CLINICAL STUDY PROTOCOL

Study title:

Virtual pulmonary rehabilitation program for patients with COPD;

a pilot study

Finnish:

Virtuaalinen kuntoutusohjelma keuhkoahtaumatautipotilaille;

pilottitutkimus

Short name:	**e-PURE**
Version:	1.3
Date:	4.11.2024

The study will be conducted in accordance with the principles of Good Clinical Practice (GCP)

Principal Investigator:	Matthijs Feuth
Institute:	Turku University Hospital
Sponsor:	Turku University Hospital, Department of Lung Diseases and Allergology

SIGNATURES

Approved by:

Principal Investigator: _____ Date: ___/___/___

Name

LIST OF INVESTIGATORS AND CONTACT INFORMATION

Henrik Söderström[1]	(HS) Study doctor, specialist in Lung Diseases and Allergology Henrik.Soderstrom@varha.fi; 040-5552238
Maritta Kilpeläinen, MD PhD[1]	(MK) Senior investigator, specialist in Lung Diseases and Allergology, Head of Department Maritta.Kilpelainen@varha.fi; 040-5052545
Matthijs (Thijs) Feuth, MD PhD[1,2]	(TF) Principal investigator; specialist in Lung Diseases and Allergology, clinical lecturer matfeu@utu.fi; 045-156 4939
Riika Liukkonen, MD[1]	(RL) Specialist in Lung Diseases and Allergology riika.liukkonen@varha.fi; 050-4119741
Chrisna Ravyse[3]	(CR) HealthFOX, PhD Clinical Exercise Physiology chrisna.ravyse@healthfox.fi; 044-9839161

1: Turku University Hospital, Department of Lung Diseases and Allergology, Turku; Finland.

2: University of Turku, faculty of Medicine, Turku, Finland.

3: HealthFOX Oy, Finland.

TABLE OF CONTENTS

LIST OF INVESTIGATORS AND CONTACT INFORMATION 2

1 INTRODUCTION 4

2 STUDY OBJECTIVES AND PURPOSE 5

3 STUDY DESIGN 6

3.1 Type and design of the study 6

3.2 General study outline and study schedule 6

4 SUBJECT SELECTION 6

4.1 Source population 6

4.2 Number of subjects 6

4.3 Inclusion and exclusion 7

4.4 Subject withdrawal 7

5 CONTENT OF THE REHABILITATION PROGRAM 8

6 OUTCOME VARIABLES 10

6.1 Assessment of efficacy 10

6.2 Assessment of safety 10

6.3 Focus group discussions 10

7 ADVERSE EVENTS 11

8 STATISTICS 11

8.1 Statistical hypotheses 11

8.2 Sample size 11

8.3 Statistical plan and analysis 12

8.4 Qualitative analyses 12

8.5 Interim analysis 13

9 QUALITY CONTROL AND QUALITY ASSURANCE 13

9.1 Information of study personnel and training 13

9.2 Monitoring and audits 13

9.3 Protocol amendments 13

10 DATA HANDLING AND RECORD KEEPING 13

10.1 Source data 13

10.2 COPD rehabilitation database 13

10.3 Pseudonymization of data and patient key....14
10.4 Electronic data collection....14
10.5 Data management....14
10.6 Study subject registed....14
11 ETHICS....15
11.1 Ethical review....15
11.2 Ethical conduct of the study....15
11.3 Subject information and informed consent....15
12 FINANCING AND INSURANCE....15
13 STUDY REPORT AND PUBLICATION(S)....16
14 ARCHIVING....16
15 REFERENCES....16
16 ABBREVIATIONS AND DEFINITION OF TERMS....17
17 APPENDICES....17

1 INTRODUCTION

Pulmonary rehabilitation (PR) is “a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health enhancing behaviours”.(*1*) PR is highly effective in patients with chronic lung disease including chronic obstructive pulmonary disease (COPD), with large effects on health-related quality of life (QoL) and exercise capacity.(*2*) Its core components include exercise training, which is structured, progressive, and individually tailored, self-management education, outcome measurement, and it should be delivered by a multidisciplinary team of healthcare professionals. (*3, 4*) PR may relieve symptoms like dyspnoea and fatigue, improves emotional function and enhances the sense of autonomy.(*5*) Furthermore, evidence from Finland suggest that PR may reduce hospitalization days.(*6*) However, uptake of PR is limited. In a cross-sectional study of COPD patients in Canada, less than 1% of COPD patients had reportedly attended PR.(*7*) In the United Stated of America, 3.7 % of COPD patients attended PR in 2012.(*8*) Similarly, availability and accessibility of PR is probably limited in Finland, although we have no existing data from literature.

