

## Special Article

# Gaming Console Home-Based Exercise for Adults with Cystic Fibrosis: Study Protocol

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### Abstract

**Background:** Despite evidence of exercise benefits to lung function, adherence to routine exercise in adults with cystic fibrosis (CF) is low. The incorporation of interactive virtual reality video exergame activities in home-based programs as an incentive may help improve motivation and adherence to exercise. This proposed study will attempt to improve the physical fitness and respiratory function of sedentary adults with CF by engaging them in a Nintendo Wii Fit Plus™ home-based exercise program.

**Methods:** A single group pretest-posttest design will be used to examine the immediate (12-weeks) and long-term effect (24-weeks) of a home-based exergame program on improving pulmonary-related function (physical fitness and respiratory function) in sedentary adults with CF. Participants will receive a one-time orientation to the Wii Fit Plus, and will be requested to use it to exercise according to the recommended guidelines 3 times a week for 30 min in the following 24 weeks. Monthly phone monitoring will be conducted during the first 12 weeks. Besides evaluating the efficacy of a home-based exergame program on improving aerobic capacity, physical activity, and respiratory-related symptoms, we will examine the impact of the exergame on airway ion transport as measured by nasal potential difference, which will be collected at baseline and at the end of 12-weeks only.

**Discussion:** This is the first study to evaluate the feasibility, acceptability and potential effectiveness of a low-cost exercise avenue (i.e., exergames) for adults with CF to improve their pulmonary-related function, which is important for CF disease management and prevention of complications. In addition, the proposed study will be the first to investigate the therapeutic efficacy of home-based exergames on airway ion transport among adults with CF. Through an increase in physical activity, it is expected that participants will improve their physical fitness and respiratory function at the end of the study.

**Trial registration:** ClinicalTrials.gov ID: NCT02277860.

**Keywords:** video games, exercise/physiology, physical fitness, cystic fibrosis/rehabilitation

### Background

Exercise is an important part of the treatment to improve the care and outcomes for persons with cystic fibrosis (CF) (Prasad & Cerny, 2002). In

fact, exercise is recommended in consensus documents for the care management of people with CF (Castellani et al., 2018; Swisher et al., 2015; Yankaskas, Marshall, Sufian, Simon, & Rodman,

2004). Studies have demonstrated that people with CF who participated in regular exercise can improve aerobic capacity (Radtke, Nevitt, Hebestreit, & Kriemler, 2017; Shelley, Boddy, Knowles, Stewart, & Dawson, 2019), enhance sputum clearance (Kriemler, Radtke, Christen, Kerstan-Huber, & Hebestreit, 2016), improve pulmonary function and protect against its decline (Radtke et al., 2017), and improve health-related quality of life (Radtke et al., 2017). Furthermore, the survival of patients with CF was found to be related to their aerobic fitness levels (Pianosi, Leblanc, & Almudevar, 2005). However, the majority of adults with CF either do not exercise at all or exercise below recommended levels (Shelley et al., 2019). In a large scale survey of adults with CF ( $n = 563$ ), only 24% of the respondents reported that they always adhere to exercise recommendations (Myers, 2009). In another study, only about 30-40% of adults with CF reported exercising at a beneficial level, which is 3 times a week or more for 30-60 min (White, Stiller, & Haensel, 2007).

Home-based exercise programs mitigate transportation and scheduling difficulties as participants are not required to attend classes in a center. Therefore, adherence level to home-based exercise programs for adults with CF was better, ranging from 57% to 88% (O'Donohoe & Fullen, 2014).

The incorporation of interactive virtual reality video exergame activities in home-based programs as an incentive may further improve motivation and adherence to exercise (Wardini et al., 2013). Adults with CF reported an overall higher level of enjoyment when engaging in games-embedded exercise than in rote or treadmill exercise (Kuys et al., 2011). In addition, energy expenditure from playing exergames was found to be equivalent to participating in cycle ergometer or treadmill exercise (Carbonera, Vendrusculo, & Donadio, 2016; Holmes et al., 2013; Kuys et al., 2011).

