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Management of Cystic Fibrosis during COVID-19: Patient Reported Outcomes based remote follow-up among CF patients in Denmark – A feasibility study



Lotte Rodkjær^{a,b,c,#,*}, Majbritt Jeppesen^{a,b,#}, Liv Schougaard^{b,c,d}

^a Department of Infectious Diseases, Aarhus University Hospital, Denmark

^b Department of Clinical Medicine, Aarhus University, Denmark

^c Research Centre for Patient Involvement, Aarhus University, Central Denmark Region, Denmark

^d AmbuFlex, Center for Patient-reported Outcomes, Regional Hospital West Jutland, Herning, Denmark

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ABSTRACT

Background: Patients with cystic fibrosis (CF) are considered to be a COVID-19 risk group. In March 2020, a fast-track Patient Reported Outcome (PRO) solution was developed to ensure access to CF care without in-person hospital visits. This study investigated the feasibility of urgently replacing in-person appointments with remote monitoring using telephone consultations combined with PROs. We investigated patients and health care professionals' (HCPs) acceptance, recruitment rate, response rate, missing data, and attrition.

Methods: We included adult CF patients from the Department of Infectious Diseases at Aarhus University Hospital, Denmark between April and June 2020. Patients filled in a disease-specific questionnaire including relevant clinical aspects, performed home spirometry, and sent in a sputum sample before a scheduled telephone consultation. Twelve participants who completed the questionnaire and had a telephone consultation were interviewed. Three physicians and three nurses from the CF clinical team participated in a focus group interview.

Results: Eighty patients were recruited for remote monitoring, and 41 patients filled in at least one questionnaire. Overall, both patients and HCPs found remote monitoring and use of PROs acceptable and useful. Patients experienced greater flexibility and found the questionnaire relevant and understandable but pointed out the need for items regarding mental health status and more adequate information about changes in follow-up and workflow.

Conclusion: Urgent reorganization of outpatient follow-up among CF patients due to COVID-19 was feasible in routine clinical practice. However, patient involvement should be a future point of attention to ensure a sustainable telehealth PRO solution.

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1. Introduction

Cystic fibrosis (CF) requires frequent outpatient visits with monitoring of lung function, microbiology, and nutritional status. Treatment burden has increased over recent years, and most pa-

tients take multiple drugs, several times daily [1]. Treatment regimens including mucolytics, antibiotics, pancreatic enzymes, and insulin, have addressed organ system manifestations rather than treating the underlying ion channel dysfunction. In combination with exercise and physiotherapy, these treatments have been considered to be the best supportive care and have increased life expectancy significantly [2].

Cystic fibrosis transmembrane conductance regulator (CFTR) modulator triple combination therapy was introduced in Denmark (DK) in October 2020. [3]. Most adult and adolescent patients have initiated Elexacaftor-tezacaftor-ivacaftor therapy, which is expected to stabilize clinical disease, reduce hospitalization, and markedly increase survival and improve quality of life [4]. This will eventually

* Corresponding author. Lotte Rodkjær, RN, MPH, PhD, Associate Professor, Infectious Diseases, Aarhus University Hospital, Department of Clinical Medicine, Aarhus University & Research Centre for Patient Involvement (ResCenPI), Department of Public Health, Aarhus University, Ph.: +45 22 30 80 60

E-mail addresses: lottrod@rm.dk (L. Rodkjær), majbjep@rm.dk (M. Jeppesen), livschou@rm.dk (L. Schougaard).

Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark

lead to patient-requested de-escalation of treatment and consultation frequency, increasing the need for individualized flexible solutions including remote follow-up [5].

CF care in DK is centralized at two public university hospitals (in Aarhus and Copenhagen). Treatment is conducted according to European standards of care [6] by skilled and highly trained physicians, nurses, physiotherapists, and dieticians, and includes access to psychotherapy and social worker counselling. Self-administered home treatment with inhaled and intravenous antibiotics, based on prior instruction in the CF clinic, has been implemented as routine. Home spirometry was validated in a previous study to integrate this into future individualized care [7].

CF patients constitute one of the special risk groups that the Danish National Board of Health has designated as being particularly susceptible to COVID-19 [8]. Their vulnerability has been exacerbated by the cancellation of outpatient activity due to COVID-19. Because CF treatment is a highly specialized function in DK, many patients live far from their nearest CF center. By attending a center in person, they potentially risk exposure to COVID-19 transmission through the use of public transport as well as their attendance at the hospital clinic itself.

