Online supplementary material

TELEREHABILITATION PROGRAMME AS A MAINTENANCE STRATEGY FOR COPD PATIENTS: A 12-MONTH RANDOMISED CLINICAL TRIAL

Introduction

This supplementary material provides additional details of some features of the design and execution of the trial (selection criteria, intensive and maintenance interventions, allocation procedures and definition of outcome measures). It also provides more detailed information on adherence, in terms of compliance with scheduled sessions in the intervention group (IG), and on HRQoL outcome measures.

I. Selection criteria

A. Inclusion criteria

The inclusion criteria were a diagnosis of COPD, according to the GOLD guidelines[1] with spirometric grade II-IV severity; age between 18 and 75 years; non-smoker and ex-smoker or smoker with an intention to quit; BODE index value[2] between 3-7, and no acute exacerbation event during the last 4 weeks prior to enrolment.

Exacerbation was defined as worsening of two or more of the following main symptoms for at least 2 consecutive days: dyspnoea, increased sputum volume, sputum purulence or worsening of any major symptom along with one of the following minor symptoms for at least 2 consecutive days: sore throat; cold (runny nose and/or nasal congestion); fever

without any other cause; cough or wheezing. Further, the degree of worsening led the patient to seek medical assessment and antibiotics and/or corticosteroids were prescribed by the physician.

B. Exclusion criteria

We excluded COPD patients with a bronchodilator response (FEV1 increase >15% of the baseline value after 200 mcg of inhaled bronchodilator), a clinical diagnosis of respiratory disease other than COPD, a history of severe coronary artery disease, orthopaedic diseases seriously limiting mobility, life expectancy of less than 2 years, or inability to co-operate.

Medical treatment for all patients, other than treatment specific for the COPD management, was supervised by the primary care physician and was not changed in the programme. Exacerbations were treated according to usual clinical practice by the patient's primary care medical team or pulmonologist on an outpatient basis or at the emergency department in both groups. Some episodes required hospital admission for more intensive therapeutic management. Patients were told about the trial and given sufficient time and opportunity to consider whether to participate and, if so, give written informed consent. They were informed of the need to be used to dealing with a mobile phone-based app if they were eventually assigned to the IG and willing to meet all the requirements of the study.

II. Intensive PR and randomisation

A. Intensive programme

All patients attended an initial 8-week outpatient PR programme, with three sessions a week lasting approximately 2 hours. These consisted of 1.- Chest physiotherapy training consisting of 30-minute sessions of breathing retraining, and if indicated, postural drainage; and 2.- Exercise training sessions with a) arm training consisting of a 30-minute

weight lifting session, starting with 1/2 kg in each hand, and progressively increasing by 1 kg every week until peak tolerance; and b) lower extremity training consisting of a 30-minute session of pedalling on a cycle ergometer. To determine the level of effort to be indicated for training, the patients performed a symptom-limited progressive cycle ergometer exercise test. The exercise started with a workload equivalent to 50% of the maximal load (Wmax) achieved during the baseline progressive exercise test. The workload increased gradually by increments of 10 watts and was considered acceptable if the patient's heart rate (HR) (+/- 10 beats/minute), SpO2 (+/- 2%) and blood pressure remained stable (within the accepted normal range), and exercise was well tolerated. The sessions ended with relaxation techniques. Additionally, four educative sessions were scheduled over the 8-week period, targeted to the patient and their family, including basic knowledge of pulmonary disease, alarm signs, instruction in medication management and energy saving.

B. Randomisation

Following completion of intensive PR, patients were allocated at random to one of the two maintenance strategies; this randomisation was implemented through the generation of a computer-based random allocation sequence, stratified by centre, with a 1:1 allocation ratio, that used permuted blocks of varying size to maximize balance in sample size between groups. The allocation list was kept at the Clinical Epidemiology Unit of the coordinating centre. Maintenance treatment was assigned centrally only after ensuring that the patient met all selection criteria and confirmation by the recruiting staff at each site that the informed consent form had been signed.

III. Maintenance period

A. Intervention group (IG):

All patients assigned to the IG group received the system kit (mobile phone, pulse oximeter, dumbbells, exercise bicycle) and a user guide on how to use the telerehabilitation software and mobile interface. Exercises performed at home by each patient at each maintenance session were recorded on the mobile-phone app. The patient was instructed to send through the mobile all required data to the web-based platform after each session had taken place. Physiotherapists were able to review the exercise pattern of their patients.

