EFFECTIVENESS OF A HOME-BASEDACTIVE VIDEO GAME PROGRAMME IN YOUNG CYSTIC FIBROSIS PATIENTS

Abstract

Background: Exercise-based rehabilitation is already a part of cystic fibrosis (CF) treatment; however, patient adherence is low.

Objectives: To assess the effectiveness of a home exercise programme using active video games (AVGs) as a training modality for children and adolescents with CF.

Methods: Thirty-nine children with CF were randomised to a control group (CG, n=20, age 11±6 years; FEV_1 86.2±20.5% of predicted) or training group (AVGG, n=19, age 13±3 years; FEV_1 82.7±1.7% of predicted). The home training protocol consisted of 30–60 min/ses, 5d/wk for 6wk, using a Nintendo Wii™ platform. Exercise capacity was measured by the 6MWT and modified shuttle walk test (MSWT); muscular strength: horizontal jump test (HJT), medicine ball throw (MBT) and handgrip strength (RHG; LHG); and quality of life: Cystic Fibrosis Questionnaire-Revised (CFQ-R). All the children were measured at baseline, post-rehabilitation, and at 12months.

Results: For the group×time interaction ANOVA: the AVGG showed significant between-group differences in exercise capacity: 6MWD, 38.4m, p<.01; and MSWD, 78.4m ,p<.05). Muscular strength:(HJT 9.8cm; MBT 30.8cm; RHG,7kg; and LHG 6.5kg, p<.01) pre vs post all. The CFQ-R reported significantly higher scores on respiratory symptoms after the intervention and favoured the AVGG, and there was an improvement in other domains after 12 months. Adherence to the home exercise programme was 95% during the 6-week intervention period.

Conclusion: A home-based programme using AVGs can effectively improve exercise capacity, muscular strength and quality of life in the short-term in children and adolescents with CF. The effects of training on muscle performance and quality of life

were sustained over 12 months.

Clinical trial registered with www.clinicaltrials.gov (NCT02552043)

Introduction

Cystic fibrosis (CF) is the most common autosomal recessive genetic disease in the white population; the prevalence of CF is 0.737 per 10,000inhabitantsin Europe[1]. CF is a multisystem disorder that is characterised by nutritional deficiencies and recurrent respiratory infections caused by thick mucus[2].Declines in physical activity (PA) are related to exercise intolerance and peripheral muscle weakness and have been shown to be a key predictor of disease prognosis and mortality in patients with CF[3].

Exercise capacity is limited by several factors in CF, including pulmonary function (ventilatory limitation) and peripheral muscle dysfunction (including muscle strength [4] and muscle endurance [5]). Furthermore, nutritional imbalance and systemic inflammation have been suggested as a contributing factors to muscle dysfunction[6,7]. Beyond disease-related factors, a lack of PA might contribute to peripheral muscle abnormalities[5,8].Physical exercise training has potential therapeutic effects on exercise capacity, pulmonary function, peripheral muscle dysfunction and health-related quality of life (HRQoL)[5,9,10]. Despite these benefits, most, but not all, patients with CF display low levels of PA and exercise training[11].

CF management includes airway clearance, medication, nutritional advice and exercise training; these daily treatments can be burdensome, time-consuming and costly[12]. In general, poor levels of exercise adherence have been reported for this population and are caused by the long-term and arduous nature of the therapeutic regimens[13];in another study, however, evidence of good adherence (57%–88%) was found over other therapies[14].Young patients with CF experience difficulty adhering to exercise routines when the activity is tedious or disliked [15].Thus, it is important to incorporate, facilitate and encourage the use of new tools that increase habitual PA and new programmes that consider the complex psychosocial realities and experiences of these patients.

Recently, a new generation of video games that require interactive PA, which are known as active video games (AVGs), have become popular. The potential health effects of these active games on children have been extensively demonstrated[16–20],and these effects include increased energy expenditure, the attainment of moderate PA levels, decreased sedentary time, increased overall muscle strength and improved cardiopulmonary fitness. In children with CF, studies have reported that AVGs produce high physiological demands similar to conventional exercise programmes [21–23].Likewise, previous studies have shown that participants experience greater enjoyment, lower dyspnoea, and increased muscle performance when using AVG comparison to high-intensity cycling[24]. An important feature of AVGs use is the entertainment factor, because some users find AVGs to be more motivating than traditional exercise modes. A recent review [25] confirms that engaging in a home exercise programme can result in improved PA participation among patients with CF. It has also been reported that many adolescents regularly play AVGs at intensity levels above global PA recommendations [26]. However, the relevant studies failed to verify the effects of using AVGs a training protocol and to determine whether these effects are maintained after the intervention. Hence, AVGs appear to be a potentially innovative alternative to traditional exercise programmes that can be used to reduce sedentary time, increase adherence and promote PA enjoyment; and these games could be incorporated into more structured home pulmonary rehabilitation programmes. Thus, the purpose of this study was to assess the effectiveness of a home exercise programme that uses an AVG platform as a training modality among adolescents and children with CF. We hypothesised that this intervention would increase exercise capacity and muscular strength and that these improvements would be sustained over time.

Methods

Study design

This study was a single-blind, randomised clinical trial. The participants were randomised into two groups: the control group (CG) and the active video games group (AVGG). To ensure blinding, an external individual who was not involved in the study allocated participants to each group using GraphPad Software© (1:1 simple randomisation), and the treatment allocations were adequately concealed in sealed envelopes. The participants were not blinded. However, the study staff who administered the questionnaires and performed the tests to collect outcome data were blinded to the participants' treatment allocations. All the patients received routine management, including inhaled antibiotics for respiratory infections, chest physiotherapy and nutritional supplementation, and were asked to continue their normal exercise routine. In addition, the AVGG performeda6-weekhome-based exercise programme. Both groups were followed for a 12-month period, and only the AVGG received a specific exercise prescription during the follow-up period.

Study group

The study population included patients who were from 7 to 18 years of age and diagnosed with CF. Patients were recruited from July 2015 to July2016 from the Cystic Fibrosis Association of Madrid (Madrid)and the Cystic Fibrosis Association of Valencia (Valencia), in Spain. All the patients were clinically stable without disease exacerbations in the six weeks prior to the study's start date. Patients were excluded if they presented clinical evidence of cardiovascular, neuromuscular or osteoarticular comorbidities that would have limited their ability to participate in exercise programmes. Lung transplant candidates and patients who participated in a rehabilitation programme within the 12 months prior to the study were also excluded. Finally, participants who were not able to attend at least 80% of the intervention sessions and participants who met any exclusion criteria during the 6 weeks of the study were also excluded. After the protocol was approved by the Human Subjects Ethics Committee of *Hospital Ramón y Cajal* in Madrid (Spain), the protocol was approved by each CF association. Written informed consent was obtained from all the children and from their parents or legal guardians.