Because of the expected effects of CFTR modulator treatment, the reorganization of CF clinics was already considered to be a priority in many centers, and this development has been accelerated by the pandemic [9,10]. Patient Reported Outcomes (PROs) use standardized and validated questionnaires completed by patients to provide information on their perceived functional well-being and health status [11]. A PRO solution appeared to be relevant during the COVID-19 pandemic as a way of maintaining regular consultations with stable CF patients by replacing hospital visits with telephone consultations and home monitoring. In March 2020, it was decided to urgently develop a PRO solution for adult CF patients at Aarhus University Hospital to ensure their access to care.

A question emerged about how the resulting PRO solution is perceived by CF patients when it becomes a supplement to their treatment and care. The overall aim of this study was to investigate the feasibility of urgently replacing in-person appointments with remote monitoring using telephone consultations combined with PRO data for CF patients. It also aimed to investigate acceptance by both patients and health care professionals (HCPs), and other feasibility outcomes such as recruitment rate, questionnaire response rate, item distribution, and missing data.

2. Methods

2.1. PRO-based remote follow-up

In March 2020, patients in a stable condition were informed by an HCP that their follow-up method had changed from all in-person appointments to alternating in-person consultations and telephone consultations combined with the use of PRO data.

Due to the COVID-19 pandemic, a 2-week fast-track remote PRO solution was developed for adult CF patients using the AmbuFlex model. AmbuFlex is a public organization in the Central Denmark Region that develops and facilitates the implementation of clinical PRO solutions in the Danish health care system [10]. PRO solutions developed on the AmbuFlex model often consist of three generic elements: PRO data collection, a PRO-based algorithm, and a PRO-based graphical overview [12].

Our PRO solution targeted CF patients over the age of 18 years who could read and understand Danish. The use of PRO data aimed to facilitate patient-centered communication by addressing important issues for patients in their conversations with HCPs. In addition, using PRO data during outpatient follow-up with CF patients facilitated closer monitoring of disease activity compared to

conventional telephone consultations. Patients were initially enrolled during an in-person encounter to introduce them to the electronic system, and thereafter received an invitation via an electronic (Eboks) invitation. The subsequent follow up appointment was being replaced with the questionnaire plus telephone consultation. They were supplied with a link to fill in the questionnaire electronically 2–3 days before a scheduled telephone consultation via secure login at the web page "cfmitelbred.dk". Patients were given both oral and written information and received equipment and guidance to measure their lung function and weight at home and to send a sputum sample to the hospital. Patients had access to their own PRO data at the Danish national health portal "Sundhed.dk". Patients were instructed to contact the clinic by phone as usual if they experienced acute symptoms, needs, or signs of deterioration.

HCPs had access to a PRO-based graphical overview (Fig. 1) embedded in the electronic health record system. Patients' questionnaire responses were assessed by a nurse and physician before scheduled telephone consultations. The responses were processed using a specific PRO-based algorithm and color-coded green (mild symptoms), yellow (moderate symptoms), or red (severe symptoms). Patients with mild to moderate symptoms could be supported virtually and stay at home. Red alerted HCPs to a possible need for supplementary treatment. The questionnaire, combined with a patient-submitted lung function measurement and sputum sample, helped the physicians to target the conversation during the subsequent telephone consultation and more quickly decide whether patients should receive additional treatment, e.g., antibiotic treatment, either at home or in hospital.

2.1.1. CF questionnaire

A disease-specific questionnaire was developed that aimed to identify whether patients had a clinical need for treatment alterations during outpatient follow-up and to focus on the problems most important to individual patients. The questionnaire was developed with clinical experts (doctors and nurses from the CF team in Aarhus) and PRO experts from AmbuFlex. Patients were not involved in this process due to an extremely strict schedule. First, clinically relevant domains to be included in the questionnaire were identified. Clinical experts then allocated how each included item would be treated by the PRO-based algorithm, resulting in a green, yellow, or red color according to the level of clinical importance and its use in the clinical decision-making process to assess whether patients needed treatment alterations or an in-person appointment. The questionnaire included 22 items clinically relevant to CF patients, e.g., breathing, coughing, mucus, eating problems, problems gaining weight, diarrhea, abdominal pain, constipation, and fatigue. The questionnaire also included items regarding lung function and whether patients lacked medicine or equipment that was usually delivered at an in-person hospital appointment. In total, [13] items were measured using the Danish version of the validated Cystic Fibrosis Questionnaire-Revised (CFQ-R) [11], and the remaining 9 were self-constructed ad hoc items.

