symptoms	54.4 ± 13.9	56.2 ± 11
Hospital anxiety and depression scale		
Anxiety	4.7 ± 2.5	4.6 ± 2.2
Depression	3.4 ± 3.2	3.6 ± 3.6
EQ-5D-5L		
Index value	0.77 ± 0.17	0.77 ± 0.17
EQ-VAS scale	63.1 ± 24.9	64.4 ± 21.9
VAS score symptoms		
General well-being	5.6 ± 0.36	5.5 ± 0.31
Cough	4.6 ± 0.45	4.7 ± 0.33
Dyspnea	4.9 ± 0.38	5.8 ± 0.34
Fatigue	4.8 ± 0.43	5.3 ± 0.38
Stability IPF	6.7 ± 0.31	6.5 ± 0.36

Definition of abbreviations: $D_{LCO}c = D_{LCO}$ corrected for Hb; IPF = idiopathic pulmonary fibrosis; K-BILD = King's Brief Interstitial Lung Disease questionnaire; VAS = visual analog scale.
Data are shown as mean ± SD unless otherwise noted.

Results

Between January 2018 and January 2019, 90 patients were enrolled; 46 patients were assigned to the home monitoring group and 44 were assigned to standard care (Figure 1).

Baseline characteristics of patients were evenly distributed between treatment groups (Table 1). The percentage of males was numerically higher in the standard care group, but the difference was not statistically significant ($P = 0.06$). Overall mean (±SD) age was 71 (6.9) years, and 91% were male. Mean total K-BILD score was 56.6 (9.3), mean FVC was 80.1 (17) % predicted, and mean D_{LCO} was 48.2% (13.5%). Pirfenidone was prescribed in 57% and nintedanib in 43% of patients. In total, 38 (83%) patients in the home monitoring group and 39 (89%) patients in the standard care group completed the study.

PROMs

From baseline to 24 weeks, mean (±SD) total K-BILD score improved, with 2.70 (9.5) points in the home monitoring group and 0.03 (10.4) points in the standard care group. Between-group difference was 2.67 points (95% confidence interval [CI], −1.85 to 7.17; $P = 0.24$; Figure 2). Mean score of the K-BILD psychological domain increased 5.12 (15.8) points in the home monitoring group and declined 0.48 (13.3) points in the standard care group; between-group difference was 5.6 points (95% CI, −1.13 to 12.3; $P = 0.10$). The mean K-BILD breathlessness and activities domain score declined 1.8 (10.7) points in the home monitoring group and 0.93 (12.8) points in the standard care group; between-group difference was 0.9 points (95% CI, −6.3 to −4.4; $P = 0.73$). The mean score of the K-BILD chest domain increased 1.58 (13.3) points in the home monitoring group and declined 2.12 (20.1) points in the standard care group; between-group difference was 3.7 points (95% CI, −4.5 to 11.5; $P = 0.35$).

HADS scores remained stable during the study (Table 2); anxiety scores (between-group difference = 0.05 points; 95% CI, −1.08 to 0.99; $P = 0.93$) and depression scores (between-group difference = 0.4 points; 95% CI, −1.61 to 0.81; $P = 0.51$) were similar in the home monitoring and standard care group. Changes in HRQOL and symptom scores did not differ between treatment groups, except for the general well-being score (between-group difference = 1.04 points; 95% CI, 0.09–2.00; $P = 0.032$). Between-group differences in GRC and VAS for stability of disease tended toward statistical significance (Table 2).