Currently available evidence suggests that telerehabilitation can be a safe alternative that is non-inferior to traditional centre-based pulmonary rehabilitation.(*9*) However, the existing evidence on digital interventions is still limited, especially regarding long term effects.(*10*)

As of Southwest Finland, rehabilitation programs for COPD patients have been on hold since the beginning of the COVID-19 pandemic – in first instance to prevent COVID-19 transmission in vulnerable patients, and in second instance because of lack of resources and/or prioritizing. In 2022-2023, the researchers of this study developed a remote rehabilitation program for COPD patients in a multidisciplinary team including a physiotherapist, a nutritional therapist, a smoking cessation nurse, in close collaboration with the commercial partner HealthFOX Oy. The program is to be incorporated in routine clinical care for COPD patients from April 2024.

2 STUDY OBJECTIVES AND PURPOSE

The general objectives of this pilot study are:

- To facilitate a safe rollout of the remote rehabilitation program for COPD patients in Southwest Finland.
- To identify and subsequently improve limitations of the rehabilitation program.
- To evaluate the levels of participant engagement and adherence to the digital COPD rehabilitation program over an extended period to understand its sustainability and long-term impact.
- To determine the effectiveness of the digital COPD rehabilitation program in improving lung function, exercise capacity, and quality of life among participants
- To assess the impact of the digital program on healthcare resource utilization, including hospital readmissions, emergency room visits, and outpatient visits related to COPD management.
- To measure participant satisfaction, usability, and overall experience with the digital platform to identify areas for improvement and enhance user engagement.
- To evaluate the cost-effectiveness of implementing the digital program compared to conventional rehabilitation methods, considering direct healthcare costs.

3 STUDY DESIGN

3.1 Type and design of the study

This is a single-arm observational pilot study.

3.2 General study outline and study schedule

Study subjects will be recruited from the 15th of April 2024 to the 30th of June 2026.

The rehabilitation program will be initiated preferably within one week but, at the latest within, 4 weeks from signing an informed consent, and the program will last up to 12 weeks. Follow-up will include 1 distant evaluation (questionnaires) at week 16 and a final visit at 26 weeks (+/- 2 weeks), including a 6-minute walking test. Follow-up may last up to 28 weeks from recruitment.

The final study report will be written in the years 2026-2027.

4 SUBJECT SELECTION

4.1 Source population

The source population comprises patients enrolled in the remote rehabilitation program for COPD patients in Southwest Finland. Patients will be selected from the inpatient- and outpatient clinics of Tyks Department of Lung Diseases and Allergology for enrolment in the rehabilitation program. Whether or not one participates in the pilot study will not influence one's ability to join the program. No control group will be recruited for this study.

Whether or not one participates in the pilot study will not influence one’s ability to join the program. No control group will be recruited for this study.

Healthcare professionals working with this study population and guiding them using the mobile application will also be included in the study for interview and feedback on their experience with working with digital tools to interact with patients and guide them through the rehabilitation plan. This will be voluntary and will not affect in any way their position in the workplace.

4.2 Number of subjects

Patients:

A maximum of 50 patients will be recruited for the pilot study.

Healthcare professionals:

All professionals involved in this study will be invited to participate in the feedback interviews.

4.3 Inclusion and exclusion

The study's inclusion criteria and rehabilitation program eligibility criteria can be found in Table 1. For enrolment in the program, the clinician may deviate from the eligibility criteria on an individual basis, if agreed upon with the patient and the program coordinators and if safety issues are sufficiently addressed.

Table 1

<table>
<tr><td colspan="2">Inclusion criteria for the pilot study</td></tr>
<tr><td colspan="2">- Age 18 years or older
- Participation in the remote rehabilitation program for COPD patients
- Signed informed consent</td></tr>
<tr><td>Eligibility criteria for the rehabilitation program</td><td>Exclusion criteria for the rehabilitation program</td></tr>
<tr><td>- Documented COPD diagnosis (ICD 10 code J44)
- Expected survival > 1 year
- Sufficient technical and language skills for safe participation in the program</td><td>- Severe comorbidities with expected survival of less than 1 year, such as:
o active cancer
o unstable heart disease
o Substance dependence interfering with cognitive function
o Clinically significant dementia
Clinical suspicion that remote rehabilitation may be unsafe.</td></tr>
</table>

4.4 Subject withdrawal

Participants can withdraw from the study at any time and without consequences for participating in the rehabilitation program or other clinical care. In case of withdrawal, the study subject may be replaced.