2.2. Study design and population

This feasibility study evaluated the usage and acceptability among patients, and acceptability among HCPs of a new remote PRO-based follow-up solution as part of daily clinical practice for CF patients. We used three data sources: semi-structured interviews with patients, a focus group interview with HCPs, and the AmbuFlex system [12]. Participants were enrolled from CF patients being treated at the Department of Infectious Diseases at Aarhus University Hospital during April 2020 who fulfilled the

AmbuFlex / Cystic Fibrosis



Fig. 1. PRO-based graphical overview seen by HCPs in patients' electronic health records. The colored dots in the upper row are the output of the PRO-based algorithm (green: mild symptoms, yellow: moderate symptoms, red: severe symptoms). The color of the bars corresponds to this output for each of the items shown. Items in blue are not covered by the PRO-based algorithm. The length of the bars indicates the degree of symptoms. Note: the text in the figure has been translated from Danish.

eligibility criteria: 18 years of age or older, in a stable condition, not transplant recipients, and able to read and write Danish. Only patients who had filled in at least one questionnaire via the website "cfmithelbred.dk" were recruited for individual interviews.

2.3. Ethics

As this was a quality assurance project, ethics committee approval and informed consent were not required for access to patient data and subsequent publication. This included the pilot testing of the questionnaire. However, the study, including the accessing of patient data, was registered with the Danish Data Protection Agency by AmbuFlex as required, and all aspects were performed in accordance with relevant Danish law and regulations.

2.4. Feasibility outcomes

2.4.1. Patient and HCP feedback

All interviews were performed by the first author. Evaluation covered the PRO solution's usability, acceptability, and relevance.

Interviews with patients: Individual semi-structured interviews based on an interview guide were conducted with patients by telephone. These focused on the questionnaire, the IT system, and the treatment. The interviewer asked summary questions at the end of each interview.

Interview with HCPs: A focus group interview based on a semi-structured interview guide was conducted with the CF team face-to-face in the outpatient clinic. This focused on the technical setup, ease of use, understanding, implementation, workflow, resource allocation, and patient involvement.

2.4.2. Descriptive data from the AmbuFlex system

We used data from the AmbuFlex system to assess recruitment rate, questionnaire response rate, item response distribution, and missing data.

2.5. Data analysis

2.5.1. Interviews

Digital audio recordings of the interviews were transcribed verbatim. Analysis of the data was then conducted using methods from Kvale & Brinkmann [14]: 1) reading and re-reading the interviews to gain a sense of the whole, i.e., a general understanding of what the participants had expressed, 2) creating a summary of feedback for each area in the interview guide, and 3) creating a concise summary of key results.

2.5.2. Data from AmbuFlex

Descriptive analyses were performed for patient characteristics and each item in the questionnaire to determine the distribution of response categories, the extent of missing values, and floor and ceiling effects. Differences between responders and non-responders were evaluated by an X² test for gender and by a Kruskal-Wallis test for age. Stata 16 (StataCorp, College Station, TX, USA) was used for all analyses.

3. Results

3.1. Patient and item characteristics

Between April and June 2020, 80 CF patients were transferred to remote PRO-based follow-up. The mean age was 31 years (SD 8.9 years), and 49% were female (Table 1). Forty-one patients (51%) completed at least one questionnaire before a scheduled telephone consultation. Non-responders were mostly men. Table 2 shows the item level distribution of the completed questionnaires. There was a tendency towards ceiling effects in all items, and missing data amounted to less than 5% in the majority of items. However, a few items had a high level of missing, for example, the lung function measurement item (83%), the weight item (10%), and the temperature item (7%). Missing lung function data was often due to the questionnaire being filled out before the spirometry or patients in-

Table 1

Characteristics of responders and non-responders to the questionnaire participants (CF patients) were asked to fill in before a scheduled telephone consultation.