Medication Use and Hospital Visits

Expectations regarding effectiveness, side effects, and ease of use of antifibrotic medication before start of treatment were relatively high and similar in both groups (Table 3). In the home monitoring group, medication was significantly more often adjusted during the study period (on average, 1 vs. 0.3 adjustments per patient; between-group difference = 0.7; 95% CI, 0.2 to 1.3; $P = 0.027$). All adjustments in medication were due to side effects. In general, patients were relatively satisfied with their antifibrotic medication, with a mean (±SD) score of 2.06 (1.89) on a scale of −5 to 5 (Table 3). Satisfaction with medication regarding efficacy, side effects, and ease of use was similar in both groups. The reported number and bothersomeness of side effects did not differ between groups. Furthermore, the number of side effects was not significantly correlated with

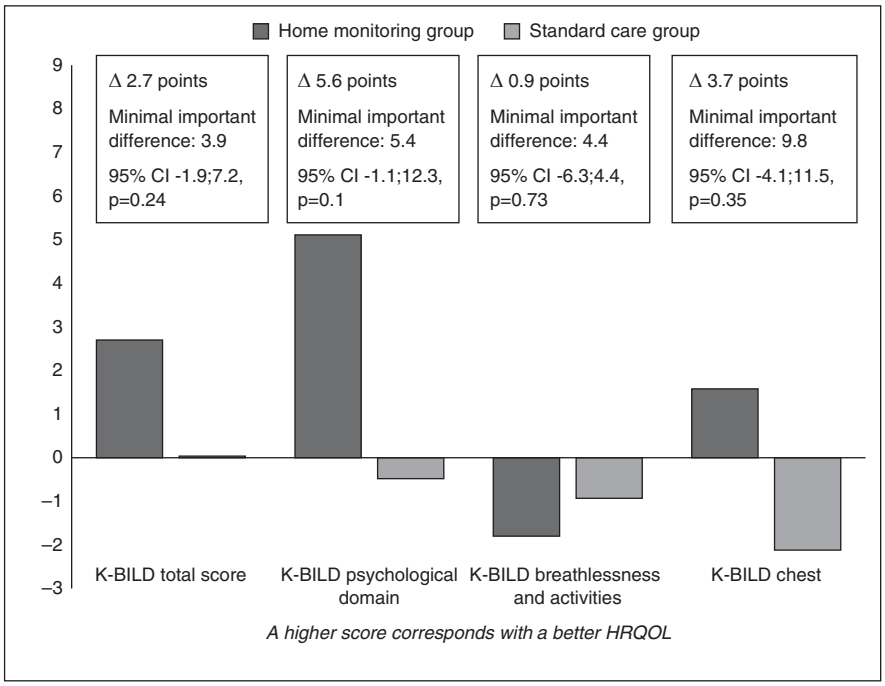

Figure 2. Change in King's Brief Interstitial Lung Disease (K-BILD) questionnaire score from baseline to 24 weeks. CI = confidence interval; HRQOL = health-related quality of life.

patients' experiences with side effects ($r = 0.27$; $P = 0.06$) and only weakly correlated with satisfaction with medication ($r = 0.28$; $P = 0.02$). Expectations about effectiveness ($r = 0.21$; $P = 0.12$), side effects ($r = 0.05$; $P = 0.79$), and ease of use ($r = 0.09$; $P = 0.47$) were not significantly correlated with overall medication satisfaction. During the study, 10 hospitalizations occurred: 6 in the home monitoring group and 4 in the control group. Four hospitalizations were respiratory related (one acute exacerbation). One hospitalization was due to side effects of medication. Overall, 13 patients in the home monitoring group and 10 patients in the control group had extra appointments with a healthcare provider in between regular visits.

Patient Satisfaction and Use of the Home Monitoring Program

Median adherence to daily home spirometry was 97% (52–100%); mean adherence was 93% (Table 4). Overall, 143 automated FVC alerts were sent to the research team: 33 alerts because patients did not send their FVC results and 110 because of a lower FVC. Most frequent reasons for lower FVC measurements were technique issues and symptoms (cough/dyspnea/chest pain). In one patient, FVC alerts were due to an acute exacerbation. More than half of patients used the information library at least once. During the study, 281 eConsultations were sent, corresponding with an average of one eConsultation per patient per month. In total, 347 automated e-mail alerts about bothersome side effects were sent to the research team.