1. Components of the TelePR programme

The home-based telerehabilitation programme included the following components (e Figures 1 and 2): a) individualized action plan; b) access to the call centre (enabling them to speak to a system technician if any technical problem occurred with the data management platform); and c) arm and leg exercises. Exercises were individually tailored to suit each patient's capacity. The exercises were similar to those that the patient had performed during the 2-month intensive period of rehabilitation with the exercise load and intensity equivalent to those used and tolerated by the patient in their last week at the hospital.

The home exercise was periodically monitored by the physiotherapist, using the web-based platform, to provide feedback to patients regarding activity levels and exercise training load. The exercises were adjusted according to compliance and patient's reported symptoms and recorded vital sign parameters.

Each rehabilitation session lasted approximately an hour and a half. The patient was asked to follow the sequence of home exercise routines programmed by the physiotherapist and stored in the app. The session usually included 10 minutes of chest physiotherapy, 30 minutes of arm training with weight lifting and 30 minutes of leg training with cycle ergometer in sequences of 15 minutes cycling, 10 minutes rest and 15 minutes cycling (at least 3 days per week) (e Figure 3).

Patients were asked to enter information on their oxygen saturation and heart rate readings into the mobile phone before and after each session. They also needed to type scores of

dyspnoea perception and leg discomfort (graded according to the Borg scale) into the mobile app on completion of each exercise sequence (e Figure 4).

2. Safety assessment and assurance

The patient was instructed to perform the exercises according to safety guidelines: i) use of dumbbells: if O_2 Sat ≤ 91% and/or dyspnoea score ≥4 then the patient was advised not to perform the scheduled exercises and to enter these data in the app; and ii) leg exercises: if O_2 Sat ≤ 91% and/or dyspnoea score ≥ 6 and/or heart rate ≥ 90% of the maximal tolerated rate (see definition below), the patient was advised not to perform the scheduled exercises and to enter these data in the app.

The physiotherapist was enabled to monitor the amount of exercise done by each patient. A traffic light system was devised as an aid to use platform-based data:

Dumbbells:

Red light: O_2 Sat ≤ 89% and/or Borg dyspnoea score ≥ 6

Yellow light: O_2 Sat ≤ 91% and/or Borg dyspnoea score ≥4

Bicycle:

Red light: O_2 Sat ≤ 89% and/or Borg dyspnoea score ≥ 6 and/or heart rate ≥ 90% of maximal tolerated rate.

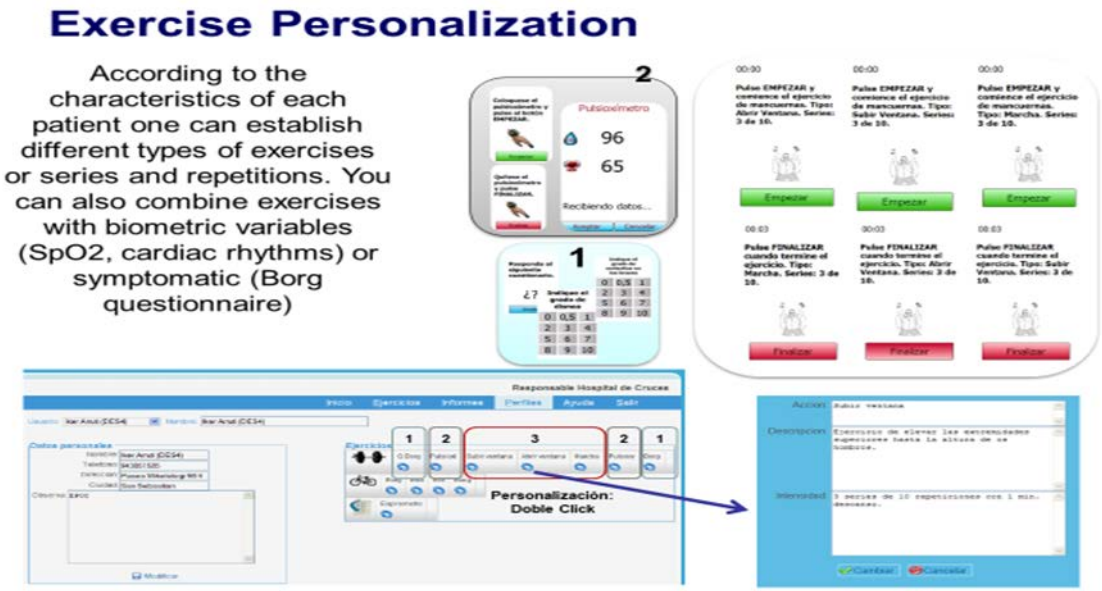
Yellow light: O_2 Sat ≤ 91% and/or Borg dyspnoea score ≥ 6 and/or heart rate ≥ 90% of maximal tolerated rate.