	Total N = 80	Respondents n = 41	Non-respondents n = 39	P-value
Gender, n (%)				
Female	39 (49)	28 (68)	11 (28)	
Male	41 (51)	13 (32)	28 (72)	p < 0.001
Age, years				
Mean (SD)	31.0 (8.9)	29.8 (8.6)	32.2 (9.3)	
Median (IQR)	29.2 (24.9–34.5)	27.1 (24.8–32.7)	30.4 (26.5–40.5)	p = 0.21

SD: standard deviation; IQR: interquartile range

Table 2

Item level distribution of items included in the questionnaire used during outpatient follow-up among CF patients (N = 41).

Item	Symptom difficulties Indicate how you have been feeling during the past two weeks	Distribution (%) of response options				
		A great deal	Somewhat	A little	Not at all	Missing
CFQ-R-39	Have you had trouble gaining weight?	0	1 (2.4)	6 (14.6)	32 (78.1)	2 (4.9)
CFQ-R-40	Have you been congested?	2 (4.9)	2 (4.9)	20 (48.8)	16 (39.0)	1 (2.4)
CFQ-R-41	Have you been coughing during the day?	2 (4.9)	6 (14.6)	31 (75.6)	1 (2.4)	1 (2.4)
CFQ-R-42	Have you had to cough up mucus?	1 (2.4)	4 (9.8)	27 (65.9)	8 (19.5)	1 (2.4)
Ad hoc	Have you had constipation?	0	2 (4.9)	5 (12.2)	33 (80.5)	1 (2.4)
Ad hoc	Have you had jaw and/or forehead pain?	1 (2.4)	2 (4.9)	8 (19.5)	29 (70.7)	1 (2.4)
Ad hoc	Have you had fatigue, lethargy, and/or malaise?	2 (4.9)	4 (9.8)	19 (46.3)	15 (36.6)	1 (2.4)
	How often during the past two weeks:	Always	Often	Sometimes	Never	Missing
CFQ-R-44	Have you been wheezing?	0	0	18 (43.9)	22 (53.7)	1 (2.4)
CFQ-R-45	Have you had trouble breathing?	0	1 (2.4)	7 (17.1)	32 (78.1)	1 (2.4)
CFQ-R-46	Have you woken up during the night because you were coughing?	0	1 (2.4)	15 (36.6)	24 (58.5)	1 (2.4)
CFQ-R-47	Have you had problems with wind?	2 (4.9)	8 (19.5)	19 (46.3)	11 (26.8)	1 (2.4)
CFQ-R-48	Have you had diarrhea?	0	0	13 (31.7)	27 (65.9)	1 (2.4)
CFQ-R-49	Have you had abdominal pain?	0	6 (14.6)	10 (24.4)	24 (58.5)	1 (2.4)
CFQ-R-50	Have you had problems eating?	0	1 (2.4)	6 (14.6)	33 (80.5)	1 (2.4)
		Excellent	Good	Fair	Poor	Missing
CFQ-R-18	How do you think your health is now?	9 (22)	26 (63.4)	4 (9.8)	1 (2.4)	1 (2.4)

CFQ-R: Cystic Fibrosis Questionnaire-Revised

security about which data to fill in, and the patient would often report data during the telephone consultation (See Supplementary material for further information about additional items).

3.2. Interviews with patients

Twelve participants who had completed the questionnaire and a telephone consultation were interviewed. They were selected to ensure diversity in gender, age, *Forced Expiratory Volume in the first second* (FEV1), socioeconomic status, and distance from the CF center.

Participant characteristics: Gender: men (6), women (6); Age: 18–25 (5), 26–35 (6), 36–50 (1); Job: full-time work (5), part time work (1)/retired (1), student (5); Distance to hospital: 10–20 km (4), 21–50 km (1), 51–100 km (1), 101–220 km (6); Living: alone (6), with parents (2), with spouse (4).

Each interview lasted around 30 minutes (Table 3).

3.3. Summary of feedback from patients

Most participants answered the questionnaire without significant problems, but certain questions should be reformulated to address some participants' difficulties understanding them. Some participants suggested additions, such as questions relating to mental health. The participants perceived the questionnaire as relevant, and most considered the form/system would be beneficial when preparing for in-clinic appointments as well as telephone consultations.