Assessments

Measurements included weight, height and spirometry, which was assessed with a portable spirometer (Spirobank USB®, MIR, Rome, Italy) [27].All outcome measures were assessed at each measurement time point: preintervention (baseline), postintervention (6 weeks) and follow-up (12 months). The exercise capacity tests were performed on two consecutive days in randomised order to avoid participant fatigue and learning bias.

Primary Outcome

The modified shuttle walk test (MSWT) is a valid and reliable test for measuring exercise capacity in children with CF[28]. The participants were asked to walk rapidly at gradually increasing speeds (15 levels total) along a 10-metre corridor, and they were allowed to run as necessary. Two tests were performed separated by 30 minutes of rest, and the farthest walking distance (MSWD) was registered [29].

Secondary Outcomes

The 6-minute walk test (6MWT) is a valid and reliable test for evaluating functional exercise capacity in children with CF[30]. The patients were asked to walk as far as possible along a 20-metre corridor, and standardised encouragement was given after each minute. Two tests were performed separated by 30 minutes of rest, and the farthest walking distance (6MWD) was recorded [29].

The horizontal jump test (HJT) is a reliable test for evaluating the functional power of the lower limb[31]. Jumps are made with the feet placed at shoulder width. Taking an extra step or touching the floor to regain balance is recorded as an invalid result. Three jumps were made, and the farthest distance was recorded.

The medicine ball throw (MBT) is a valid and reliable measure of arm strength in children [32]. The participants sat on their knees and threw the medicine ball forwardusing an overhead motion (2kg: ≤12 years of age and3kg: ≥13 years of age). The distance of the farthest of three throws was recorded.

The handgrip device is a valid and reliable tool for measuring the isometric strength of the hand and forearm [33]. All the participants held a hand dynamometer (JAMAR®, Patterson Medical, IL, USA) at a 90° angle to their elbow. Three separate tests were administered for the right handgrip (RHG) and left hand grip (LHG), with 30sof rest between tests. The highest value was recorded (kg).

The Spanish version of the Cystic Fibrosis Questionnaire-Revised (CFQ-R)[34,35] is are liable and valid measure of HRQoL for patients with CF. This questionnaire consists of self-reported items within various domains. Three different versions of the questionnaire (CFQ-R 6-11, CFQ-R 14+, and CFQ-R Parents) were used. All the answers were reported on a 4-point scale, with the respondents rating and selecting statements (including physical functioning, respiratory symptoms, etc.) that described the patient’s situation. Higher scores indicate higher degrees of impairment.

Videogame exercise programme

The6-week home training protocol consisted of 30–60 min sessions, 5 days per week, using a Nintendo Wii™ platform with the game EA SPORTS™ ACTIVE 2. This game involved activities such as running, squats, lunges and bicep curls. The game is supervised by a virtual personal trainer and includes a heart rate (HR) monitor. Once a week, at the beginning of the training session, the videogame included a maximum HR test. This test consisted of short and intense exercise (foot fires) for more than one minute to increase the HR, and then a cool-down time by walking until the HR returns to normal. With this test, patients could control their HR evolution, which helped them monitor daily exercise intensity. The patient was advised to perform all activities at a fitness level of three, which is equivalent to a 70%–80% maximal HR. We chose this video game based on the results of a previous study, in which investigators observed high physiological demands capable of generating training effects in patients with CF[22].The exercise activities were loaded into each participant's console and adjusted according to age to improve motivation among the children (i.e., fun fitness activities)(group 1, ≤12 years of age; group 2, ≥13 years of age).The training load was increased every week. An initial series of training sessions was provided in the first week of the programme at the two specialised CF institutions to ensure that the participants performed the exercises correctly. These three training sessions also served to monitor the patients' exercise response and to teach them to avoid risky situations during training sessions at home. The subsequent training sessions were supervised by parents or caregivers at home. To increase patient adherence, a physiotherapist provided weekly telephone check-ins. After the training period, the AVGG patients were instructed to continue their individualised exercise programme using the same AVG at home for a 12-monthfollow-up period, with an exercise prescription of a minimum of 2 days per week, 20 min per session. All the participants were in possession of the necessary technological requirements (video game console and AVG) during the 12-month study. At the end of the intervention, all the patients were asked to answer a questionnaire about the acceptability of the AVG. The items in the questionnaire are aimed to evaluate the perceived degree of 'enjoyment,' 'comfort,' 'acceptability' and 'desire to continue.' A Likert scale was used to score each item with 0 as the worst and 5 the best, and the predefined values 'yes' or 'no.' Adherence levels were measured using the Youth/Adolescent Activity Questionnaire (YAAQ) at baseline and at 12 months in both groups (CG and AVGG). The YAAQ reports on the amount of time spent on PA in the previous year[36]. In addition, based on a previous study [37], adherence was measured monthly by email. The participants were instructed to send a log of all exercise and training days in the previous month.

Sample size

The sample size was calculated with G*Power version 3.1.7 (G*Power© University of Dusseldorf, Germany). Between-group differences in the exercise capacity test (6MWD) were used to determine the power calculations. A pilot study with a sample of 18 participants (AVGG, n=10 patients with CF and CG, n=8 healthy volunteers), established an expected effect size of 0.27 (moderate). Using a power of 0.90 (1- β error) and a significance level of 0.05 (α error), 18 patients per group was deemed to be the minimum study sample size. Assuming a 15% dropout rate, the study sample size was set at 41 patients.

Statistical analysis

The data analysis was performed with SPSS version 21.0 (SPSS Inc, Chicago, Illinois, USA). The normal distribution of the variables was demonstrated using the Kolmogorov-Smirnov test (p>.05). The continuous variables are presented as the mean±standard deviation (SD) and 95% confidence intervals (CI), and the categorical variables are presented as the absolute number and relative frequency percentages. A separate 2×2 mixed-model analysis of variance (ANOVA) was used to examine the effects of the intervention on the primary and secondary outcomes. For the group×time interaction in the ANOVAs, the factors analysed were group (CG and AVGG) and time (preintervention, postintervention).For this test, a partial eta-squared (η^2_p) of 0.01–0.059 represents a small effect, a value of 0.06–0.139 represents a medium effect and a value >0.14 represents a large effect [38]. A multiple comparison analysis was performed using the Bonferroni correction. Effect sizes were calculated according to Cohen's*d* coefficient; the magnitude of the effect was classified as small (0.20–0.49), medium (0.50–0.79) or large (≥0.8) [39]. A value of $p<.05$ was considered to be statistically significant for all the analyses. The analysis was performed using an intention-to-treat (ITT) approach and a per protocol (PP) analysis. In the ITT analysis, all the randomised patients were calculated, and the patients who did not complete the study were counted; whereas, in the PP analysis, the patients who discontinued the study protocol or who were noncompliant with the assigned therapy were excluded.