Maximal tolerated heart rate was calculated individually for each patient, based on the maximum heart rate measured during the cycle tests performed at the hospital in the last week of intensive PR.

Physiotherapists were given general advice to review these signals on a regular basis and contact the patient either if a sequence of three yellow signals was flagged or there were two red signals, at most two sessions apart. They were also made aware of any potential exacerbation through phone contact with the patient when substantial departures from the scheduled programme were observed.

Exacerbation episodes were managed through the usual care pathways (primary care or outpatient hospital ward attended by a pulmonologist, with some episodes dealt with at the hospital emergency department or requiring hospital admission). The patient was then contacted periodically until they reached the point where they felt they could return to the exercise programme. At any point, patients were able to choose to abandon the programme, if they felt they could no longer continue. After an exacerbation, it was usually necessary to start the exercise sessions at a lower intensity than before the event; the intensity and workload of exercises were adjusted by physiotherapists, according to local criteria and procedures.

e Figure 1. Snapshots showing instructions for patients to follow on the TelePR app.



e Figure 2. Snapshots of the software's interface showing patient-tailored exercise plan and instructions on the use of the pulse oximeter and scoring of perceived dyspnoea using the Borg scale.

e Figure 3. Snapshots of the software's interface showing data from a sample day of exercise.

e Figure 4. Example of a leg exercise session with instructions on exercise sequencing and how to score perceived leg discomfort between sequences.

Control group (CG):

Patients in the CG group were advised to keep active and exercise regularly. No supervision of their level of activity was organised and they only visited the hospital for scheduled evaluations. We did not provide them with cycle ergometers, but we advised them to walk at least 1 hour daily. If they had access to a cycle ergometer, they were advised to do exercises similar to those performed at the hospital.

IV. Outcome measures

A. BODE Index

The BODE Index is a multidimensional scale in which higher scores indicate a higher risk of death. The index includes body-mass index (B), the degree of airflow

obstruction (O) dyspnoea measured by the MRC scale (D), and exercise tolerance (E) as assessed by the 6-minute walk test (6MWT). Its score ranges from 0 to 10 points, and the higher the score, the worse the patient's clinical condition.[2, 3]

B. Exercise tolerance

A 6MWT was conducted according to the ATS statement.[4] Improvement after training greater than or equal to 35 meters was considered clinically important.[5]

C. Health-related quality of life (HRQoL)

To assess HRQoL, we used two questionnaires: the Short Form-36 (SF-36) and the Chronic Respiratory Questionnaire (CRQ). The SF-36[6] is a general questionnaire that measures HRQoL and covers eight domains: physical functioning, role physical, role emotional, social functioning, general health perceptions, mental health, bodily pain and vitality. For all measures, scores were linearly transformed to scales of 0 to 100, higher scores indicating greater impairment. Physical component (PCS) and mental component (MCS) summaries were used to compare intervention and control groups.[7]