Although there is some preliminary evidence on the efficacy of playing exergames in improving muscle strength, exercise capacity, and respiratory-related symptoms in children and adolescents with CF (Del Corral et al., 2018), to date, no study has been conducted to investigate the therapeutic efficacy of home-based exergames on airway ion

transport among adults with CF. There are studies to support the immediate benefits of a single bout of aerobic exercise (15-20 min) in the improvement of airway bioelectric abnormalities (i.e., an increase  $Cl^-$  secretion through altering ion regulation) as measured by nasal potential difference (NPD) in the CF population (Alsuwaidan et al., 1994; Schmitt et al., 2011; Wheatley et al., 2015), where moderate-intensity exercise resulted in a significant reduction in the abnormally high NPD values of patients with CF.

It is suggested that moderate-intensity exercise partially blocks the amiloride-sensitive sodium conductance in the respiratory epithelium (Schmitt et al., 2011). The inhibition of luminal sodium conductance can reduce reabsorption and increase water content of the mucus, and favors airway fluid secretion and mucociliary clearance in the CF lung (Alsuwaidan et al., 1994; Schmitt et al., 2011). This may, in part, explain the beneficial effects of exercise in patients with CF. However, the benefits of habitual endurance exercise training (e.g., 12 weeks) on improving airway ion transport in adults with CF is not known. The proposed study will be the first to investigate this important outcome.

The aim of this proposed study is to evaluate the efficacy of a home-based exergame program designed to improve pulmonary-related function in adults with CF. Specifically, the objectives are to determine:

1. Whether adults with CF who engage in a home-based exergame program will exhibit an improvement in physical function-related endpoints, including aerobic capacity as measured by peak oxygen consumption ( $VO_2$ ), physical activity as measured by an ActiGraph (activity monitor), respiratory-related symptoms as assessed by the Cystic Fibrosis Questionnaire-Revised (CFQ-R), at immediate post-exergame (i.e., 12-weeks) and 24-weeks follow-up when compared to the pretest scores.
2. Whether adults with CF who engage in a home-based exergame program will exhibit an improvement in respiratory specific endpoints, including airway ion transport as measured by nasal potential difference (NPD) at the end of the 12-week exergame program when compared to the pretest scores.

## Methods

### Research design

The proposed study will employ a single group pretest-posttest design to investigate the impact of a home-based exergame program on improvement in aerobic capacity, airway ion transport, physical activity, and reduction of severity in respiratory-related symptoms among adults with CF. Seven adults with CF will receive a brief education on the importance of exercise and one-time orientation using the Nintendo Wii Fit Plus™, and be requested to use it to exercise 3 times a week for 30 min. The primary outcome measures will be aerobic capacity as measured by peak VO<sub>2</sub>, activity level for a week as measured by ActiGraph (an activity monitor), and self-reported respiratory-related symptoms as measured by the CFQ-R. These endpoints will be collected at baseline, at 12-weeks (i.e., immediately after the completion of the 12-week intervention) and 24-weeks follow-up. The secondary outcome measures will be airway ion transport as measured by NPD, and will be collected at baseline and at 12-weeks only.

### Study participants

Participant inclusion criteria are: (a) a confirmed diagnosis of CF based on two positive sweat Cl<sup>-</sup> tests (>60 mmol/L) and the identification of two causative mutations in CF transmembrane conductance regulator; (b) ≥ 19 years-of-age; (c) ambulatory without the use of an assistive device; (d) stable clinical condition (i.e., no pulmonary exacerbation for at least 6 weeks); (e) currently sedentary (i.e., exercise or participate in sports less than 3 times per week for 20 min in the past 6 months) and do not play any exergames; (f) able to read and follow exercise directions in English on the television screen; (g) able to provide informed consent by understanding the nature of participation; and (h) have permission from their treating physician to participate in moderate-intensity exercise.