Patient satisfaction with the home monitoring program was high. The vast majority of patients would recommend the home monitoring program to others and mentioned that they gained better insights in to their disease course, felt reassured, and that the program enabled low-threshold communication with the hospital (Table 4). Patients considered use of the home

Table 2. Secondary Endpoints

	Home Monitoring ($n = 38$)	Standard Care ($n = 39$)	Difference (95% CI)	*P* Value
Patients with extra hospital or GP visits, *n* (%)	13 (31.7)	10 (25.6)	—	0.55
Hospitalizations, *n**	6	4	—	0.27
Change from baseline in HADS score at 24 wk				
Anxiety†	0.13 ± 0.35	0.18 ± 0.38	−0.05 (−1.08 to 0.99)	0.93
Depression†	0.34 ± 0.43	0.74 ± 0.43	−0.40 (−1.61 to 0.81)	0.51
Change from baseline in EQ-5D-5L score at 24 wk				
Index value‡	0.02 ± 0.02	−0.03 (0.17)	0.05 (−0.01 to 0.10)	0.11
VAS scale‡	−0.89 ± 3.6	−4.84 ± 2.8	3.95 (−5.20 to 13.10)	0.39
Change from baseline in GRC score at 24 wk‡	0.34 ± 0.35	−0.70 ± 0.40	1.03 (−0.02 to 2.09)	0.055
Change from baseline in VAS scores at 24 wk				
General well-being‡	0.65 ± 0.36	−0.39 ± 0.31	1.04 (0.09 to 2.00)	0.032
Cough†	0.51 ± 0.45	−0.31 ± 0.50	0.82 (−0.52 to 2.17)	0.23
Dyspnea†	0.41 ± 0.32	−0.23 ± 0.30	0.63 (−0.23 to 1.50)	0.15
Fatigue†	0.46 ± 0.40	0.28 ± 0.35	0.18 (−0.88 to 1.23)	0.74
Stability IPF‡	0.49 ± 0.31	−0.6 ± 0.52	1.09 (−0.12 to 2.29)	0.076

Definition of abbreviations: CI = confidence interval; GP = general practitioner; GRC = Global Rating of Change; HADS = Hospital Anxiety and Depression Scale; IPF = idiopathic pulmonary fibrosis; VAS = visual analog scale.
Data are shown as mean ± SD unless otherwise noted.
*Mann-Whitney *U* test.
†A higher score indicates worse symptoms.
‡A higher score indicates better quality of life or symptoms.

Table 3. Medication Use

	Home Monitoring ($n = 41$)	Standard Care ($n = 39$)	Difference (95% CI)	*P* Value
Average number of medication adjustments per patient	1.0	0.3	0.7 (0.2 to 1.3)	0.027
Number of patients who discontinued medication	2	2	—	—
PESaM questionnaire—baseline				
Expectations—effectiveness	2.90 ± 0.80	2.66 ± 0.77	−0.25 (−0.66 to 0.17)	0.24
Expectations—side effects	2.54 ± 0.72	2.50 ± 0.83	−0.04 (−0.51 to 0.43)	0.86
Expectations—ease of use	3.66 ± 0.48	3.64 ± 0.67	−0.02 (−0.28 to 0.25)	0.90
PESaM questionnaire—24 wk				
Satisfaction with medication efficacy	1.52 ± 1.69	1.59 ± 1.97	0.06 (−0.77 to 0.88)	0.89
Satisfaction with side effects	1.70 ± 1.90	1.41 ± 2.23	−0.29 (−1.23 to 0.64)	0.53
Satisfaction with ease of use	2.65 ± 1.59	2.75 ± 1.78	0.10 (−0.66 to 0.86)	0.80
Overall satisfaction with medication	2.01 ± 1.90	2.11 ± 1.91	0.11 (−0.75 to 0.97)	0.81
Number of reported side effects per patient*	6.2 ± 5	4.8 ± 4.5	−1.4 (−3.4 to 0.6)	0.16
Bothersomeness of side effects	1.46 ± 0.63	1.47 ± 0.84	0.01 (−0.4 to 0.3)	0.94

Definition of abbreviations: CI = confidence interval; PESaM = Patient Experiences and Satisfaction with Medication questionnaire.
Data are shown as mean ± SD unless otherwise noted.
*Reported side effects after 24 weeks.

monitoring program and spirometer easy and useful, found it pleasant to have an overview of results, and did not consider home monitoring burdensome (Figure 3).