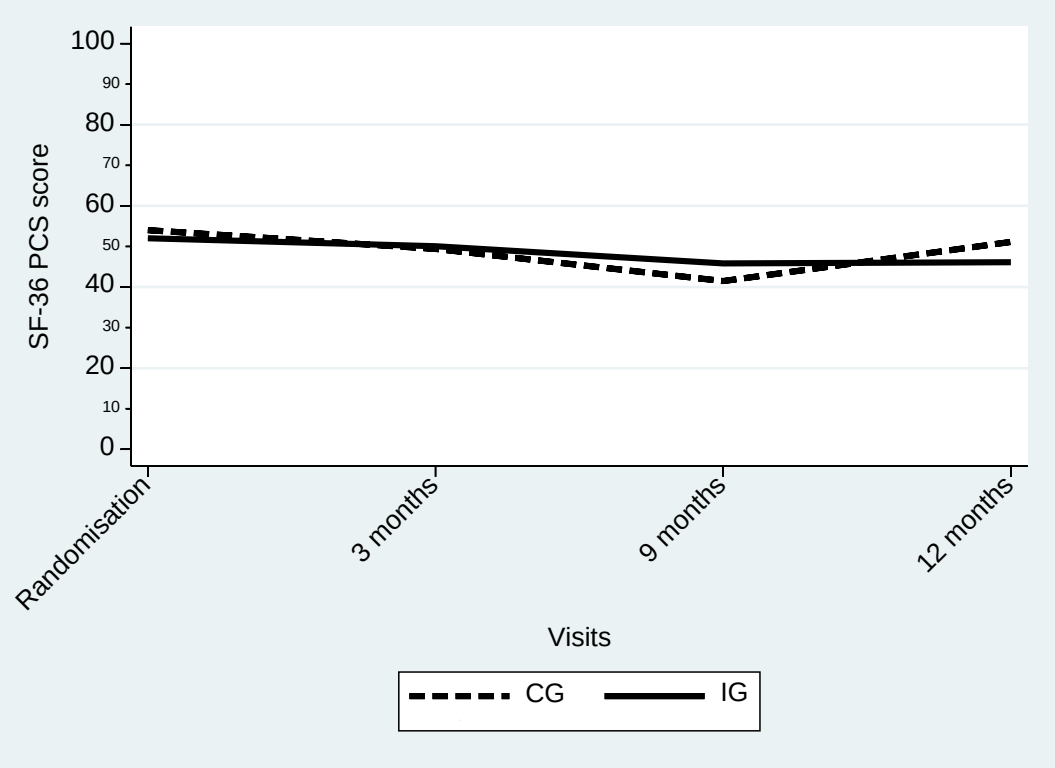
The interviewer-administered version of the CRQ is a specific questionnaire that has been translated and validated for use in Spanish.[8] The questionnaire includes 20 items covering four domains: dyspnoea (CRQ-D, five items), fatigue (CRQ-F, four items), emotional function (CRQ-E, seven items) and mastery (CRQ-M, four items). Each item was rated on a 7-point scale, higher scores indicating better perceived quality of life. We defined the minimal important difference as a change of 0.5 per item.[9] All the tests were performed in both groups 1 week prior to the start of the intensive PR programme and repeated immediately after the intensive period and at the 3, 9 and 12-month visits during the maintenance period.

V. Adverse events and dropouts

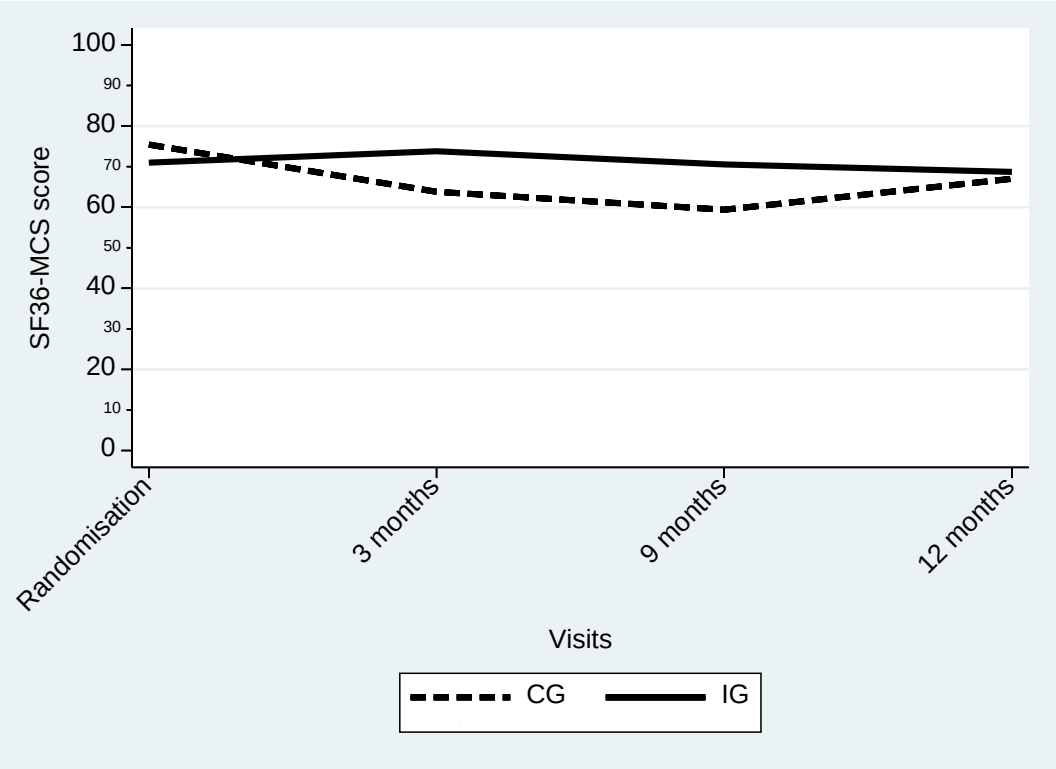
Adverse events (including deaths, injuries and other events potentially attributable to the rehabilitation programmes) were to be recorded in the specific web-based case report form (CRF). Technical problems were recorded by each participating centre in a separate database. Patients who notified the research team that they refused to participate any longer in the study and therefore withdrew their consent were considered dropouts. Patients who stopped actively participating in the intervention were kept in the study, advised to attend follow-up visits and analysed according to the intention-to-treat approach. Patients were able the leave the study at any time. Withdrawal times and reasons were recorded in the study CRF. Any death that occurred during the study time had to be notified without delay to the sponsor and the Ethics Committee.