Exclusion Criteria are: (a) nasal surgery for polyposis in the past 2 years; (b) currently participating or have participated (in the past 30 days) in another clinical trial which can affect the outcomes of the proposed study; (c) contraindication for moderate-intensity exercise

(e.g., recurrent pneumothorax (in the past 6 months), hemoptysis (hospitalized in the past 6 months), experience severe musculoskeletal pain during moderate-intensity exercise, stage 2 hypertension, anemia (hemoglobin < 8 g/dL), history of uncontrolled CF-related diabetes (HbA1c > 10%), or epilepsy); or (d) planning to move out of the state of Alabama, within the next 9 months.

### Recruitment of study participants

Potential participants will be recruited from patients visiting the adult CF clinic at University of Alabama at Birmingham (UAB). There are about 15-20 patients with CF received care in the clinic weekly. CF health providers (e.g., pulmonologist, nurse practitioners, physical therapist) in the clinic will be informed about the proposed study at a regular departmental meeting; they will be asked to inform and refer appropriate patients to participate in the proposed study. The majority of CF patients require regular follow-up (i.e., every 3 months), and return for continued care and consultation; therefore, a continuous flow of patients will be available for recruitment.

Concurrently, on behalf of the attending pulmonologists, the research coordinator (RC) will contact all patients (living in the state of Alabama) in the adult CF clinic by phone and inform them of the study. The research coordinator (RC) will explain the study to potential participants, including requirements for participation, and return to UAB 3 times during the 6-month study period (baseline, 12-weeks, and 24-weeks). In addition, a letter of invitation, signed by the principal investigator and the medical director of adult CF clinic, a recruitment flyer, and a stamped, return-addressed envelope will be sent to the appropriate patients who have had a comprehensive medical assessment within 12 months at the CF clinic, or those patients who cannot be reached by phone/texting or e-mail.

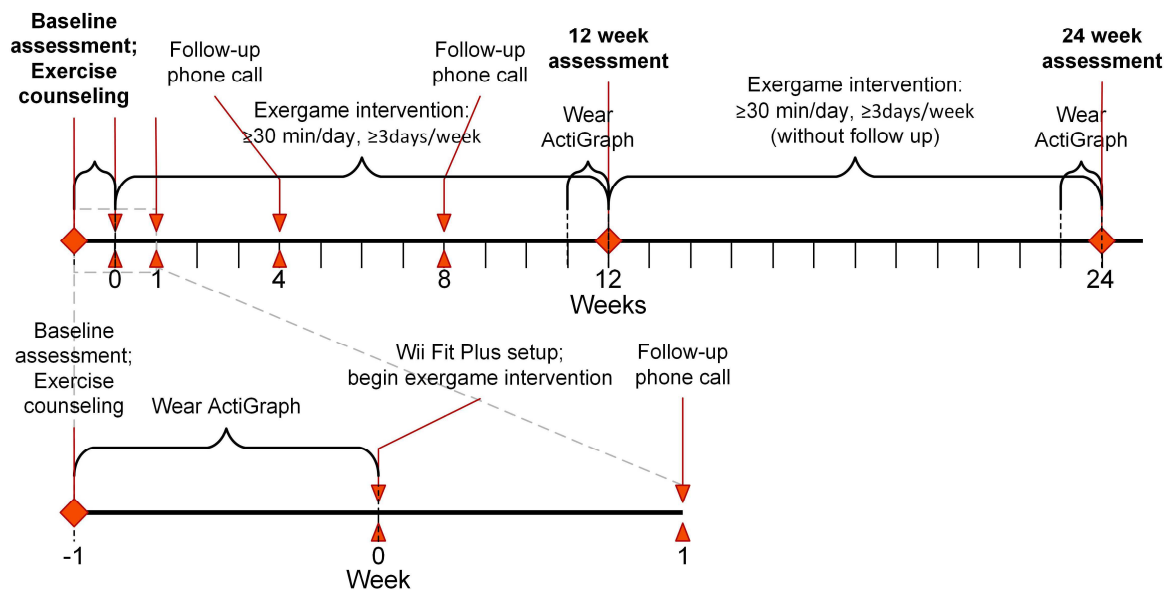
### Baseline assessment

For those patients who agree to participate and meet the eligibility criteria (based on self-report), the attending pulmonologist will review their current medical record, including results of laboratory tests and medical history to determine final eligibility for participation. The RC will then