Results

A total of 41 patients were recruited. Figure 1 shows a flow diagram of participant enrolment, allocation, follow-up and analysis. The baseline characteristics of the participants are presented in Table 1. During the AVG programme, common musclestiffness was the only adverse effect reported during or after exercise.

Adherence to the home exercise programme was 95% during the 6-week intervention period. Exercise adherence during the 12-month follow-up period was lower: 35% (n=8) of the patients performed the exercise prescription of a minimum of two days per week, 20 min per session using the same AVG, and 65% (n=11) of the patients reported no exercise using the AVG. We found no significant between-group differences in annual activity, as reported by the YAAQ. The AVGG patients showed 100% acceptability of the AVG intervention, 60% good enjoyment, 46.7% very good comfort and 53.3% no desire to continue with the training.

Per protocol analysis

Statistically significant differences were found in the ANOVAs for the group×time interaction for walking distance (6MWD [F=4.96; p=.016; η^2_p=0.131]; MSWD [F=3.24; p=.045; η^2_p=0.089]); arm isometric strength (RHG [F=15.58; p<.001; η^2_p=0.384]; LHG [F=15.92; p<.001; η^2_p=0.389]); and HRQoL (CFQ-R 6-11: eating disturbances [F=5.43; p=.008; η^2_p=0.205], respiratory symptoms [F=4.69; p=.014; η^2_p=0.176]).

The change in scores at the postintervention assessment showed statistically significant differences for the variables measuring walking distance (6MWD and MSWD) compared to the scores of the control group (Cohen's*d*>0.80). All the muscle strength variables (HJT, MBT, RHG and LHG) increased after the intervention (Cohen's*d*>0.80), as did HRQoL (eating disturbances and respiratory symptoms domains). During the follow-up period, the only significant between-group differences were observed in the MSWT distance and the isometric arm strength (effect size ranged from -0.74 to -1.54). All the above outcomes favoured the AVGG. The *post hoc* analyses are presented in Table 2, and the HRQoL analyses are presented in Appendix A.

Intention-to-treat analysis

Statistically significant differences were found in the ANOVAs for the group×time interaction for walking distance (6MWD [$F=5.61$; $p=.012$; $\eta^2_p=0.132$]),leg strength (HJT [$F=4.7$; $p=.019$; $\eta^2_p=0.139$]) and arm isometric strength (RHG [$F=9.77$; $p<.001$; $\eta^2_p=0.259$] and LHG [$F=10.05$; $p=.001$; $\eta^2_p=0.264$]).

The results obtained in the *post hoc* analyses using ITT analysis were the same as those found in the PP analysis, except for MSWD and leg strength. The following differences between the analyses (ITT and PP) were noted: (1) no between-group differences in MSWD were observed at follow-up; and (2) the CG showed statistically significant within-group differences for leg strength at follow-up compared with baseline. In general, the effect sizes were similar to those found in the PP analysis, with a greater effect size observed in the LHG at the postintervention assessment (d = -2.41). The *post hoc* analyses for the walking distance and muscle strength variables are presented in Table 3 and Figure 2. The HRQoL analyses are presented in Appendix B.

Discussion

This study is the first to demonstrate that training with AVGs produces a significant and sustainable improvement in exercise capacity and muscle strength in young patients with CF. The results of this study show that AVGs represent an alternative home training strategy for this population, which can be adequately adapted based on patient age and personal preferences. To our knowledge, this study is the first randomised controlled trial to investigate the short- to long-term effects of using AVGs as a training protocol in children and adolescents with CF, and the first study to directly assess the feasibility of implementing pulmonary rehabilitation programmes performed by using AVGs at home in this population.

A previous study performed by Kuys et al. [40] observed higher estimated energy expenditure in hospitalised adults with CF who used AVGs compared with patients who used conventional training exercises. Likewise, Holmes et al. [41]obtained a high exercise intensity (equivalent to 6.1 METS) using the Microsoft© Xbox Kinect in adults with CF. O'Donovan et al.[21] measured energy cost and intensity to demonstrate that AVGs can be a moderate aerobic exercise modality for children with CF. Our results demonstrate that the use of a specific AVG as a training modality can increase exercise capacity. The observed improvements in MSWD (58.95m in the ITT analysis and 70m in the PP analysis)are above the minimal clinically important difference of 40 m in adults with CF[42].These results suggest that the AVG home programme represents a feasible and effective way to improve exercise capacity in patients with CF who follow the programme.

These results can be explained based on the following factors: (1) training intensity (5 days per week for 6 weeks); (2) type of AVG; and (3) training protocol, which was designed to include a combination of aerobic exercise, muscular strength, body endurance and flexibility. Based on a previous study performed by our research group [22], this training protocol targeted upper and lower limb activities that produced high exercise intensities, which could be sustained throughout the session. As reported by Helgerud et al.[43],high-intensity training is associated with better training effects than low-intensity training. Additionally, we observed a significant effect on muscle strength, as measured by functional muscle tests after the training intervention. The AVG model chosen for the study included arm and leg activities that used a strengthening elastic band(TheraBand™),which can improve physical performance in terms of muscular strength and endurance[44]. Finally, the training protocol that combined an aerobic training program with strength training and that engaged both anaerobic and aerobic metabolisms might have led to enhanced results [45].These improvements were maintained long-term, which is consistent with the results of other studies [46,47]. Possible explanations could include physiological adaptations to the high exercise intensities, along with the fact that participants comprised a physically active population (the increased day-to-day activity levels), or the improvements could have been caused by the growth process in children. Also, exercise training strategies with a longer duration and strategies that require self-directed behaviours might have greater impacts on PA participation. Schneiderman-Walker et al. [48] observed high compliance and positive self-reported attitudes towards exercise when patients with CF were able to choose aerobic activities according to their individual interests.

The results of this study show that AVGs represent an alternative home training strategy for this population that can be adequately adapted based on age and interests. The latter factor is critical for motivating children to exercise and to increase their physical fitness[49]. In addition, routine exercise activities using AVGs can be easily implemented in daily life at home and could reinforce patients' attitudes to practice regular exercise in the short term. In terms of adherence, long-term adherence to the AVG home programme progressively decreased. A possible explanation for these low adherence rates could be related to supervision, which has been observed to be a key factor for succeeding in pulmonary rehabilitation[37]. Another reason could be that after the high-intensity training period, the exercise programme was somewhat monotonous; we did not change the type and intensity of activity over the follow-up. Finally, by time, the overloaded daily schedule of the children could have resulted in lower adherence because they did not perceived the immediate benefits as those produced by medication or mucus drainage techniques.