Home and Hospital Spirometry

Mean change in hospital-based FVC in the standard care group (−87.9 ml; range, −209 to 33.2 ml) was not significantly different from FVC change in the home monitoring group (−7.9 ml; range, −96 to 69.4 ml; $P = 0.25$). In the home monitoring group, mean change over time in home-based FVC was −16.8 (range, −124 to 90.9) ml. Correlation between home and hospital spirometry was very strong at all time points ($r = 0.97$, $P < 0.001$ at baseline and 12 wk; $r = 0.96$, $P < 0.001$ at 24 wk). Slopes of hospital- and home-based FVC over time were comparable (interaction < 0.0001; $P = 0.81$), and correlation between slopes was moderately strong ($r = 0.58$; $P < 0.001$). Mean within-patient variability was 5.2% (SD = 1.7; range, 2.6–9.5%). An example of six individual patients with a wide range in FVC from all trial sites is provided in Figure 4.

Discussion

This first-ever randomized trial of eHealth in IPF investigated whether a comprehensive home monitoring program on top of standard care improved HRQOL compared with standard care alone. The results of our study show that this home monitoring program did not significantly improve overall HRQOL measured with K-BILD. Despite this, psychological well-being tended to improve, and general well-being was significantly higher in the home monitoring group after 24 weeks. Home monitoring was greatly appreciated by patients, allowed for individually tailored treatment adjustments, and did not increase anxiety levels. Furthermore, daily home spirometry was feasible and provided reliable results similar to hospital-based spirometry.

The main purpose of our home monitoring program was to enhance comprehensive care by targeting multiple domains: stimulating self-management, improving medication use, providing disease-specific information, and enabling low-threshold communication. Capturing these diverse effects in one outcome measure is challenging, as many outcomes are not tangible, nor have validated outcome measures to quantify the effect. In this study, we have chosen the K-BILD as primary endpoint as it seems the most comprehensive HRQOL questionnaire in ILD. Moreover, K-BILD is the only ILD questionnaire to date that has managed to capture improvement in HRQOL in a randomized study evaluating a supportive measure (ambulatory oxygen) (20). However, the K-BILD measures overall health status, whereas our home monitoring program seemed to have more influence on psychological well-being. This was highlighted by the finding that the difference in K-BILD psychological score between both groups after 24 weeks exceeded the MCID. Besides, patients in the home monitoring group reported higher

Table 4. Patient Experiences with Home Monitoring

	Home Monitoring Group ($n = 42$)
Use of home monitoring program	
Adherence to daily home spirometry, median %	97
PROM completion rate, %	93
Use of information library, % of patients	58
Total eConsultations, *n*	281
Patient experiences ($n = 38$), %	
Would recommend it to others	95
Better insights in disease course	89
Feeling reassured	88
More accessible communication with hospital	87

Definition of abbreviation: PROM = patient-reported outcome measure.