schedule a baseline clinical evaluation for these patients. Prior to baseline assessment, informed consent will be explained and completed. The RC will emphasize the importance of the commitment to return to UAB for follow-up evaluations. Baseline evaluations will include collecting the participants' socio-demographic information, physical activity pattern and exercise habits, peak VO<sub>2</sub>, CFQ-R, and NPD. Measurement of peak VO<sub>2</sub> will be completed in the Exercise Clinical Trials Facility at the UAB Center for Exercise Medicine. Measurement of NDP will be conducted in the UAB Gregory Fleming James Cystic Fibrosis Research Center's Clinical and Translational Core.

**Procedures**

After the clinical evaluation (See Figure 1 for participant activities), participants will receive a pamphlet, "Day-to-Day Exercise and Cystic Fibrosis" published by the Cystic Fibrosis Foundation (<https://www.cff.org/Life-With-CF/Daily-Life/Fitness-and-Nutrition/Fitness/Day-to-Day-Exercise-and-CF.pdf>). The RC will briefly go over the important points in the pamphlet to increase the participants' awareness of the importance of regular exercise and suggest to the participants that they exercise using the Wii Fit Plus at least 3 times a week for 30 minutes as recommended in the pamphlet.



**Figure 1. Participant Activities (diamond = assessment; double triangle = communication with the research coordinator)**

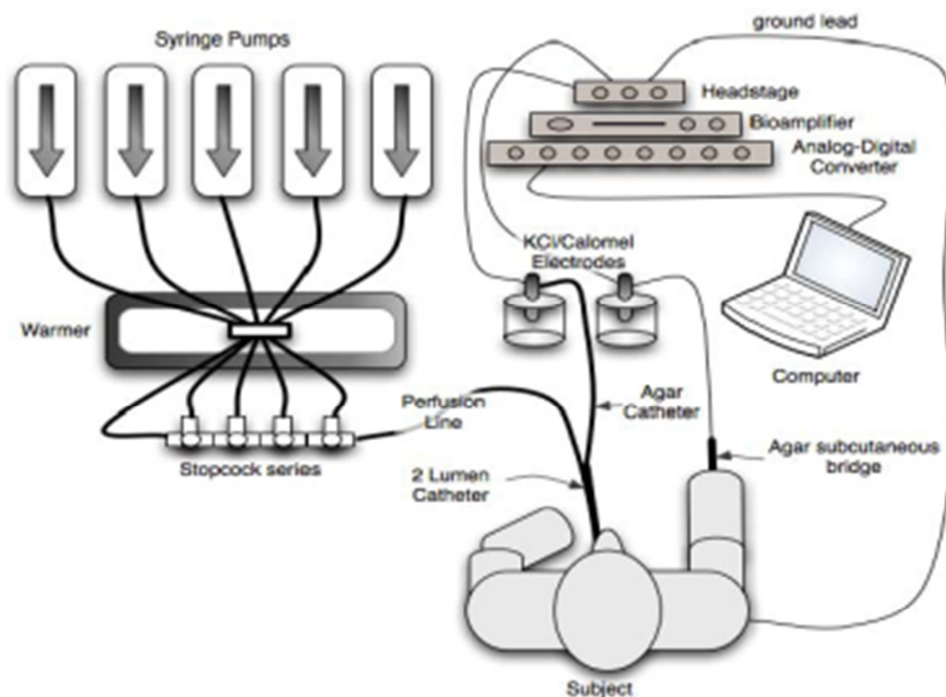
Participants will receive an activity monitor (ActiGraph) and be informed that the purpose of the activity monitor is to keep track of their daily activity level. Participants will be asked to wear the ActiGraph at the waist during awake hours for the ensuing 7 consecutive days (i.e., before the exergame program) (Hart, Swartz, Cashin, & Strath, 2011). Participants will also be told to continue their usual physical activity while wearing the ActiGraph. Participants will be asked to mail the Actigraph back in a pre-addressed,