The AVG also impacted quality of life. Significant improvements in CFQ-R domains, such as respiratory symptoms, were observed. The observed improvements in the respiratory symptoms domain in both analyses were larger than the minimal clinically important difference (4.0 points) for stable patients [50].Perceived improved respiratory functioning could translate into higher treatment adherence and improved clinical outcomes. These results could be directly related to the motivation generated by the programme, especially due to the use of a new and interesting tool for exercise training that most of the patients viewed as a fun game. Although the respiratory symptoms domain improvement was no longer significant at the end of the follow-up period, there was an improvement in other domains after 12 months.

This study had some limitations. The first limitation is the length of the follow-up period (12 months) due to difficulties in time management in a complex population with therapeutic overload, and the unsupervised follow-up, which increase the risk of nonadherence. Both factors could strongly decrease the efficacy of the intervention; however, this is a commonly used model in long-term pulmonary rehabilitation programmes. We anticipated a 15% dropout rate due to the follow-up time frame and the severity of the complications (Figure1). Only one patient in the AVGG (5%) did not finish the exercise programme, and four patients (10%) were lost to follow-up (two patients in the AVGG, and two patients in the CG). A second limitation is related to achieved levels of exercise and adherence during the follow-up period. A monthly email for encouraging patients was sent to increase programme adherence during follow-up. We feel that adequate adherence was achieved during the intervention period, but adherence to the exercise recommendations decreased exponentially during follow-up.

However, noncompliance and missing outcomes are common situation in long-term randomised controlled trials. The ITT analysis is a conservative method that provides an unbiased estimate and avoids overoptimistic estimates of treatment effect, given it reflects the practical clinical scenario because it admits noncompliance and protocol deviations. Further research is required to develop other strategies (e.g., combination of different types of games, competition between players, strategies based on game prizes such as achieving more complex or higher levels) to improve long-term adherence rates. Fourth, standardised assessments using laboratory exercise testing are strongly preferred to field tests for measuring the impact of interventions in patients with CF [51]; however, we used the field tests because such tests have additional advantages, such as easy application, portability and few material requirements, which are easily implemented in the clinical setting. In the same way, the most used measure of lower limb muscle strength is the maximal isometric voluntary force of the quadriceps instead of the horizontal jump test [5]. Further studies should make use of laboratory exercise tests to provide more specific physiological data on metabolism, oxygen consumption and formal measure of quadriceps strength. Finally, we recruited children with a diagnosis of CF who were medically stable; thus, the effects of our home-based rehabilitation model in patients with exacerbated CF, in adults who have a specific need for exercise interventions or in patients with other chronic respiratory disorders remain to be established.

The principal clinical implication of this study is that home-based pulmonary rehabilitation using AVGs could be useful for enhancing PA accessibility among children and adolescents with CF who cannot engage with or who are uninterested in traditional programmes. Conventional treatment usually requires attendance at an outpatient centre, and this requirement could place an extra burden upon the patient because it is time-consuming and expensive, whereas the common cost of the AVG equipment is approximately 150€. AVGs can serve as an adjunct to traditional therapy and should be tested in combination with conventional exercise strategies, because AVGs offer the ability to increase exercise effort and motivate subjects to engage in a regular exercise practice. Future studies assessing the optimal doses and the effects of this combined intervention of typical exercise interventions and AVGs are needed. New AVGs with enough diversity and competition between players should be designed by game designers in collaboration with specialist health care professionals to encourage greater adherence and effectiveness for rehabilitation programmes.

In summary, exercising using AVGs at home produced short- to long-term training effects (improved muscle performance and quality of life) in young patients with CF. However, long-term adherence to the home programme progressively decreased. These results suggest that AVGs could be incorporated into pulmonary rehabilitation programmes for children and adolescents with CF; however, the greatest benefits would be produced at short periods of time (up to 6 weeks) to ensure adherence. The feasibility of using this system at home is supported by the present results.

Acknowledgements

CF patients, CF Associations, medical doctors (Dr.López Andreu and Dr.Cortell Aznar)*Unidad de Fibrosis Quística del Hospital UniversitariiPolitècnic La Fe, Valencia (España).*

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1 Farrell PM: The prevalence of cystic fibrosis in the European Union. J Cyst Fibros 2008 Sep;7:450–3.

2 Orenstein DM, Higgins LW: Update on the role of exercise in cystic fibrosis. Curr Opin Pulm Med 2005 Nov;11:519–23.

3 Nixon PA, Orenstein DM, Kelsey SF, Doershuk CF: The prognostic value of exercise testing in patients with cystic fibrosis. N Engl J Med 1992 Dec 17;327:1785–8.

4 de Meer K, Gulmans VA, van Der Laag J: Peripheral muscle weakness and exercise capacity in children with cystic fibrosis. Am J Respir Crit Care Med 1999 Mar;159:748–54.

5 Gruet M, Troosters T, Verges S: Peripheral muscle abnormalities in cystic fibrosis: Etiology, clinical implications and response to therapeutic interventions. J Cyst Fibros 2017 Mar 2; DOI: 10.1016/j.jcf.2017.02.007

6 Wood LG, Fitzgerald DA, Gibson PG, Cooper DM, Collins CE, Garg ML: Oxidative stress in cystic fibrosis: dietary and metabolic factors. J Am Coll Nutr 2001 Apr;20:157–65.

7 Shah AR, Gozal D, Keens TG: Determinants of aerobic and anaerobic exercise performance in cystic fibrosis. Am J Respir Crit Care Med 1998 Apr;157:1145–50.

8 Troosters T, Langer D, Vrijsen B, Segers J, Wouters K, Janssens W, et al.: Skeletal muscle weakness, exercise tolerance and physical activity in adults with cystic fibrosis. Eur Respir J 2009 Jan;33:99–106.

9 Radtke T, Nolan SJ, Hebestreit H, Kriemler S: Physical exercise training for cystic fibrosis. Cochrane database Syst Rev 2015 Jan;6:CD002768.

10 Burtin C, Hebestreit H: Rehabilitation in Patients with Chronic Respiratory Disease Other than Chronic Obstructive Pulmonary Disease: Exercise and Physical Activity Interventions in Cystic Fibrosis and Non-Cystic Fibrosis Bronchiectasis. Respiration 2015;89:181–189.

11 Nixon PA, Orenstein DM, Kelsey SF: Habitual physical activity in children and adolescents with cystic fibrosis. Med Sci Sports Exerc 2001 Jan;33:30–35.