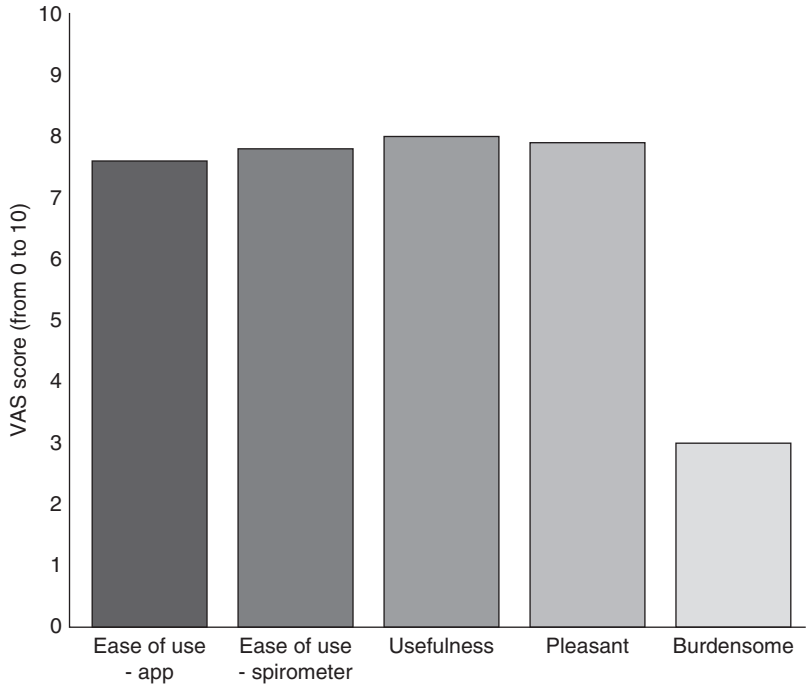

Figure 3. Patient experiences with the home monitoring program, scored on visual analog scale (VAS) from 0 to 10 ($n = 38$).

scores for general well-being on a VAS scale. Even though these were secondary outcome measures, this suggests that home monitoring could have positive effects on well-being and health perception. Our results are comparable with previously published studies using eHealth interventions in chronic obstructive pulmonary disease and asthma; patient satisfaction with the intervention was generally high, but results regarding HRQOL were mixed (5, 21, 22).

This study was designed to assess the effects of a home monitoring program as add-on to standard care. However, it is important to note that IPF care in the Netherlands is already well organized. Patients are treated in expert centers and closely monitored by ILD specialist nurses, which reduces differences between standard care and add-on home monitoring. This may also have contributed to the low medication discontinuation rate in the current study (5%) in comparison with previous trials in IPF (2, 3). Future studies are needed to determine whether outpatient clinic visits can be partly replaced by home monitoring, including video consultations. This could not only reduce the burden of frequent hospital visits on patients with IPF and their families but potentially lead to more efficient healthcare delivery and cost reduction, both for the healthcare system as well as for patients and their families.

Observational studies in IPF and chronic obstructive pulmonary disease hypothesized that home monitoring could be psychologically distressing, because patients may become more preoccupied with their disease (9, 23). Our data revealed that home monitoring did not increase anxiety and depression levels after 24 weeks. Patients actually appreciated that they gained more insights in their disease course and felt reassured by the information and feedback they received. It has previously been suggested that daily spirometry could be intrusive for patients if performed for a prolonged period (9, 10, 24). Importantly, patients in our study did not consider daily spirometry burdensome. The vast majority would recommend it to others and wished to continue with home monitoring after the study was completed. The high patient satisfaction was also reflected in the good adherence and completion rate, which were better than in some previous studies (10, 11). Another reason for the high satisfaction and compliance might be that the home monitoring program has been developed together with patients from the beginning; it has been tested and evaluated during two pilot studies, and patient suggestions have been incorporated to improve the program (12, 13). This highlights the importance of active patient participation in the design of eHealth interventions. We previously described that people may be hesitant to use