5 CONTENT OF THE REHABILITATION PROGRAM

Development of the application

The application is not a clinical device but a communication tool between healthcare providers and patients. The rehabilitation program is developed by a team of TYKS healthcare workers of multiple disciplines in tight collaboration with HealthFOX. The multidisciplinary team included three pulmonologists (MK, MF, HS), one physiotherapist, two nutritional therapists, and one nurse specialized in smoking cessation.

Content of the rehabilitation program

Patients receive patient education materials throughout the program in text and video formats. These materials provide information on COPD management, lifestyle modifications, and strategies to enhance their well-being. Furthermore, the program contains an individually tailored exercise program., consisting of the following phases:

i. Phase 1: Patient Assessment and Questionnaires

a. Patients are enrolled in the digital COPD therapeutics program through a referral from their healthcare provider or self-enrolment.
b. Patients are prompted to complete a series of validated questionnaires and assessments, including:
    i. CAT (COPD Assessment Test) questionnaire to assess their symptom severity.
    ii. St George respiratory questionnaire, Finnish version
    iii. Nutrition risk screening questionnaire (NRS2002) to evaluate their dietary habits and nutritional status.
    iv. Physical activity participation questionnaire (unvalidated questionnaire that is currently used in TYKS clinical setting to score their current level of physical activity).
    v. Smoking (Standardised nicotine dependence questionnaire, and stop smoking questionnaire) and alcohol question to assess their tobacco and alcohol consumption.
    vi. Depression scale (DEPS) to screen for depression

ii. Phase 2: Clinical Input and Evaluation

a. Review of clinical parameters by a medical doctor, including:
    i. Pulmonary function test results (including spirometry)
    ii. 6-minutes walking test

iii. Blood test results, including hemoglobulin, albumin, C-reactive protein, partial pressure of CO_2 (PCO_2).
iv. Electrocardiogram
v. Medication history
vi. Current medications
vii. And other relevant medical data.

b. The combination of patient input and clinical parameters is used to individualize the COPD therapeutics program for each patient. This will be done by the study investigators and healthcare professionals, and parts will be automatized. The automatically generated aspects will be evaluated and, if needed, adjusted by the study investigators and/or healthcare professionals.

iii. Phase 3: Individualized Program Development

a. Patients who are identified as smokers are provided with a Cognitive Behavioural Therapy (CBT)-based program to support smoking cessation.
b. Based on the risk profile, participants are assigned to different types of breathing exercises, which are timed and progressively increased in intensity over time to improve lung function.

iv. Phase 4: Nutritional Advice

a. Patients receive personalized nutritional advice based on **their input and nutritional status assessment.** The program aims to improve their dietary habits and overall nutritional status.

v. Phase 5: Physical Activity Program Initiation

a. a physical activity program will start in the fifth week of the program. The intensity and duration of the program are determined based on their 6-minute walk test results according to the guidelines of the American College of Sports Medicine (ACSM) as applied in routine medical practice. Each patient receives an individually tailored program, which is approved by the TYKS physiotherapist. (*11*)
b. Over time, the program gradually increases the intensity and duration of the walking program to help patients build endurance.

vi. Phase 6: Strength Training

a. After approximately eight weeks in the program, **depending on patients' clinical parameters** patients are introduced to strength training exercises to improve their overall physical strength and quality of life. Progression is slow and builds over time based on their risk profile.

vii. Phase 7: completing the program and follow-up

a. The training program finishes after 14 weeks. In this phase, the patient is interviewed about their experience
b. In weeks 16 (+/- 2 weeks) and 26 (+/- 2 weeks), the symptoms will be scored with mMRC and St George respiratory questionnaire. In addition, a 6-minute walking test will be repeated in week 26 (+/- 2 weeks).

Tailoring of the program at the individual level

Regular monitoring by the digital care-master (COPD expert nurse/physiotherapist) will ensure patient adherence to care, follow-up on progress and adjust the program if needed based on their evolving needs and goalsor make referral back to the clinical team (TF, MK, HS,RL)

Gradual Program Advancement

As the program is rolled out, its content may be adjusted based on clinical experience and patient feedback from and beyond this pilot study.