return postage-paid envelope after one week of data collection. The RC will issue the ActiGraph again (via mail) ~2 weeks before the end of the 12th-week and 24th-week of the exergame program. Participants will return the ActGraph to the research team at 12-weeks and 24-weeks evaluation visits. Participants will be reminded every day to wear the ActiGraph during these 3 weeks of monitoring.

The RC will set up the Wii Fit Plus before the participants left UAB campus so that they can start playing the exergames in a timely fashion without delay due to problems associated with delivery or technical issues related to set up. The RC remind the participants not to engage in the exergames until they have donned the activity monitor for a week, and mailed it back to the research team. The RC will show the participant how to use the Wii remote controller, how to navigate through the menus, how to play the game, and create his/her own "Mii," which is an avatar representing the participant in the Wii Fit Plus games. In addition, the RC will review the recommended Wii Fit Plus exercise program protocol. The RC will call and check on the participant the following week to ensure he/she does not have any technical

problems following the exergame program protocol.

During the first 12 weeks, participants' exergame engagement will be monitored with monthly phone calls; and from week 13 to 24, the program will be maintained by the participant without any monthly calls. During the study period, participants will continue their regular therapies, including airway clearance therapy, enzymes, vitamins, and other medical treatment. Evaluations at each post-intervention will be exactly the same as those taken at baseline and will be conducted by the same evaluators. Throughout the 6-month study period, any changes in medications, healthcare utilization (hospitalization, emergency visit) will be obtained from patient medical records. The RC will keep a log regarding content of each phone monitoring call.



**Figure 2. Setup for measurement of nasal membrane transepithelial potential difference**

#### Protocol of the exergame program

The RC will introduce the protocol for each exercise session which begins with a 5-min warm

up. Since the mean metabolic equivalent (MET) values of all the activities in the Yoga and Balance Games modules are less than 3, which is regarded

as light intensity, the participants can select any activities from these two modules that they want to start as their first 5 minutes warm up. However, we will also provide them a handout to guide them in the selection of some of the more common activities people use for warm up (e.g., stretching and/or deep breathing). After warming up, participants will engage in various moderate-intensity activities selected from the Training Plus, Aerobics, and Strength Training modules. Each session will end with a 5-min cool-down involving deep breathing and/or slow stepping and walking, or selection of any of the light-intensity activities from the Yoga and Balance Games modules. Initially, the aerobic exercise may last for 10-20 min depending on the participant's tolerance, however the goal will be to gradually increase to 30 min or more per session on at least 3 days per week over the 12-week period, which is the current physical activity recommendation for adults ("American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults," 1998). Participants will be allowed to increase their frequency and/or duration of exercise, if desired, and will be encouraged to choose the recommended exercise games they enjoy. The RC will give the participant a handout with categories of game activities from Wii Fit Plus classified into levels of energy expenditure, and recommend that participants gradually increase their exercise intensity by selecting the appropriate category (Miyachi, Yamamoto, Ohkawara, & Tanaka, 2010).