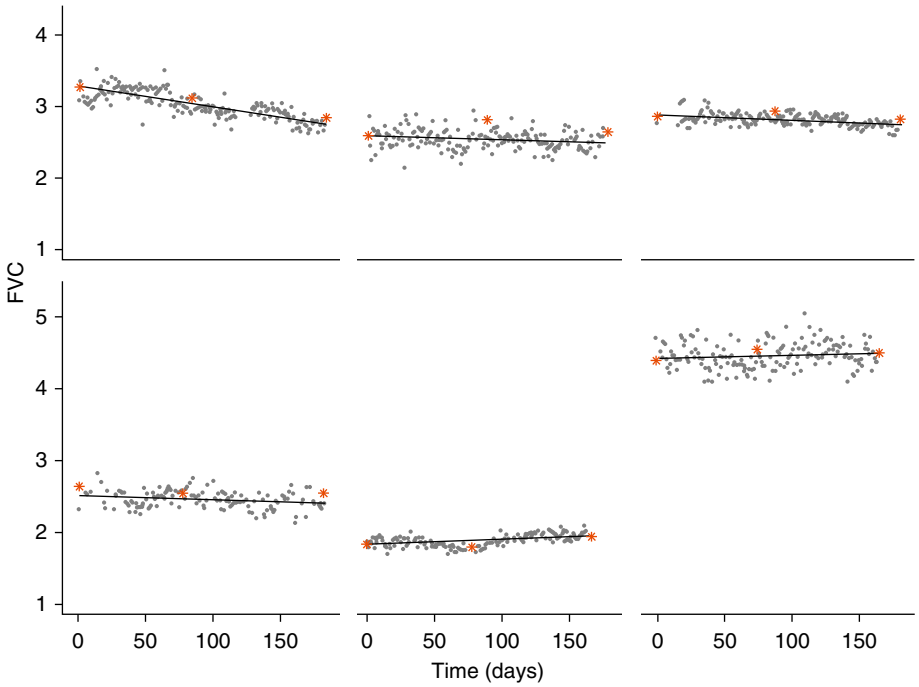

Figure 4. Example of hospital- and home-based FVC change (L) over 24 weeks in six individual patients from different trial sites. The grey dots in each plot represent home-based spirometry, whereas the red asterisks in each plot represent the hospital-based spirometry.

online applications in this elderly patient population (12). However, the high rate of patients willing to participate in the current study (80% of invited patients) shows that this is not a major concern in patients with IPF. Even a few patients without internet access at home were able to participate, because a tablet and 4-G sim card were provided. These are encouraging results for future use of eHealth solutions for research and daily care purposes in IPF.

The automated e-mail alerts about burdensome side effects allowed for an individually tailored treatment schedule; medication was significantly more often adjusted in the home monitoring group than in the standard care group. Strikingly, medication adjustments did not lead to significant differences in patient satisfaction with medication between the groups. One of the reasons could be that patient satisfaction with medication was relatively high in the whole group. Furthermore, we found that neither expectations before start of treatment nor the number and perceived severity of side effects correlated with patient experiences and satisfaction. A systematic review in other chronic diseases also suggested that eHealth tools may enable personalized medication adjustments (7). In line with our data, no evidence was found that medication changes had a positive impact on patient satisfaction (7). Because of the relatively short study duration, it was not possible to assess whether treatment adjustments lead to better long-term outcomes and compliance. Prospective observational studies with a longer duration are needed to answer these important questions.

Recently, there has been quite some debate about the use and reliability of home spirometry in pulmonary fibrosis (24). Our study demonstrated that daily home spirometry was feasible in a multicenter trial. Patient adherence remained high during our study, and only a few technical problems were encountered. Home spirometry yielded reliable results similar to hospital-based spirometry, in line with other nonrandomized home spirometry studies (9–11, 13). We found that slopes of home- and hospital-based FVC over time were comparable. In contrast, a randomized trial of pirfenidone in progressive unclassifiable ILD using home spirometry showed rather conflicting results (24). In that trial, multiple challenges with home spirometry were encountered, mainly owing to technical and adherence problems, leading to highly variable FVC results and analytical issues (24). In most previous studies, patients were blinded to their own results, did not receive reminders to perform spirometry, and results were not directly available to the study team. We believe that many of the challenges with home spirometry can be overcome by using an online home monitoring program with real-time feedback and alerts, easy access to a technical helpdesk, and extensive instruction of patients as we did in the current study. Therefore, we believe that we should not discard home spirometry too early as a tool for close monitoring and follow-up of patients in research and also, potentially, in daily practice.