General feedback: 1) The solution supported individual needs and gave participants flexibility in their daily life. 2) It was positive that patients were involved in the development of the questionnaire and this new solution. 3) It required a change of mindset about treatment and how to be a patient. 4) The solutions cannot entirely replace personal contact with HCPs.

3.4. Focus group interview with HCPs

Three doctors and three nurses participated in a one-hour focus group interview at the hospital outpatient clinic (4).

3.5. Overall conclusion from patients' and HCPs' feedback

The PRO-based remote follow-up solution is relevant but needs further development including revision of the questionnaire, increased information for patients about the solution's purpose, and discussions about which patients can benefit from it and the implementation process in clinical practice.

4. Discussion

This study examined the feasibility of urgently replacing in-person outpatient appointments for CF patients with remote monitoring using telephone consultations combined with PRO data. We investigated the acceptability, usability, and relevance of the PRO solution developed for both patients and HCPs, as well as other feasibility outcomes such as recruitment rate, questionnaire response rate, item distribution, and missing data.

Table 3
Feedback from interviews with patients.

Areas discussed	Patient observations	Quotes
Questionnaire	<p>Overall, the participants agreed that the questions were relevant and understandable and gave only some minor suggestions for corrections of the language.</p> <p>None thought the form was too long or time-consuming.</p> <p>It took about 10 minutes to fill in the questionnaire if they had measured their lung function and weight beforehand.</p> <p>The questions focused primarily on physical issues, and it was suggested that there should also be questions relating to psychological issues in order to focus on the whole person.</p> <p>Many expressed the view that addressing mental health issues is a prerequisite for good quality of life and vice versa. These two aspects are interconnected.</p> <p>It was important that the questionnaire was not too long, or they would not take the time to complete it.</p>	<p><i>It did not take that long to complete and provides a nice overview. But some of the answer categories are not so easy to understand – e.g., how to define the difference between often and sometimes.</i></p> <p><i>I think there are questions missing about your mental health as this influences your physical health. You cannot separate the two – you have to focus on the whole person.</i></p> <p><i>The psychic part has a big influence on me, especially now that corona has arrived. It shows up on my tests if I am not feeling well mentally.</i></p> <p><i>The questionnaire must not be too long, and the questions have to be relevant to me, otherwise I will not bother to fill it out. It is important that we as patients participate in the development of the questionnaire and this new solution overall. It has to be relevant for us.</i></p>
Information	<p>Due to the urgent implementation, not all participants said that they had received adequate information about the purpose of the solution and an introduction to measuring their lung function.</p> <p>Some said further information about the importance of measuring lung function and weight before completing the questionnaire would have been useful. Some of the participants did not have scales at home.</p> <p>Some found that there was a lot of text information to read and understand before filling out the questionnaire.</p> <p>The amount of information to absorb and number of things to coordinate made it seem complex in comparison to physical attendance, when everything could be arranged at the same time.</p> <p>A number of participants suggested replacing some of the text with visuals, including the different timelines (e.g., schedules for taking their own measurements and having their telephone appointments).</p> <p>Some said that they needed more detailed guidance on how to conduct their consultation by telephone compared to their usual consultation at the hospital.</p>	<p><i>There was a lot of information, and it was difficult to get an overview of it all. For example, I had not measured my lung function before I started filling out the form and could not measure my weight, because I have no scales, and I could not move on in the form until these things were entered.</i></p> <p><i>I think it is nice I can measure my lung function myself, but I am not quite comfortable with it yet, but I think I will get used to it. I know I can call the hospital if there is anything I doubt. There was a lot of text and things to do at different times, and it was difficult to quickly get an overview. It could be an idea to give visuals of the information and the treatment.</i></p> <p><i>It's a different way to go to check, and I think I lacked knowledge about how to have a telephone consultation compared to physical attendance.</i></p>
Technical setup	Participants found the IT system easy to use.	
Patient treatment	<p>Almost all the participants expressed satisfaction with their telephone consultation and reported that the doctor had used their answers in the consultation. The consultation took less time and focused on their needs.</p> <p>The new solution saved participants time, as they did not have to spend time travelling. Furthermore, they did not have to time off work or their studies.</p> <p>It supported individualized outpatient care as participants experience CF as a dynamic disease which therefore needs a flexible course of treatment.</p> <p>It provided more freedom for them to plan their daily life because they have many things, they need to take care of in addition to their treatment, such as family and school.</p> <p>Some expressed that they felt less ill because they didn't have to visit the hospital.</p> <p>Patient-centered communication was encouraged in the consultation.</p> <p>It was important that this was an offer so participants felt committed.</p> <p>Participants required structure to remember to fill out the questionnaire before the consultation.</p> <p>Many underlined that their relationship with HCPs was important and that the PRO solution could not entirely replace meeting them in person.</p>	<p><i>The doctor used my answers in the conversation and was prepared. I think it became much more targeted to my needs and focused. It was really good not to have to spend time talking about everything that had happened but about my future plan.</i></p> <p><i>I live far away and spend a lot of time travelling, which means I have to take a day off work every time I go to the hospital. So I think it's really good if you can have the opportunity for flexible treatment where I can choose whether it should be in person or by phone.</i></p> <p><i>I have a child, am studying, and need to take care of my treatment. It takes a lot of time and therefore I have plenty to look after in my everyday life. Therefore, it would make it easier for me if I did not have to go to the hospital unless it was necessary. I also think I feel less sick and do not neglect my studies either.</i></p> <p><i>It's important it's a choice and not something you have to do. I am aware that it can give you flexibility, but on the other hand, it is also much easier to show up and get everything fixed at the hospital. I live close to the hospital. Here, I have to do a lot beforehand and there are many timescales to find my way around, and it demands a lot of structure.</i></p> <p><i>You have to change your mindset as it is a new way to practice, but it is a good idea.</i></p>