Initially, participants will be instructed to exercise at an intensity corresponding to a perceived dyspnea level of 3-5 using the Borg Category-Ratio (Borg CR-10) scale, which is at or below the anaerobic threshold (Zamunér, Moreno, Camargo, & Graetz, 2011). The Borg CR-10 scale (Borg, 1982) can be used to measure a person's perceived exertion or dyspnea during physical activity. It is a category-ratio scale with values ranging from 1 to 10 and verbal anchors (e.g., 3=moderate, 4=somewhat heavy, 5=heavy). Participants will be instructed not to exceed a rating of 5 on the Borg CR-10 scale regardless of their response to the exercise session. This intensity will elicit some breathlessness but still allow participants to carry

on a conversation (Kuys et al., 2011). The perceived exertion level is a sufficient guide for the participant to monitor their exertion. We will also instruct participants to "listen to their body" and halt exercising should they experience pain, dizziness or nausea. The rather conservative intensity guidelines are designed to maximize exercise safety and to minimize the risk of exacerbating fatigue or breathlessness during this unsupervised program. All of these procedures follow the guidelines of the American College of Sports Medicine for a safe exercise conditioning program ("American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults," 1998), and are similar to those described in the literature for exercise programs used with patients who have CF (Kuys et al., 2011).

Although participants will be provided with recommendations regarding exercise intensity and frequency of training, they will be allowed to choose exercise intensity, duration, and frequency with which they feel comfortable. This will increase the ecological validity of the training program (Warburton et al., 2007). Participants are allowed to invite their family members or friends to engage in the exergames. Since performance of the Wii Fit exercise depends on one's personal information (i.e., weight, height, and age), and each user selects his or her own Mii to play, participants will be told that no one besides themselves should play as their Mii avatar. Other persons can enter their personal information and select their own avatars for use.

### **Outcome measures**

The three primary outcome variables for this proposed study are: aerobic capacity, physical activity level for a week, and self-reported respiratory-related symptoms. The secondary outcome variable is airway ion transport. Table 1 summarizes the characteristics of these four outcome variables.

### **Aerobic capacity**

Aerobic capacity as measured by peak  $VO_2$  (Carlson, 1995) will be determined via indirect calorimetry using a symptom-limited maximal

exercise test, the modified Bruce treadmill protocol (including stages 0 and 0.5). Expired volumes of oxygen and carbon dioxide will be continuously measured by open-circuit spirometry and analyzed by using a metabolic measurement cart. Continuous electrocardiography and pulse oximetry will be used to monitor heart rate and

assess for exercise-induced dysrhythmias and oxygen desaturation. Indications of a maximal test include: (1) plateauing of  $\text{VO}_2$ , (2) respiratory exchange ratio  $> 1.0$ , and (3) maximal heart rate within 10 beats of age-predicted maximum (Hebestreit et al., 2015).

**Table 1. Characteristics of the outcome measures**

Variable	Measure	Data collection	Type	Unit/Scale
Aerobic capacity	Peak $\text{VO}_2$	Baseline, 12, & 24-wk	Clinical assessment	ml/kg/min
Physical activity	ActiGraph	Baseline, 12, & 24-wk	Field assessment	counts·min <sup>-1</sup> & MET
Respiratory-related symptoms	CFQ-R	Baseline, 12, & 24-wk	Self-report	points
Airway ion transport	NPD	Baseline, 12-wk	Clinical assessment	mV

### Physical activity

Physical activity will be measured by the ActiGraph (model AM-7164, 50 x 41 x 15 mm, 43 g), a uniaxial accelerometer that measures movement in the vertical plane. ActiGraph can detect acceleration ranging in magnitude from 0.05 to 2.00 G with a frequency response from 0.25 to 2.50 Hz, and converts accelerations in activity counts. Activity counts are recorded during a user-specified time interval (epoch). ActiGraph is initialized to collect activity count data in 1-s epochs. Activity counts (counts·min<sup>-1</sup>) can be converted into METs (Freedson, Melanson, & Sirard, 1998). For example, the cutoff points for moderate physical activity (MPA) will be set to 1,952–5,724 counts per min (i.e., 3.0-5.9 METs) (Freedson et al., 1998).