Home monitoring could potentially allow for early detection of intercurrent events. As only a small number of intercurrent problems and respiratory-related hospitalizations occurred in our study, no conclusions can be drawn regarding the potential of eHealth tools to detect acute exacerbations and prevent hospitalizations in IPF. Presently, an observational study of a longer duration is investigating whether a home monitoring program, including home spirometry, allows for early detection of acute exacerbations (clinical trial NCT03979430).

This study has some limitations. The healthcare situation and organization of care for IPF in the Netherlands might not be representative for other countries. However, it can be speculated that home monitoring could be even more relevant in countries with other healthcare systems and longer travel distances to the hospital. Furthermore, the study team received, on average, one eConsultation and less than two e-mail alerts per patient per month—a limitation of this study is that we did not structurally evaluate the time investment and burden on the study team. Finally, no good, validated questionnaires exist to evaluate patient satisfaction with eHealth compared with usual care. Consequently, we used a nonvalidated questionnaire to assess patient satisfaction in the home monitoring group, which was one of the secondary outcomes. Next to patient satisfaction and HRQOL, it could have been useful to measure other PROMs, such as confidence in self-management and sense of self-control. Validated questionnaires to measure these outcomes (e.g., the Patient Activation Measure and Pearlin Mastery Scale) have been used in other diseases and may be of added value in future eHealth studies in IPF (25–27).

In conclusion, a comprehensive home monitoring program for patients with IPF tended to improve psychological well-being but did not improve overall HRQOL measured with K-BILD. Nevertheless, patient satisfaction was high, and home monitoring allowed for individually tailored medication adjustments. Home spirometry was feasible and provided reliable results over time. Hence, we believe that eHealth tools have the potential to enhance personalized treatment for IPF in the future. ■

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References

1. Lederer DJ, Martinez FJ. Idiopathic pulmonary fibrosis. *N Engl J Med* 2018;378:1811–1823.
2. King TE Jr, Bradford WZ, Castro-Bernardini S, Fagan EA, Glaspole I, Glassberg MK, *et al*.; ASCEND Study Group. A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. *N Engl J Med* 2014;370:2083–2092.
3. Richeldi L, du Bois RM, Raghu G, Azuma A, Brown KK, Costabel U, *et al*.; INPULSIS Trial Investigators. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370:2071–2082.
4. Maher TM, Strek ME. Antifibrotic therapy for idiopathic pulmonary fibrosis: time to treat. *Respir Res* 2019;20:205.
5. Tupper OD, Gregersen TL, Ringbaek T, Brøndum E, Frausing E, Green A, *et al*. Effect of tele-health care on quality of life in patients with severe COPD: a randomized clinical trial. *Int J Chron Obstruct Pulmon Dis* 2018;13:2657–2662.