Eighty patients were recruited to remote follow-up, and 41 filled in at least one questionnaire. Overall, both patients and HCPs found remote monitoring and use of PROs acceptable and useful. Patients experienced greater flexibility, and found the questionnaire relevant and understandable, but pointed out the need for items regarding mental health status and more information about the change in follow-up, e.g., the solution's purpose, their role, an introduction to measuring their own lung function measure, and

organization of workflow. Most participants considered that filling in the questionnaire would be beneficial when preparing for in-clinic appointments as well as telephone consultations.

The use of digital technology, such as various telehealth solutions, has increased in CF treatment, as highlighted in a systematic review by Calthorpe et al. [15]. Many patients live far from their CF center and support the development of more flexible solutions such as options for remote delivery. The patients in our

Table 4
Feedback from focus group interview with HCPs.

Areas discussed	HCP observations	Quotes
Technical setup/Ease of use	The HCPs experienced no technical problems in using the system, including the graphics, layout, and function, and they found it easy to navigate individual patients' responses.	<i>It makes really good sense and gives me a good overview. Important information from the patients has appeared in the free text box.</i>
Understanding	They found the questionnaire relevant, and it provided a good overview of each individual's situation. Some of the questions needed to be revised and additional questions needed to be added, e.g., about mental health.	<i>A few clinical questions and questions about their mental health are missing. My experience is that if the patient is affected mentally, it influences the treatment and increases non-adherence. It can help us to be aware of the mental aspect and take action before things go wrong.</i>
Implementation	It was not certain that this was a solution that was suitable for everyone, so the information about what it is about and what it entails needs to be made clearer. Several HCPs found that individual participants had not set aside as much time for the telephone conversation as they would to attend the clinic, or made sure they were in a quiet place with no one else present. Some took the call while they were at work or taking a walk.	<i>I could hear that the patient was out of breath and that it was windy so I asked where he was. He replied that he was at work and standing on the roof. I was not able to continue the conversation with him on the roof and suggested another time for a consultation. Another patient was at the beach when I called him and there was a lot of noise and music.</i>
Workflow/Resource allocation	The solution has led to changes in workflow. While these are manageable, future implementation of the solution will need further adjustments to daily routines and role distribution.	<i>We have introduced a quick morning meeting where we check the PROs from the patients, we have appointments with. Then we are prepared for the conversations and have ordered medication to be sent to the patients.</i>
Patient involvement	The solution was a good basis for dialogue with patients.	<i>It is important to show that you have checked the questionnaire and use their answers in the consultation. They have spent time filling it out. I think communication and the content of the consultations have been more focused. We did not spend time asking about things that we knew were OK but focused the time on the patients' needs.</i>