VI. Results

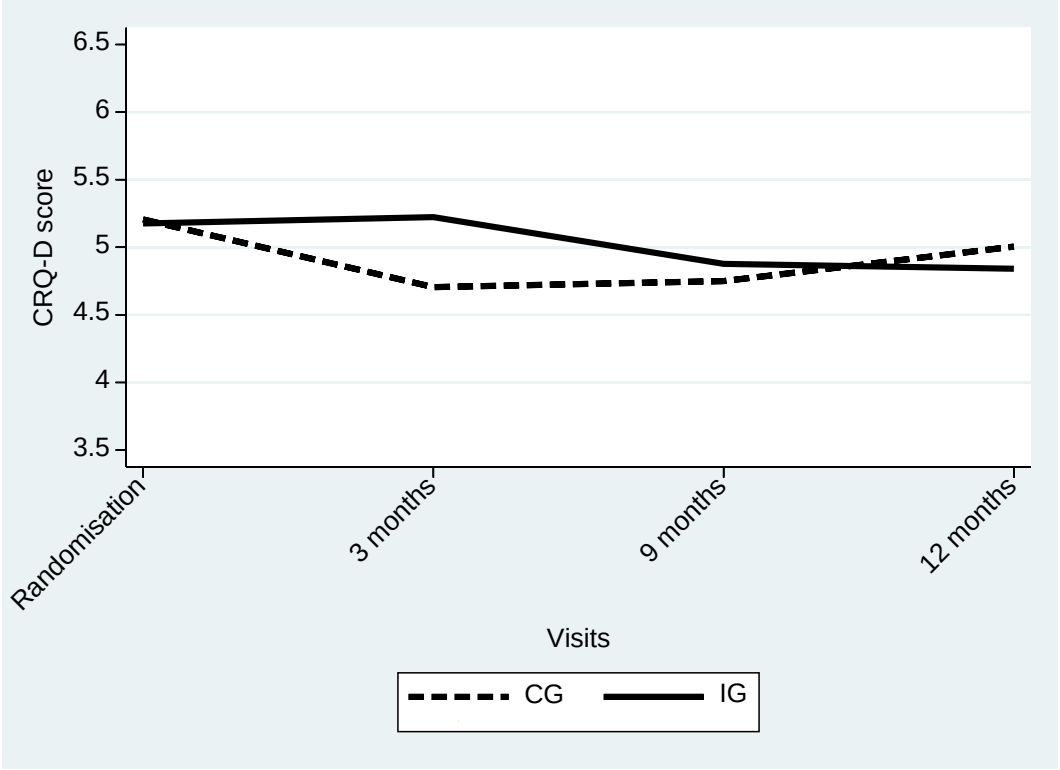
A. Comparative changes in HRQoL results



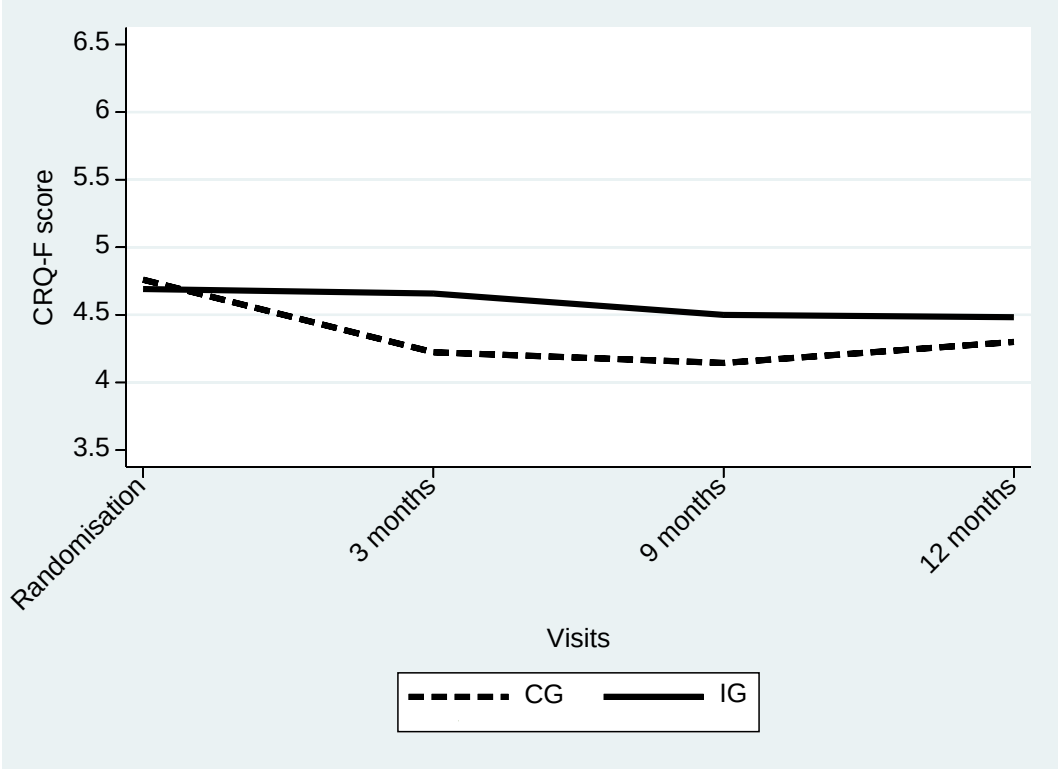
e Figure 5. Mean Short Form-36 physical component summary (SF-36 PCS) score by visit and treatment group (CG: control group IG: intervention group).



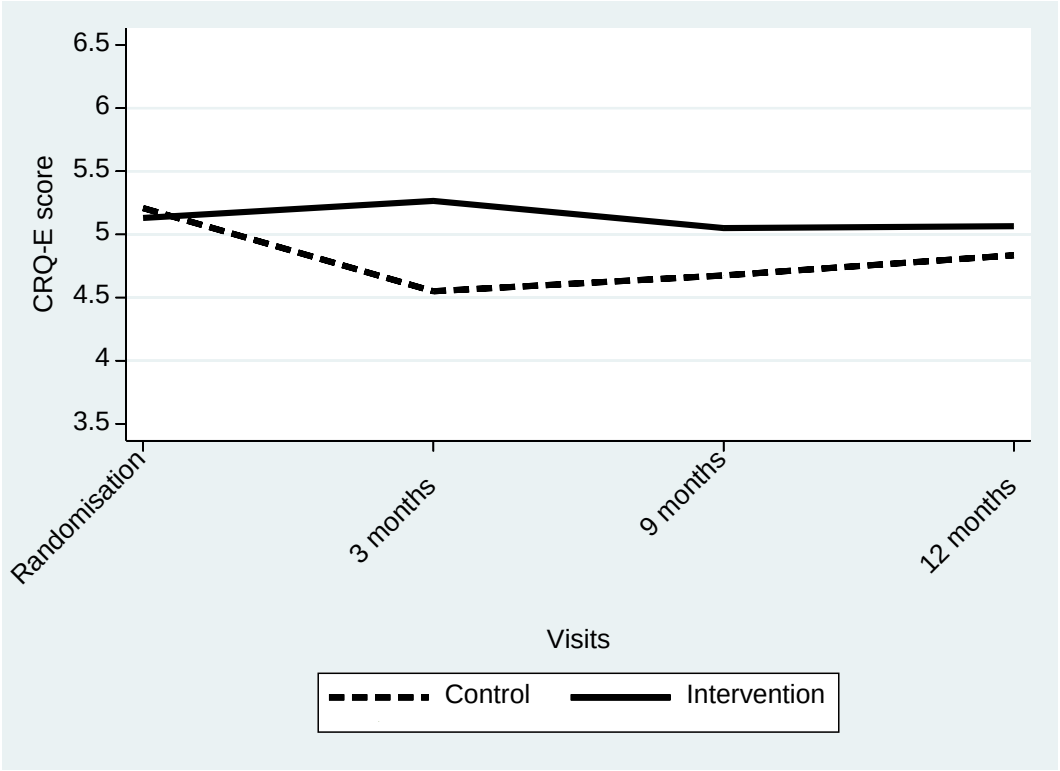
e Figure 6. Mean Short Form-36 mental component summary (SF-36 MCS) score by visit and treatment group (CG: control group IG: intervention group).