12 Sawicki GS, Sellers DE, Robinson WM: High treatment burden in adults with cystic fibrosis: challenges to disease self-management. J Cyst Fibros 2009 Mar;8:91–6.

13 Myers LB: An exploratory study investigating factors associated with adherence to chest physiotherapy and exercise in adults with cystic fibrosis. J Cyst Fibros 2009 Dec;8:425–7.

14 O'Donohoe R, Fullen BM: Adherence of subjects with cystic fibrosis to their home program: a systematic review. Respir Care 2014 Nov;59:1731–46.

15 Swisher AK, Erickson M: Perceptions of physical activity in a group of adolescents with cystic fibrosis. Cardiopulm Phys Ther J 2008 Dec;19:107–13.

16 Liang Y, Lau PWC: Effects of Active Videogames on Physical Activity and Related Outcomes Among Healthy Children: A Systematic Review. Games Health J 2014 Jun;3:122–44.

17 Barnett A, Cerin E, Baranowski T: Active video games for youth: a systematic review. J Phys Act Health 2011 Jul;8:724–37.

18 LeBlanc AG, Chaput J-P, McFarlane A, Colley RC, Thivel D, Biddle SJH, et al.: Active video games and health indicators in children and youth: a systematic review. PLoS One 2013;8:e65351.

19 Peng W, Crouse JC, Lin J-H: Using active video games for physical activity

promotion: a systematic review of the current state of research. Health Educ Behav 2013 Apr;40:171–92.

20 Biddiss E, Irwin J: Active video games to promote physical activity in children and youth: a systematic review. Arch Pediatr Adolesc Med 2010 Jul;164:664–72.

21 O'Donovan C, Greally P, Canny G, McNally P, Hussey J: Active video games as an exercise tool for children with cystic fibrosis. J Cyst Fibros 2014 May;13:341–6.

22 Del Corral T, Percegona J, Seborga M, Rabinovich RA, Vilaró J: Physiological response during activity programs using Wii-based video games in patients with cystic fibrosis (CF). J Cyst Fibros 2014 Dec;13:706–11.

23 Carbonera RP, Vendrusculo FM, Donadio MVF: Physiological responses during exercise with video games in patients with cystic fibrosis: A systematic review. Respir Med 2016 Oct;119:63–69.

24 Salonini E, Gambazza S, Meneghelli I, Tridello G, Sanguanini M, Cazzarolli C, et al.: Active Video Game Playing in Children and Adolescents With Cystic Fibrosis: Exercise or Just Fun? Respir Care 2015 Aug 1;60:1172–1179.

25 Cox NS, Alison JA, Holland AE: Interventions for promoting physical activity in people with cystic fibrosis. Cochrane database Syst Rev 2013 Jan;12:CD009448.

26 O'Loughlin EK, Dugas EN, Sabiston CM, O'Loughlin JL: Prevalence and correlates of exergaming in youth. Pediatrics 2012 Nov;130:806–14.

27 Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al.: Standardisation of spirometry. Eur Respir J 2005 Aug;26:319–38.

28 Selvadurai HC, Cooper PJ, Meyers N, Blimkie CJ, Smith L, Mellis CM, et al.: Validation of shuttle tests in children with cystic fibrosis. Pediatr Pulmonol 2003 Feb;35:133–8.

29 Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, et al.: An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur Respir J 2014 Dec;44:1428–46.

30 Gulmans VA, van Veldhoven NH, de Meer K, Helders PJ: The six-minute walking test in children with cystic fibrosis: reliability and validity. Pediatr Pulmonol 1996 Aug;22:85–9.

31 Maulder P, Cronin J: Horizontal and vertical jump assessment: reliability, symmetry, discriminative and predictive ability. Phys Ther Sport 2005 May 1;6:74–82.

32 Davis KL, Kang M, Boswell BB, DuBose KD, Altman SR, Binkley HM: Validity and reliability of the medicine ball throw for kindergarten children. J Strength Cond Res 2008 Nov;22:1958–63.

33 Peolsson A, Hedlund R, Oberg B: Intra- and inter-tester reliability and reference values for hand strength. J Rehabil Med 2001 Jan;33:36–41.

34 Quittner AL, Buu A, Messer MA, Modi AC, Watrous M: Development and validation of The Cystic Fibrosis Questionnaire in the United States: a health-related quality-of-life measure for cystic fibrosis. Chest 2005 Oct;128:2347–54.

35 Olveira G, Olveira C, Gaspar I, Cruz I, Dorado A, Pérez-Ruiz E, et al.: [Validation of the Spanish version of the Revised Cystic Fibrosis Quality of Life Questionnaire in adolescents and adults (CFQR 14+ Spain)]. Arch Bronconeumol 2010 Apr;46:165–75.

36 Aaron DJ, Kriska AM, Dearwater SR, Cauley JA, Metz KF, LaPorte RE: Reproducibility and validity of an epidemiologic questionnaire to assess past year physical activity in adolescents. Am J Epidemiol 1995 Jul 15;142:191–201.

37 Emery CF, Shermer RL, Hauck ER, Hsiao ET, MacIntyre NR: Cognitive and psychological outcomes of exercise in a 1-year follow-up study of patients with chronic obstructive pulmonary disease. Health Psychol 2003 Nov;22:598–604.

38 Cohen J: Eta-squared and partial eta-squared in fixed factor ANOVA designs. Educ Psychol Meas 1973;33:107–112.

39 Cohen J: Statistical power analysis for the behavioral sciences. Hillsdale, 1988.

40 Kuys SS, Hall K, Peasey M, Wood M, Cobb R, Bell SC: Gaming console exercise and cycle or treadmill exercise provide similar cardiovascular demand in adults with cystic fibrosis: a randomised cross-over trial. J Physiother 2011 Jan;57:35–40.

41 Holmes H, Wood J, Jenkins S, Winship P, Lunt D, Bostock S, et al.: Xbox Kinect™ represents high intensity exercise for adults with cystic fibrosis. J Cyst Fibros 2013 Dec;12:604–8.

42 Bradley J, Howard J, Wallace E, Elborn S: Reliability, repeatability, and sensitivity of the modified shuttle test in adult cystic fibrosis. Chest 2000 Jun;117:1666–71.

43 Helgerud J, Høydal K, Wang E, Karlsen T, Berg P, Bjerkaas M, et al.: Aerobic high-intensity intervals improve VO2max more than moderate training. Med Sci Sports Exerc 2007 Apr;39:665–71.

44 Sahlberg ME, Svantesson U, Thomas EMLM, Strandvik B: Muscular strength and function in patients with cystic fibrosis. Chest 2005 May;127:1587–92.