ActiGraph is the most commonly used accelerometer and provides information regarding the intensity, duration, and frequency of the user's physical activity bouts. ActiGraph accurately estimates of step counts and activity intensity at most walking and running speeds (Abel et al., 2008). ActiGraph also accurately reports summary statistics relating to time spent in specific physical activity intensity categories (Rothney, Schaefer,

Neumann, Choi, & Chen, 2008). ActiGraph was also reported to be highly reliable in tracking activity over a 7-day period in natural settings (Sirard, Forsyth, Oakes, & Schmitz, 2011).

For the proposed study, a physical activity index (counts per min per day) will be established from ActiGraph data, calculated by dividing the average of the total daily counts by the average of daily time monitored (excluding time with zero count periods). Periods of zero values for more than 20 min will be excluded from the analysis. "Inactivity" will be classified as activity below an arbitrary level of 100 counts per min, including sporadic zero values less than 20 continuous min (Yngve, Nilsson, Sjoström, & Ekelund, 2003). Time in MPA bouts of 2 min or more of continuous activity and the number of bouts of continuous activity at MPA lasting at least 10 min will be computed.

We will exclude data from the first day of monitoring to eliminate any reactivity to wearing the ActiGraph itself. The activity level data (i.e., amount / step count, and intensity) collected from the ActiGraph during the first week will be compared to that collected at the last week of the

12th- and 24th-week of the exergame program, respectively.

### **Respiratory-related symptoms**

The adolescent and adult computerized version of the Cystic Fibrosis Questionnaire-Revised (CFQ-R) is a self-administered questionnaire used to measure respiratory-related symptoms (i.e., health-related quality of life) (Quittner, Buu, Messer, Modi, & Watrous, 2005). The tool consists of 44 items organized into 12 generic and disease-specific scales. The scales most appropriate as outcome measures for the proposed study are physical functioning (8 items), respiratory symptoms (6 items), and vitality (4 items).

### **Airway ion transport**

Airway ion transport will be measured by NPD. Measurement of nasal membrane transepithelial potential difference will be conducted according to the Cystic Fibrosis Foundation Therapeutics Development Network Standard Operating Procedure (Solomon et al., 2018; Solomon et al., 2010). In brief, participants are seated, facing the NPD technician who first places a subcutaneous bridge on the dorsal forearm. A rhinoscope is used to visualize the right inferior turbinate and the nasal probe is inserted and voltage recorded for ~5 sec at distances of 3.0, 2.0, 1.5, 1.0, and 0.5 cm. Basal measures are repeated on the left nostril. Repeated measures are made with perfusion solutions (Ringer's, Amiloride, zero [Cl<sup>-</sup>], isoproterenol, and ATP) per nostril at the site of the most negative basal potential. The computer based data acquisition system provides continuous recording during measurements and facilitates repeat readings at the same distances along the nasal floor (Ergonul et al., 2004) (see Figure 2). The system was shown to give reliable results with high specificity (92%), sensitivity (79%), positive predictive value (95%) and negative predictive value (72%) (Ergonul et al., 2004). NPD measurement was shown to be reproducible with variability in the acceptable range for people with CF (Yaakov et al., 2007). The values to represent the changes in potential difference of Amiloride ( $\Delta$ Amil), zero [Cl<sup>-</sup>] + isoproterenol ( $\Delta$ Total Chloride Conductance ( $\Delta$ TCC)), and ATP ( $\Delta$ ATP) for the same nostril between baseline and at 12-weeks evaluation will be calculated.

### **Anticipated outcomes**

We anticipate a 10% improvement in peak VO<sub>2</sub>, a  $\geq 4$  point improvement in the CFQ-R score, and a decrease (improvement) of ~5 mV in NPD following the study period, and a 10-15% increase in time spent performing moderate-to-vigorous physical activity during the study period.