6 OUTCOME VARIABLES

6.1 Assessment of efficacy

The single primary outcome measurement is distance in the 6 minutes walking test at 16 weeks in comparison to baseline to assess efficacy at the individual level. Secondary outcome includes 6 minutes walking test result at week 26 and St George Respiratory Questionnaire and 6 minutes walking test after 16 weeks and after 26 weeks in comparison to the result before initiation of the program. Other outcome measurements include the participant satisfaction, and other quantitative and qualitative measures of respiratory health and well-being.

6.2 Assessment of safety

Any presentation at the emergency ward, home visit of emergence services, hospital admission and/or death is considered as a severe adverse event and will be documented as such. Furthermore, adverse events identified from the study data and/or from reporting by the patient will be documented. This is further specified in §7.

6.3 Focus group discussions

Qualitative data obtained from focussed group discussions will be analyzed using a two-step coding according to standards described elsewhere.(*12, 13*)

7 ADVERSE EVENTS

The pilot study will be performed while the remote rehabilitation program for COPD patients in Southwest Finland is enrolled as part of routine care for COPD patients. The aim of this study is to adjust the program to clinical experience. Strictly speaking, any adverse events related to the rehabilitation program are not related to the study, but to routine clinical care.

However, the pilot study will also be used to document adverse events related to the rehabilitation program, and these will be actively asked for as part of the rehabilitation program as well as part of the study. The participants can contact a healthcare provider via the application and are provided with a contact number for (suspected) adverse events during working hours and beyond. They are instructed to call the emergency services in case of any serious acute event.

Any presentation at the emergency ward, home visit of emergence services, hospital admission and/or death is considered as a severe adverse event (SAE) and will be documented as such. Exacerbations of COPD can be expected in a significant proportion of patients due to the severe morbidity. Due to high prevalence of comorbidities, other SAEs may be linked to comorbidities. Any hospitalization for acute conditions that cannot be explained by COPD or the already present comorbidities, will be regarded as a suspected unexpected serious adverse reaction (SUSAR).

After 3 months and 6 months, and at any other point if clinically indicated, the investigators will carry out a safety check by analysing safety data of all included patients. In case of suspected safety issues, the head of the Department will be informed, as well as the Ethical Committee. It will then be considered whether continuation of the rehabilitation program is justified and sufficiently safe.

8 STATISTICS

8.1 Statistical hypotheses

8.2 Sample size

By recruiting 50 patients, we expect to recruit at least 12 patients from each of the following groups:

- According to exacerbations:
    - Stable COPD patients
    - COPD patients with acute exacerbations (AE-COPD)
- According to airflow limitation:
    - GOLD 1-2 (Forced expiratory volume ≥50% of predicted)

- GOLD 3-4 (Forced expiratory volume <50% of predicted)

8.3 Statistical plan and analysis

The majority of the study's data will take a descriptive approach. To determine statistical significance of the primary outcome the Mann Whitney U test will be applied for nonparametric data. Similarly, differences in continuous data between two groups will utilize the Mann Whitney U test, while the Kurskal Wallis test will be employed for comparisons involving more than two groups. Categorical data will be analyzed using either the chi squared test or Fisher exact test. There is a possibility of conducting multivariate analysis for non-parametric data to compute adjusted odds ratios if the data sets are deemed reliable due to their small size. A significance level of $p< 0.05$ will be considered statistically significant.

Data analysis will primarily leverage the most recent version of SPSS during analysis, but the investigator's preference may lead to the use of other established programs such as GraphPad and R. If faced with complex analysis, consulting a biostatistician might be considered, although this is not anticipated until after the study commences.

8.4 Qualitative analyses

The study will also gather qualitative data through focus group discussions with patients of 8-10 participants per group will be included and will continue until data saturation is reached. Discussions with healthcare professionals will be based on availability and might be one-on-one depending on doctor's schedules. These discussions delve into subjective experiences, perceptions, and perspectives regarding the digital COPD rehabilitation program. Patient discussions will explore their engagement, challenges faced, and perceived benefits, shedding light on the program's usability and impact on daily life. Simultaneously, interviews with healthcare providers will capture insights into the program's integration into clinical practice, perceived patient response, and potential areas for program enhancement. These qualitative interviews will provide a nuanced understanding of participant experiences and healthcare provider perspectives, enriching the study's findings beyond quantitative measures.