45 Selvadurai HC, Blimkie CJ, Meyers N, Mellis CM, Cooper PJ, Van Asperen PP: Randomized controlled study of in-hospital exercise training programs in children with cystic fibrosis. Pediatr Pulmonol 2002 Mar;33:194–200.

46 Kriemler S, Kieser S, Junge S, Ballmann M, Hebestreit A, Schindler C, et al.:

Effect of supervised training on FEV1 in cystic fibrosis: a randomised controlled trial. J Cyst Fibros 2013 Dec;12:714–20.

47 Hebestreit H, Kieser S, Junge S, Ballmann M, Hebestreit A, Schindler C, et al.: Long-term effects of a partially supervised conditioning programme in cystic fibrosis. Eur Respir J 2010 Mar 1;35:578–83.

48 Schneiderman-Walker J, Pollock SL, Corey M, Wilkes DD, Canny GJ, Pedder L, et al.: A randomized controlled trial of a 3-year home exercise program in cystic fibrosis. J Pediatr 2000 Mar;136:304–10.

49 Ryan RM, Rigby CS, Przybylski A: The Motivational Pull of Video Games: A Self-Determination Theory Approach. Motiv Emot 2006 Nov 29;30:344–360.

50 Quittner AL, Modi AC, Wainwright C, Otto K, Kirihara J, Montgomery AB: Determination of the minimal clinically important difference scores for the Cystic Fibrosis Questionnaire-Revised respiratory symptom scale in two populations of patients with cystic fibrosis and chronic Pseudomonas aeruginosa airway infection. Chest 2009 Jun;135:1610–8.

51 Hebestreit H, Arets HGM, Aurora P, Boas S, Cerny F, Hulzebos EHJ, et al.: Statement on Exercise Testing in Cystic Fibrosis. Respiration 2015;90:332–51.

Table 1. Baseline characteristics ofthe participants for both groups.

	AVG group (n=20)	**Control group (n=20)**
Age (years)	12.6± 3.4	11 ± 3
Gender (m/f)	10/10	11/9
BMI (kg/m^2)	18.3± 2.7	17.4 ± 3
Lung Function		
FVC (l)	2.7± 1.1	2.5 ± 1.2
FVC (% pred)	89.4 ± 18.2	89.9 ± 15.6
FEV_1 (l)	2.1 ± 0.9	1.9 ± 1
FEV_1 (% pred)	82.7 ± 21.7	86.2 ± 20.5
FEV_1/FVC(% pred)	78 ± 10.5	81 ± 11.4
6MWD (m)	660 ± 61.6	663.5 ± 60.3
MSWD (m)	823.5 ± 270.6	1085.5 ± 255.6
HJT (cm)	139.9 ± 25.1	134.5 ± 30.7
MBT (cm)	304.5 ± 76.2	295.3 ± 112.9
RHG (Kg)	18.4 ± 6.8	16.2 ± 10.1
LHG (Kg)	16.9 ± 6.7	14.8 ± 10.1

Data are presented as mean±SD and number. AVG: active video games; m: male; f: female; BMI: body mass index; FVC: forced vital capacity; FEV_1: forced expiratory volume in the first second; 6MWD: six-minute walk test distance; MSWD: modified shuttle walk test distance; HJT: horizontal jump test; MBT: medicinal ball throw; RHG: handgrip strength right hand; LHG: handgrip strength left hand.

Table 2. Exercise capacity and muscle strength results pre-post intervention and after 12-months follow-up period using per protocol analysis.

	Group	Pre	Post	Follow-up	Within-Group Change Score a) Post vs. Pre b) Follow-up vs. Pre	Between-Group Differences in Change Score a) Post vs. Pre b) Follow-up vs. Pre
6MWD(m)	AVGG	664.53 ± 65.7	696.65 ± 76.13	685 ± 74.6	a) 32.12 (15.24 to 48.99)**; *d*= 0.45 b) 20.47 (-6.32 to 47.26); *d*= 0.29	a) 40.4 (21.42 to 59.38)**; *d*= 1.47 b) 16.36 (-13.78 to 46.49); *d*= 0.37
	CG	670.17 ± 57.9	661.9 ± 61	674.28 ± 67.14	a) -8.28 (-24.68 to 8.12); *d*=-0.14 b) 4.11 (-21.93 to 30.15); *d*= 0.07	
MSWD(m) No diftime×group	AVGG	852.94 ± 281.66	922.94 ± 287.11	937.06 ± 292.27	a) 70 (19.07 to 120.93)**; *d*= 0.25 b) 84.12 (18.42 to 149.82)**; *d*= 0.29	a) 82.22 (24.94 to 139.51)**; *d*= 0.99 b) 78.56 (4.66 to 152.46)*; *d*= 0.74
	CG	1072.78 ± 261.33	1060.56 ± 254.8	1078.33 ± 258.53	a) -12.22 (-61.71 to 37.27); *d*=-0.05 b) 5.56 (-58.29 to 69.41); *d*= 0.02	
HJT (cm) No diftime×group	AVGG	140.11 ± 26.68	149.44 ± 26.58	148.11 ± 28.97	a) 9.33 (1.93 to 16.73)*; *d*= 0.35 b) 8 (-2.52 to 18.52); *d*= 0.29	a) 9.22 (1.95 to 16.5)*; *d*= 1.16 b) 1.33 (-9.01 to 11.68); *d*= 0.11
	CG	132.61 ± 29.05	132.72 ± 25.1	139.28 ± 27.04	a) 0.11 (-5.12 to 5.34); *d*= 0.004 b) 6.67 (-0.77 to 14.11); *d*= 0.24	
MBT (cm) No diftime×group	AVGG	298.33 ± 78.18	334 ± 83.1	343.33 ± 89.02	a) 35.67 (10.66 to 60.67)**; *d*= 0.44 b) 45 (14.37 to 75.63)**; *d*= 0.54	a) 33.78 (9.2 to 58.36)**; *d*= 1.27 b) 18.56 (-11.55 to 48.66); *d*= 0.54
	CG	288.89 ± 107.81	290.78 ± 109.15	315.33 ± 124.89	a) 1.89 (-15.79 to 19.57); *d*= 0.02 b) 26.44 (4.79 to 48.1)*; *d*= 0.23	
RHG (Kg)	AVGG	17.56 ± 6.69	24.33 ± 9.04	26.67 ± 9.82	a) 6.78 (4.08 to 9.47)**; *d*= 0.85 b) 9.11 (5.68 to 12.54)**; *d*= 1.08	a) 6.83 (4.18 to 9.48)**; *d*= 1.96 b) 6.22 (2.85 to 9.6)**; *d*= 1.54
	CG	15.22 ± 8.78	15.17 ± 9.15	18.11 ± 10.19	a) 0.06 (-1.96 to 1.85); *d*= -0.006 b) 2.89 (0.46 to 5.32)*; *d*= 0.3	
LHG (Kg)	AVGG	16.56 ± 6.98	22.67 ± 8.68	23. 89 ± 9.45	a) 6.11 (4.04 to 8.18)**; *d*= 0.78 b) 7.33 (4.38 to 10.28)**; *d*= 0.88	a) 6 (3.96 to 8.04)**; *d*= 2.35 b) 5.06 (2.16 to 7.96)**; *d*= 1.51
	CG	13.89 ± 8.9	14 ± 9.23	16.17 ± 8.87	a) 0.11 (-1.35 to 1.58); *d*= 0.01 b) 2.28 (0.19 to 4.37)*; *d*= 0.26	