6. Denis F, Basch E, Septans AL, Bennouna J, Urban T, Dueck AC, *et al*. Two-year survival comparing web-based symptom monitoring vs routine surveillance following treatment for lung cancer. *JAMA* 2019;321:306–307.
7. Lancaster K, Abuzour A, Khaira M, Mathers A, Chan A, Bui V, *et al*. The use and effects of electronic health tools for patient self-monitoring and reporting of outcomes following medication use: systematic review. *J Med Internet Res* 2018;20:e294.
8. Jeminiwa R, Hohmann L, Qian J, Garza K, Hansen R, Fox BI. Impact of eHealth on medication adherence among patients with asthma: a systematic review and meta-analysis. *Respir Med* 2019; 149:59–68.
9. Russell AM, Adamali H, Molyneaux PL, Lukey PT, Marshall RP, Renzoni EA, *et al*. Daily home spirometry: an effective tool for detecting progression in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2016;194:989–997.
10. Johannson KA, Vittinghoff E, Morisset J, Lee JS, Balmes JR, Collard HR. Home monitoring improves endpoint efficiency in idiopathic pulmonary fibrosis. *Eur Respir J* 2017;50:1602406.
11. Marcoux V, Wang M, Burgoyne SJ, Fell CD, Ryerson CJ, Sajobi TT, *et al*. Mobile health monitoring in patients with idiopathic pulmonary fibrosis. *Ann Am Thorac Soc* 2019;16:1327–1329.
12. Moor CC, van Manen MJG, Tak NC, van Noort E, Wijsenbeek MS. Development and feasibility of an eHealth tool for idiopathic pulmonary fibrosis. *Eur Respir J* 2018;51:1702508.
13. Moor CC, Wapenaar M, Miedema JR, Geelhoed JJM, Chandoesing PP, Wijsenbeek MS. A home monitoring program including real-time wireless home spirometry in idiopathic pulmonary fibrosis: a pilot study on experiences and barriers. *Respir Res* 2018; 19:105.
14. Raghu G, Remy-Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ, *et al*.; American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Society. Diagnosis of idiopathic pulmonary fibrosis: an official ATS/ERS/JRS/ALAT clinical practice guideline. *Am J Respir Crit Care Med* 2018;198:e44–e68.
15. Patel AS, Siegert RJ, Brignall K, Gordon P, Steer S, Desai SR, *et al*. The development and validation of the King's Brief Interstitial Lung Disease (K-BILD) health status questionnaire. *Thorax* 2012;67: 804–810.
16. Nolan CM, Birring SS, Maddocks M, Maher TM, Patel S, Barker RE, *et al*. King's Brief Interstitial Lung Disease questionnaire: responsiveness and minimum clinically important difference. *Eur Respir J* 2019;54:1900281.
17. Kimman ML, Wijsenbeek MS, van Kuijk SMJ, Wijnsma KL, van de Kar NCAJ, Storm M, *et al*.; PESaM Collaborating Group. Validity of the patient experiences and satisfaction with medications (PESaM) questionnaire. *Patient* 2019;12:149–162.
18. Brooks R. EuroQol: the current state of play. *Health Policy* 1996;37:53–72.
19. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–370.
20. Visca D, Mori L, Tsipouri V, Fleming S, Firouzi A, Bonini M, *et al*. Effect of ambulatory oxygen on quality of life for patients with fibrotic lung disease (AmbOx): a prospective, open-label, mixed-method, crossover randomised controlled trial. *Lancet Respir Med* 2018;6:759–770.
21. Gregersen TL, Green A, Frausing E, Ringbæk T, Brøndum E, Suppli Ulrik C. Do telemedical interventions improve quality of life in patients with COPD? A systematic review. *Int J Chron Obstruct Pulmon Dis* 2016;11:809–822.
22. McLean G, Murray E, Band R, Moffat KR, Hanlon P, Bruton A, *et al*. Interactive digital interventions to promote self-management in adults with asthma: systematic review and meta-analysis. *BMC Pulm Med* 2016;16:83.
23. Talboom-Kamp EPWA, Holstege MS, Chavannes NH, Kasteleyn MJ. Effects of use of an eHealth platform e-Vita for COPD patients on disease specific quality of life domains. *Respir Res* 2019;20:146.
24. Maher TM, Corte TJ, Fischer A, Kreuter M, Lederer DJ, Molina-Molina M, *et al*. Pirfenidone in patients with unclassifiable progressive fibrosing interstitial lung disease: a double-blind, randomised, placebo-controlled, phase 2 trial. *Lancet Respir Med* 2020;8:147–157.
25. van der Hout A, van Uden-Kraan CF, Holtmaat K, Jansen F, Lissenberg-Witte BI, Nieuwenhuijzen GAP, *et al*. Role of eHealth application Oncokompas in supporting self-management of symptoms and health-related quality of life in cancer survivors: a randomised, controlled trial. *Lancet Oncol* 2020;21:80–94.
26. Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. *Health Serv Res* 2005;40:1918–1930.
27. Pearlin LI, Schooler C. The structure of coping. *J Health Soc Behav* 1978;19:2–21.