### **Sample size estimation**

For this proposed study, seven adults with CF will be recruited. The sample size is based on the number which would help support whether the home-based exergame program we are proposing is feasible in this patient population. Sample size determination for the proposed study is also guided by a previous study (Rowe et al., 2013), in which sample size between 5 and 10 was sufficient to detect a 5 mV change, an effect size that provides a meaningful within-subject change in clinical status for adults with CF.

### **Data analysis plan**

Descriptive statistics including means, standard deviations, median, interquartile range, missing data, and frequency distributions of the outcome measures at each time point (baseline, at 12-weeks and 24-weeks) will be examined to inform designs for future larger trials of similar exergame program. These descriptive analyses will constitute the primary statistical analyses for the outcome variables. Effect size will be calculated by dividing the z statistic by the square root of the number of participants within each pair of comparison, then taking the absolute value as the effect size (Fritz, Morris, & Richler, 2012).

### **Discussion**

The proposed study protocol will provide an alternative low-cost exercise avenue (i.e., exergames) for adults with CF to improve their physical fitness and pulmonary-related function, which is important for CF disease management and prevention of complications. Home-based exercise programs will have the potential to maintain sustainability as home-based exercise training has been shown to result in greater long-term adherence to exercise (Ashworth, Chad, Harrison, Reeder, & Marshall, 2005). The long-term outcome of engaging in exergames, which is beyond the scope of the proposed study, may offer



the potential for reducing mortality, or morbidity (i.e., pulmonary exacerbations) and hospitalization, thus reducing health care costs, as well as increasing work ability and employment among people with CF. Findings will allow us to gain insight into the effectiveness of such an exergame program on participants' levels of fitness over time.

Several strategies will be used to maximize participant retention. (1) Emphasis on participants' commitment to return for the post-intervention evaluations during the informed consent process. (2) Participants will receive regular monthly telephone monitoring during the first 12-week of the study as a strategy to minimize attrition. (3) For the convenience of the participants, evaluation visits can be scheduled on the same day as their physician appointment. (4) Provide monetary incentive and reimbursement of gas mileage for each evaluation visit.

### Limitations

In any home-based exercise study, it is impossible for the researcher to know exactly what the participants do in relation to exercise at home, or whether they adhered to the protocol or not without invading their privacy. However, one of the merits of the Wii Fit Plus is that it records the participants' exercise pattern (i.e. number of minutes playing Wii Fit Plus on a particular date). At the completion of the proposed study, we will request participants to download their exercise records and send them to us for verification. Another potential limitation is related to measuring participants' activity level using the ActiGraph. Participants may forget to wear it during the data collection period. We feel that daily reminders will be sufficient to ensure that participants will wear it during the data collection period.

Finally, the incidence of pulmonary exacerbation / hospitalization rates over this 5-6 month study will not be of sufficient magnitude to allow for meaningful interpretations in this pilot study; however, we will track these outcomes. This important information will serve as preliminary data for future multi-center collaboration study with larger sample size and longer duration of follow-up. A large-scale study through multi-center collaboration with long-term follow-up beyond 1-2 years will be used to validate the

efficacy of the exergame exercise program on enhancing quality of life, and reducing mortality, morbidity (i.e., pulmonary exacerbations), emergency room use, and health care costs associated with improved health. In addition, behavioral management such as the use of motivational interviewing has been advocated (Duff & Latchford, 2010) and successful in increasing exercise adherence in home-based exercise programs in other lung disease populations (Valero et al., 2009). Future studies will therefore evaluate whether adding motivational interviewing in the setting of an exergames interventions will further improve adherence including a comparison of exergame intervention versus motivational interviewing in terms of overall exercise adherence.

### Ethics approval and consent to participate

The study design was approved by The University of Alabama at Birmingham Institutional Review Board (IRB protocol number: 2017P001667). All the participants will provide written informed consent. The study is registered at ClinicalTrials.gov (NCT02277860), May 8, 2015, <https://clinicaltrials.gov/ct2/show/NCT02277860>.

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