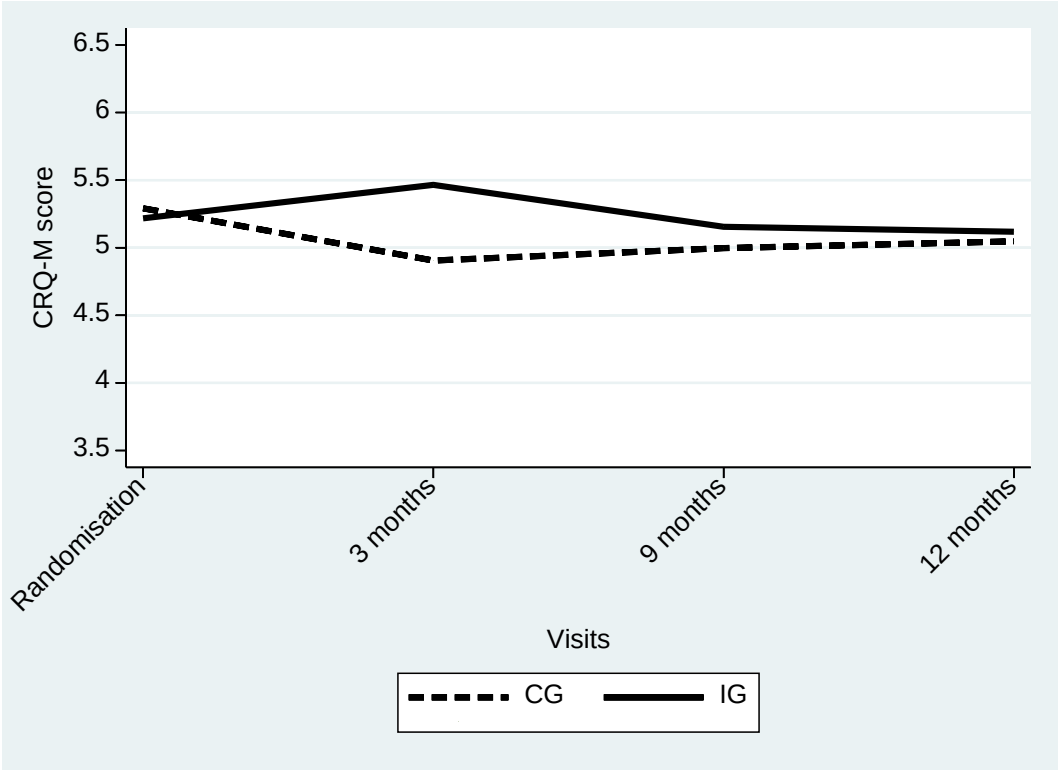
e Figure 7. Mean Chronic Respiratory Questionnaire dyspnoea (CRQ-D) score by visit and treatment group (CG: control group IG: intervention group).



e Figure 8. Mean Chronic Respiratory Questionnaire fatigue (CRQ-F) score by visit and treatment group (CG: control group IG: intervention group).



e Figure 9. Mean Chronic Respiratory Questionnaire emotional (CRQ-E) score by visit and treatment group (CG: control group IG: intervention group).