The qualitative data will be analyzed using ATLAS.ti, a robust qualitative data analysis software. The software enables systematic coding and organization of textual and multimedia data, allowing for in-depth exploration and interpretation. Initially, the interview transcripts will be imported into ATLAS. ti and a systematic coding process will be employed to identify themes, patterns, and key concepts within the data. Through iterative coding and categorization, codes will be grouped to form themes and sub-themes, fostering a comprehensive understanding of participant perspectives and

experiences. The software's tools for qualitative analysis, such as network views and query functions, will be utilized to uncover relationships between codes and themes, facilitating the synthesis of rich, contextual insights from the qualitative data collected during the interviews.

8.5 Interim analysis

Interim analysis will be performed after 3 months and after 6 months. In case of safety concerns, continuation of the study will be critically appraised. For this purpose, external experts may be consulted.

9 QUALITY CONTROL AND QUALITY ASSURANCE

9.1 Information of study personnel and training

All investigators are familiar with the Helsinki Declaration and with the principles of Good Clinical Practice (GCP). All investigators are required to have successfully completed a GCP test within 2 years before the initiation of the study.

9.2 Monitoring and audits

The study will be subject to routine monitoring and audits as performed at the research department of Turku University Hospital, Department of Lung Diseases and Allergology

9.3 Protocol amendments

A protocol amendment will be made and submitted to the Ethical Committee in case of any significant change to the study protocol.

10 DATA HANDLING AND RECORD KEEPING

10.1 Source data

The study data will be obtained from Tyks patient records, from the COPD registry owned by the Wellbeing Services of County Southwest Finland and from the COPD rehabilitation program database (further addressed in §10.2), also owned by the Wellbeing Services of County Southwest Finland.

10.2 COPD rehabilitation database

Healthfox Oy provides the electronic service for the COPD rehabilitation database via the Microsoft Azure-service. The data in the COPD rehabilitation database is entered by patients using validated questionnaires, and relevant clinical data such as disease parameters are entered by healthcare

professionals. The data is stored on the Microsoft Azure-service in Ireland and Germany. The COPD rehabilitation database data protection is in line with the General Data Protection Regulation of the European Union. VARHA is the owner of the data. Healthfox Oy has the right to make quality improvement for the electronic service by using the patient data, if needed.

10.3 Pseudonymization of data and patient key

All study data will be pseudonymized and before storage and handling using a patient key. The patient key file will be stored in a locked space in the working room of the principal investigator. An electronic version of the patient key will be kept in the Microsoft Sharepoint of the Wellbeing Services of County Southwest Finland and will be only accessible to the medical doctors of TYKS involved in this study (HS, MK, RL, TF).

10.4 Electronic data collection

Pseudonymized clinical relevant data including sex, age, comorbidities, clinical characteristics of COPD, comorbidities will be collected via an electronic Case Report Form (eCRF) into an electronic database using REDCap via the University of Turku. Data collection rights are restricted to medical doctors of Tyks involved in this study (HS, MK, RL, TF), while right to correction is reserved to only HS and TF.

10.5 Data management

Pseudonymized study data will be exported from the REDCap study database to SPSS and/or R for statistical analysis. From there, selected data will be exported to graph design programs such as PRISM Graphpad. For this purpose, only the selected relevant data will be exported, to safeguard privacy of the study subjects. Data safety of REDCap is safeguarded by strict policy of the University of Turku.

10.6 Study subject registed

Only the patient identification code (‘henkilötunnus’) will be collected and stored in the patient key file, separate from the study data.

11 ETHICS

11.1 Ethical review

The study protocol will be reviewed by the Ethical Committee of the Wellness Services of County Southwest Finland for approval.

11.2 Ethical conduct of the study

As explained in §1, PR is an established and essential part of treatment for COPD patients, but availability and accessibility of PR is poor (locally in Turku & Southwest Finland, as well as in other parts of Finland). Virtual PR has been shown to be non-inferior to traditional PR, and may improve accessibility of PR. Therefore, virtual PR will be introduced in Southwest Finland in 2024. As highlighted in §2, this study is designed to facilitate a safe rollout of the remote rehabilitation program for COPD patients in Southwest Finland.

As the remote rehabilitation program for COPD patients in Southwest Finland will be part of routine medical care during this pilot study, participation will not pose patients at risk. The decision whether to participate in this pilot or not will not have any consequence regarding the possibility to participation in the rehabilitation program, nor any other treatments or therapy.