study also supported the possibility of more flexible solutions as they could spend less time managing their disease, and not have to take time off work and their studies, allowing them to focus on their daily lives. Improved self-monitoring may help patients better understand and self-manage their condition, actively adjusting their treatment in relation to their condition. Further studies are needed to define which patients could benefit from this as the participants highlighted that the solution had both advantages (e.g., gives security and consciousness about disease, self-measurements could change perception of disease status, disease becomes more visible, more control, and larger responsibility) and disadvantages (e.g. becoming overly conscious of disease, worries about measurements, psychological impact if lung function decreases, increased focus on disease as part of everyday life, interruption of daily routines, and requires energy and time). Numerous patients in this study mentioned the same pros and cons. It is important that such flexible solutions are developed with new technology that patients find acceptable and sustainable to use as they already have a significant treatment burden [15]. Adherence to treatment is crucial, and digital technology might improve adherence. Another study by Calthorpe et al. [16] highlighted the need to focus on developing interventions that simplify care and reduce treatment burden. Overall, the participants agreed that the PRO solution supported individualized outpatient care as they experience CF as a dynamic disease that requires a flexible approach to treatment. Nonetheless, they underlined that relationships with and support from HCPs remained important and the PRO solution could not entirely replace in-person meetings. This was also the finding of the other study [16], which identified patients' families and CF teams as key support networks.

4.1. Limitations/strengths

The patients were not involved in the first phase of the development of the questionnaire due to the urgency of the process. To capture the patient's perspective, it is essential that patients are involved in development as only they can determine which health outcomes are relevant to them and whether

the questionnaire captures these outcomes in an understandable way [17]. We accommodated this by conducting interviews with patients after the pilot test, which provided knowledge about both the relevance of the current PRO questionnaire and useful changes and additions to its questions. Further we lack information from non-responders as under 50% of patients never completed a questionnaire.

The benefits for patients must outweigh the time they spend completing the questionnaire and monitoring their lung function, and it is paramount that patients' views guide further development. The solution should also benefit the CF team's clinical practice and their organization's readiness to re-organize consultations. In this study, these perspectives were highlighted in interviews with both patients and clinicians and should be taken into consideration to help ensure successful implementation. Patients selected for interview had already filled out the PRO questionnaire and could therefore have been more positive towards this initiative than the overall group of patients.

One strength of this study was its use of an established technology: the generic PRO system AmbuFlex, which has shown high usability in other clinical settings in the Danish health care system [11,20]. Furthermore, we selected most items from a Danish validated disease-specific questionnaire (CFQ-R) that has been used by patients and clinicians in the Department of Infectious Diseases for several years [18]. We are aware of other PRO instruments for CF patients [19,20,21], especially the questionnaire recently developed by McCarrier et al. [19], which will be considered in future if they cover relevant health aspects that are not included in the CFQ-R. However, the new questionnaire has not yet been translated into Danish. Home spirometry and home treatment had already been introduced at the CF center, which probably helped to facilitate the introduction of the PRO solution. However, despite the patients having a lung function device and are familiar with using it, there are barriers to report this in the questionnaire, as the lung function measurement item was missing in 83%. Important criteria for implementation success are access to a personal computer and IT literacy, which are high in DK and especially among this group of young patients [22].

4.2. Perspectives

The urgent development of the PRO solution had to accommodate both an ongoing pandemic requiring social distancing and a force majeure shutdown of the CF clinic, and an imminent CFTR modulator therapy implementation with expected improvement in patient health requiring new flexible and individualized solutions. This feasibility study provided information that will be valuable in the future development of integrated remote solutions to ensure the selection of suitable patients and long-term adherence.

In conclusion, this study of PRO-based remote follow-up among CF patients revealed high usability, acceptability, and relevance for the target population, and that the solution was feasible and safe for both patients and HCPs. The pilot provided valuable input from the participant perspective, which can be used to improve the questionnaire and future implementation.

Credit Author Statement

All authors have seen and approved the manuscript and have contributed significantly to the work. All authors have made substantial contributions to all the following: (1) the conception and design of the study, acquisition of data and analysis and interpretation of data, (2) drafting the article and revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.jcf.2021.10.010](https://doi.org/10.1016/j.jcf.2021.10.010).

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