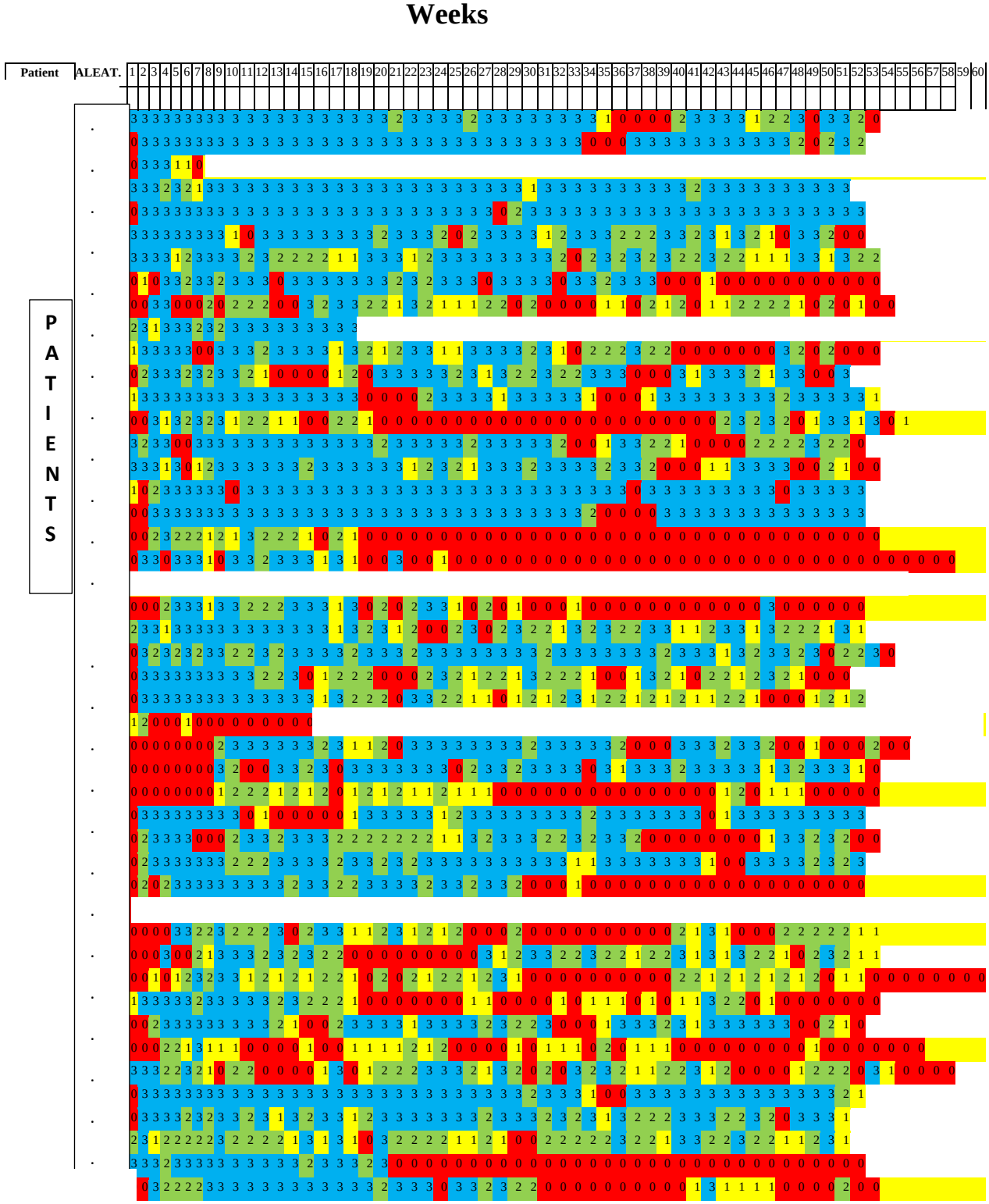


e Figure 10. Mean Chronic Respiratory Questionnaire mastery (CRQ-M) score by visit and treatment group (CG: control group IG: intervention group).

Month of visit	Difference (IG-CG)	
	CRQ-D	CRQ-M
3	0.4	0.6
9	0.1	0.3
12	-0.1	0.1

e Table 1. Differences between treatment groups in Chronic Respiratory Questionnaire dyspnoea (CRQ-D) and mastery (CRQ-M) scores by visit, showing changes over time (statistically significant interactions).

B. Compliance with prespecified sessions (IG)



e Figure 11. This figure shows weekly compliance of TelePR (IG) patients with scheduled home-based rehabilitation sessions over the course of the study. Blue, green

and yellow indicate that the patient reported exercising on at least 3 days, 2 days or 1 day that week; red indicates that the patient did not perform any maintenance session that week and white that the patient dropped out or was withdrawn from the study.

VII. References

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4. Holland AE, Spruit MA, Troosters T et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J* 2014;44:1428–1446.

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