Data are presented as mean±SD, mean difference (95%CI) and effect size (*d*). AVGG, active video games group; CG, control group; 6MWD, six-minute walk test distance; MSWD, modified shuttle walk test distance; HJT, horizontal jump test; MBT, medicinal ball throw; RHG, handgrip strength right hand; LHG, handgrip strength left hand.

* Statistically significant differences $p<0.05$

** Statistically significant differences $p<0.01$

Table 3. Exercise capacity and muscle strength results pre-post intervention and after 12-months follow-up period using intention-to-treat analysis.

	Group	Pre	Post	Follow-up	Within-Group Change Score a) Post vs. Pre b) Follow-up vs. Pre	Between-Group Differences in Change Score a) Post vs. Pre b) Follow-up vs. Pre
6MWD(m)	AVGG	660.58 ± 63.31	691.53 ± 73.43	669.21 ± 84.95	a) 30.95 (15.51 to 46.39)**; *d*= 0.45 b) 8.63 (-20.76 to 38.02); *d*= 0.01	a) 38.45 (21.03 to 55.87)**; *d*= 1.44 b) -3.17 (-36.33 to 29.99); *d*= -0.06
	CG	663.55 ± 60.31	656.05 ± 62.92	675.35 ± 65.33	a) -7.5 (-22.55 to 7.55); *d*= -0.12 b) 11.8 (-16.85 to 40.45); *d*= 0.19	
MSWD (m) No diftime×group	AVGG	838.95 ± 268.86	897.89 ± 282.68	914.21 ± 283.95	a) 58.95 (3.73 to 114.17)*; *d*= 0.21 b) 75.26 (8.9 to 141.62)*; *d*= 0.13	a) 78.45 (16.14 to 140.75)*; *d*= 0.82 b) 46.26 (-28.61 to 121.13); *d*= 0.4
	CG	1085.50 ± 255.6	1066 ± 266.27	1114.5 ± 273.66	a) -19.5 (-73.32 to 34.32); *d*= -0.07 b) 29 (-35.68 to 93.68); *d*= 0.11	
HJT (cm)	AVGG	137.36 ± 25.31	146.55 ± 26.44	141.91 ± 29.93	a) 9.18 (2.3 to 16.07)**; *d*= 0.35 b) 4.55 (-5.31 to 14.4); *d*= 0.16	a) 9.83 (2.93 to 16.73)**; *d*= 1.17 b) -3.65 (-13.53 to 6.22); *d*= -0.28
	CG	134.55 ± 30.7	133.9 ± 28.71	142.75 ± 30.34	a) 0.65 (-5.76 to 4.46); *d*= -0.02 b) 8.2 (0.89 to 15.51)*; *d*= 0.27	
MBT (cm) No diftime×group	AVGG	304.5 ± 76.25	338.6 ± 79.68	346 ± 84.35	a) 34.1 (11.51 to 56.69)**; *d*= 0.44 b) 41.5 (8.85 to 74.15)**; *d*= 0.52	a) 30.8 (8.54 to 53.06)**; *d*= 1.2 b) 6.6 (-25.56 to 38.76); *d*= 0.17
	CG	295.35 ± 112.95	298.65 ± 114.07	330.25 ± 134.26	a) 3.3 (-12.68 to 19.28); *d*= 0.03 b) 34.9 (11.82 to 57.99)**; *d*= 0.28	
RHG (Kg)	AVGG	18.4 ± 6.85	24.9 ± 8.71	26.7 ± 9.26	a) 6.5 (3.88 to 9.12)**; *d*= 0.83 b) 8.3 (4.54 to 12.06)**; *d*= 1.02	a) 7 (4.42 to 9.58)**; *d*= 1.99 b) 4.5 (0.79 to 8.21)*; *d*= 0.96
	CG	16.2 ± 10.08	15.7 ± 9.84	20 ± 12.27	a) 0.5 (-2.35 to 1.35); *d*= -0.05 b) 3.8 (1.14 to 6.46)**; *d*= 0.34	
LHG (Kg)	AVGG	16.9 ± 6.67	23 ± 8.25	23.7 ± 8.93	a) 6.1 (3.94 to 8.26)**; *d*= 0.81 b) 6.8 (3.54 to 10.06)**; *d*= 0.86	a) 6.5 (4.37 to 8.63)**; *d*= 2.41 b) 3.65 (0.43 to 6.87)*; *d*= 0.94
	CG	14.8 ± 10.12	14.40 ± 9.77	17.95 ± 11.14	a) -0.4 (-1.93 to 1.13); *d*= -0.04 b) 3.15 (0.84 to 5.46)**; *d*= 0.29	

Data are presented as mean±SD, mean difference (95%CI) and effect size (*d*). AVGG, active video games group; CG, control group; 6MWD, six-minute walk test distance; MSWT: modified shuttle walk test distance; HJT, horizontal jump test; MBT, medicinal ball throw; RHG, handgrip strength right hand; LHG, handgrip strength left hand.