11.3 Subject information and informed consent

Patients will be shortly informed about the rehabilitation program and this pilot study by their treating physician. If interested, they will be further informed by one of the investigators of this study and they will receive the patient information letter. It is the responsibility of the recruiting investigator to check whether the patient has understood the methods and objectives of this study, before signing informed consent.

12 FINANCING AND INSURANCE

This is an investigator-driven study. The use of the application in the program is paid by the Wellness Services of County Southwest Finland. Only minor administrative costs are anticipated on, such as printing costs of the patient information letter and these will be carried by the Sponsor. Other costs include refund of travel costs of study subjects beyond the routine program (eg.: for focus group discussions), data storage and programs for data analysis and presentation. The investigators well seek to publish the final report in a journal with Article Publication Charges covered by the Finnish program for Open Access agreements FinELib.

The investigators may apply for funding on an individual basis.

HealthFOX has a liability insurance for 1,000,000 €.

13 STUDY REPORT AND PUBLICATION(S)

The study protocol may be submitted for an international peer-reviewed international journal. Preliminary findings may be reported in national and /or international scientific meetings. The final report will be submitted for publication in an Open Access peer-reviewed scientific journal. Any communication of the study requires approval of the full study team and should be unbiased.

14 ARCHIVING

The study data will be stored in the research database of Turku University Hospital, Department of Lung Diseases and Allergology for the duration of 15 years. The patient key file, containing personal data, will be destroyed within 2 years from completion of the study.

15 REFERENCES

1. M. A. Spruit *et al.*, An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med* **188**, e13-64 (2013).
2. M. A. Puhan, E. Gimeno-Santos, C. J. Cates, T. Troosters, Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* **12**, CD005305 (2016).
3. C. L. Rochester *et al.*, Pulmonary Rehabilitation for Adults with Chronic Respiratory Disease: An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med* **208**, e7-e26 (2023).
4. A. E. Holland *et al.*, Defining Modern Pulmonary Rehabilitation. An Official American Thoracic Society Workshop Report. *Ann Am Thorac Soc* **18**, e12-e29 (2021).
5. B. McCarthy *et al.*, Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* **2015**, CD003793 (2015).
6. M. Katajisto, T. Laitinen, Estimating the effectiveness of pulmonary rehabilitation for COPD exacerbations: reduction of hospital inpatient days during the following year. *Int J Chron Obstruct Pulmon Dis* **12**, 2763-2769 (2017).

7. P. G. Camp *et al.*, Pulmonary rehabilitation in Canada: A report from the Canadian Thoracic Society COPD Clinical Assembly. *Can Respir J* **22**, 147-152 (2015).
8. S. P. Nishi, W. Zhang, Y. F. Kuo, G. Sharma, Pulmonary Rehabilitation Utilization in Older Adults With Chronic Obstructive Pulmonary Disease, 2003 to 2012. *J Cardiopulm Rehabil Prev* **36**, 375-382 (2016).
9. N. S. Cox *et al.*, Telerehabilitation for chronic respiratory disease. *Cochrane Database Syst Rev* **1**, CD013040 (2021).
10. S. Janjua *et al.*, Digital interventions for the management of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* **4**, CD013246 (2021).
11. T. T. Lasala, J. L. Cola, V. M. S. DiMartino, Exercise considerations and recommendations for Chronic Obstructive Pulmonary Disease. *ACSM's Health and Fitness journal* **26**, 56-59 (2022).
12. P. Lehoux, B. Poland, G. Daudelin, Focus group research and "the patient's view". *Soc Sci Med* **63**, 2091-2104 (2006).
13. J. Kitzinger, Qualitative research. Introducing focus groups. *BMJ* **311**, 299-302 (1995).

16 ABBREVIATIONS AND DEFINITION OF TERMS

AECOPD	Acute exacerbation of COPD
CAT	COPD assessment test
CBT	Cognitive Behavioural therapy
COPD	Chronic obstructive pulmonary disease
DEPS	Depression scale
GCP	Good Clinical Practice
GOLD	Global initiative for obstructive lung disease
mMRC	Modified Medical Research Council dyspnea scale
NRS2002	Nutrition Risk Screening 2002
PR	Pulmonary rehabilitation
SAE	Severe adverse event
SUSAR	Suspected unexpected serious adverse reaction
Tyks	Turku University Hospital

17 APPENDICES

Appendix 1	Written information sheet to the study subjects (5 pages)
Appendix 2	Informed consent form (1 page)