* Statistically significant differences $p<0.05$

** Statistically significant differences $p<0.01$

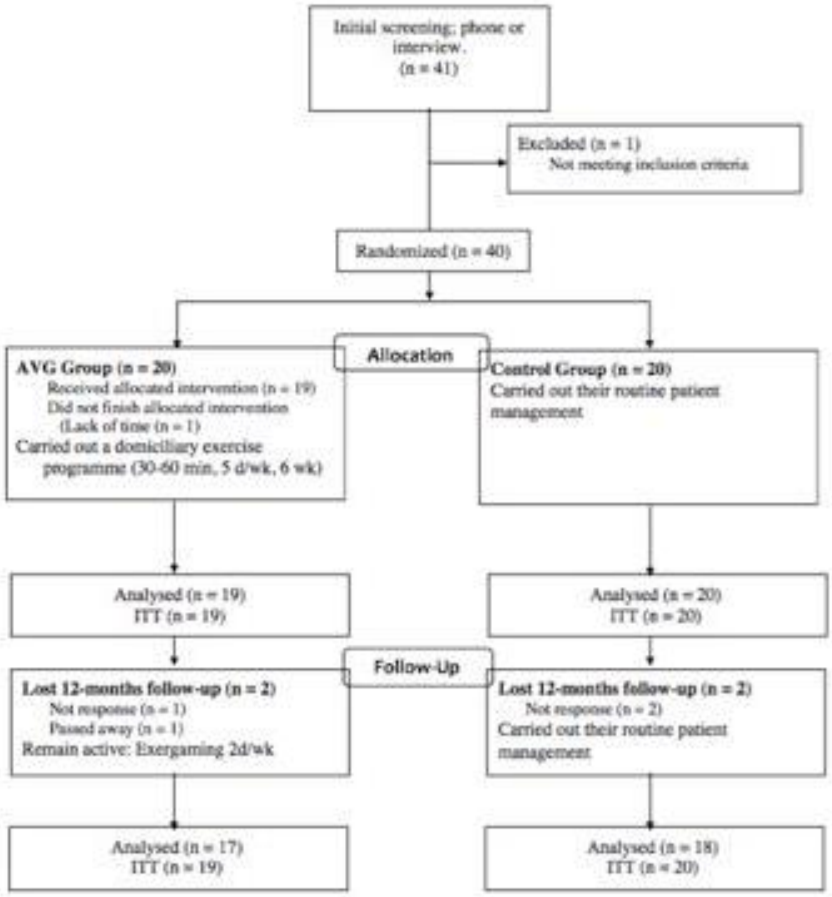
Figure legends

Figure 1. Flow diagram of participation.

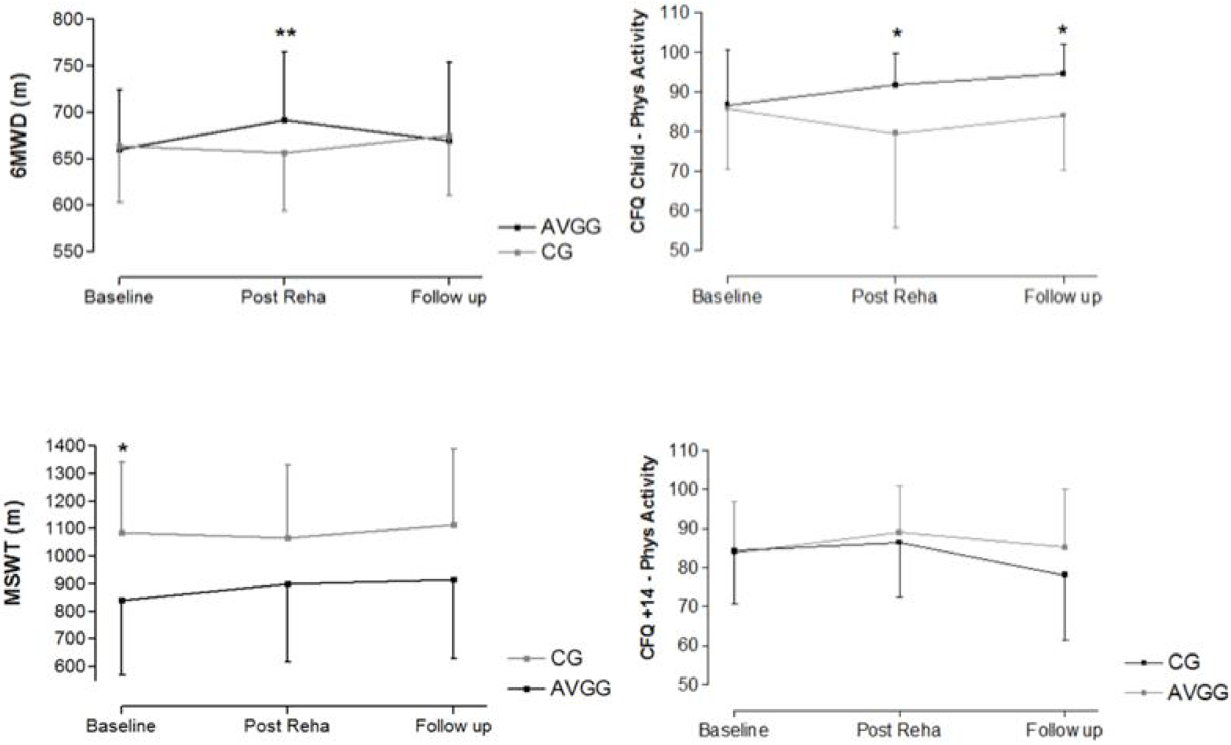
AVG, active video games and ITT, intention-to-treat analysis.

Figure 2. Between-group differencesin outcome measures from baseline to 6 weeks and baseline to 12 months using intention-to-treat analysis.

Data are presented as mean and whiskers represent 95% confidence intervals. 6MWD, six-minute walk test distance; MSWD: modified shuttle walk test distance; CG, control group; AVGG, active video games group; CFQ: Cystic Fibrosis Questionnaire physical functioning.
* Statistically significant differences $p<0.05$
** Statistically significant differences $p<0.01$



Initial screening: phone or interview.
(n = 41)
Excluded (n = 1)
Not meeting inclusion criteria
Randomized (n = 40)
Allocation
AVG Group (n = 20)
Received allocated intervention (n = 19)
Did not finish allocated intervention
(Lack of time (n = 1)
Carried out a domiciliary exercise programme (30-60 min, 5 d/wk, 6 wk)
Control Group (n = 20)
Carried out their routine patient management
Analysed (n = 19)
ITT (n = 19)
Analysed (n = 20)
ITT (n = 20)
Follow-Up
Lost 12-months follow-up (n = 2)
Not response (n = 1)
Passed away (n = 1)
Remain active: Exergaming 2d/wk
Lost 12-months follow-up (n = 2)
Not response (n = 2)
Carried out their routine patient management
Analysed (n = 17)
ITT (n = 19)
Analysed (n = 18)
ITT (n = 20)


6MWD (m)
800
750
700
650
600
550
**
AVGG
CG
Baseline
Post Reha
Follow up
CFQ Child - Phys Activity
110
100
90
80
70
60
50
*
*
Baseline
Post Reha
Follow up
MSWT (m)
1400
1300
1200
1100
1000
900
800
700
600
*
CG
AVGG
Baseline
Post Reha
Follow up
CFQ +14 - Phys Activity
110
100
90
80
70
60
50
CG
AVGG
Baseline
Post Reha
Follow up