Bronchiectasis - Exercise as Therapy (BREATH): Rationale and Study Protocol for a Multi-center Randomized Controlled Trial

Taryn Jones
Queensland University of Technology, Brisbane, QLD, Australia
Kerry-Ann F O'Grady
Queensland University of Technology, Brisbane, QLD, Australia
Vikas Goyal
Queensland Children's Hospital, Brisbane, QLD, Australia
Ian B Masters
Queensland Children's Hospital, Brisbane, QLD, Australia
Gabrielle McCallum
Menzies School of Health Research, Darwin, NT, Australia.
Christopher Drovandi
Queensland University of Technology, Brisbane, QLD, Australia
Thomas Lung
George Institute for Global Health, Sydney, NSW, Australia.
Emmah Baque
Griffith University, QLD, Australia.
Denise S K Brookes
Queensland University of Technology, Brisbane, QLD, Australia
Caroline O Terranova
Queensland University of Technology, Brisbane, QLD, Australia
Anne B Chang
Queensland University of Technology, Brisbane, QLD, Australia
Stewart G Trost (s.trost@qut.edu.au)
Queensland University of Technology, Brisbane, QLD, Australia https://orcid.org/0000-0001-9587-3944

Study protocol

Keywords: Bronchiectasis, pediatric, physical activity, exercise, exacerbation

Posted Date: August 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-764230/v1

Abstract

Background: Globally, bronchiectasis (BE) unrelated to cystic fibrosis (CF) is recognized as a major cause of respiratory morbidity, mortality and health-care utilization. Children with BE regularly experience exacerbations of their condition resulting in frequent hospitalizations and decreased health related quality of life (HRQoL). Guidelines for the treatment and management of BE call for regular exercise as it may reduce the incidence of acute exacerbations. To date, the short and long-term health benefits resulting from therapeutic exercise have not been investigated in children with BE. We aim to determine if a therapeutic exercise program is effective in reducing the proportion of children with BE who experience any exacerbation in a 12-month period. The secondary aims are to determine the cost-effectiveness of the intervention, and assess the program's impact on aerobic fitness, fundamental movement skill (FMS) proficiency, habitual physical activity, HRQoL, and lung function.

Methods: This multi-center, observer-blinded, parallel group (1:1 allocation), randomized controlled trial (RCT) will be conducted at three sites. One hundred and seventy-four children aged six to under 13 years with BE will be randomized to a developmentally appropriate, play-based therapeutic exercise program (eight, 60-minute weekly sessions, supplemented by a home-based program) or usual care. Randomization will be stratified by site. Outcome measures (aerobic fitness, fundamental movement skill proficiency, habitual physical activity, HRQoL, and lung function) will be assessed at baseline, 9 weeks, 6 and 12-months. Monthly, parental contact and medical review will document acute respiratory exacerbations and parameters for cost-effectiveness outcomes.

Discussion: Results from this study will test the effects of the therapeutic exercise program to prevent acute exacerbations and improve FMS proficiency, fitness, and HRQoL in children with BE. The program could be readily translated with low cost equipment and flexible delivery and have the potential for a major paradigm shift in the way in which therapeutic exercise is prescribed and implemented in children with chronic respiratory conditions. This RCT is required because it will provide long overdue Level 1 evidence regarding the efficacy and cost-effectiveness of tailored therapeutic exercise programs for children with BE.

Trial registration: Australian and New Zealand Clinical Trials Register (ANZCTR) number ACTRN12619001008112.

Introduction

Background and rationale {6a} {6b}

Bronchiectasis (BE) unrelated to cystic fibrosis (CF) is a major cause of respiratory morbidity and a significant contributor to health care utilization in children and adolescents globally [1-3]. It is the end point of the chronic suppurative lung disease (CSLD) continuum and is described as abnormal irreversible dilatation of the airways and associated with airway infection and inflammation [4, 5]. Children with BE regularly experience exacerbations of their condition (increased wetness and severity of

cough, breathlessness, chest pain, and/or wheeze) resulting in frequent hospitalizations and decreased of health-related quality of life (HRQoL) [2, 6]. Prevalence data in children are scarce however, a recent review of the epidemiology of CLSD estimated the prevalence of BE to range from 0.2 to 15 cases per 100,000 [7]. BE is particularly prevalent among socially disadvantaged populations, such as Indigenous communities of Australia, New Zealand, Alaska and Canada [7, 8]. A study of Central Australian Aboriginal children reported the prevalence as high as one in every 68 children [9].

The treatment goals of multi-disciplinary management are to prevent airway damage, optimise quality of life and minimize exacerbations [4]. Current clinical treatment guidelines recommend general exercise to improve aerobic fitness and QoL [9]. However, the health impacts associated with therapeutic exercise in children with BE are not well understood [10, 11]. A recent meta-analysis of the effects of exercise training on physical and psychosocial health in children with chronic respiratory disease identified no published studies investigating the impact of therapeutic exercise in this population [12]. Therapeutic exercise may benefit children with BE by reducing the frequency and severity of acute exacerbations – an independent predictor of long-term decline in lung function [6]. A randomized controlled trial (RCT) evaluating the effects of an eight-week exercise program in adults with BE reported significant reductions in the number of acute exacerbations over a 12-month period [13]. Moreover, therapeutic exercise programs may also reduce the risk of disabling secondary conditions such as obesity, depression, and anxiety [14].

It is known that children with BE are not sufficiently active to obtain the health benefits associated with regular physical activity (PA). Using an accelerometer to objectively measure daily physical activity, Joschtel and colleagues [15], found children with BE to have low levels of moderate-to-vigorous intensity physical activity (MVPA). Expressed as a percentage of the waking hours, children with BE were sedentary for 57.5% of the time, in light-intensity PA 35.8% of the time, and in MVPA just 6.7% of the time. Indeed, only two children (5.6%) achieved the recommended 60 minutes of daily MVPA described in the Australian 24-Hour Movement Guidelines for Children and Young People. In contrast, 42% of healthy children in the normative comparison group achieved the guideline. On average, children with BE accumulated 8,229 steps/day, well below the recommended 12,000 steps/day. In comparison, daily step counts in healthy children ranged from 11,500 - 14,500 steps/day.

Fundamental movement skill (FMS) proficiency is an important determinant of children's current and future physical activity status, and a significant contributor to individual health and well-being [16]. The development of FMS's early in life is critical to establishing the more complex movement patterns required for participation in all types of play, games, physical activities, and sports [16-18]. Children who are proficient in FMS's are more likely to participate in and enjoy physical activity, achieve higher levels of aerobic fitness, exhibit higher levels of perceived competence and self-esteem, and are less likely to be overweight or obese [16-18]. It has been shown that that children with BE exhibit significant delays in their FMS development, thus compromising their ability, confidence and motivation to participate in PA [19]. In a study of 46 children with BE, only nine (19.6%) achieved their age equivalency for locomotor skills, while just four (8.7%) achieved their age equivalency for object control skills. Fewer than 5% of children demonstrated mastery in the run, gallop, hop, and leap; while fewer than 10% demonstrated mastery for

the two-handed strike, overarm throw, and underarm throw. Importantly, children achieving their age equivalency for locomotor or object control skills exhibited higher levels of MVPA, perceived competence, and HRQoL than children with developmental delays in FMS's [20].

To address the concerns that children with BE are insufficiently active for health benefit and that developmental delays in fundamental movement skill proficiency are a root cause, we have developed a novel, play-based therapeutic exercise program specifically designed to improve FMS proficiency and aerobic fitness in children with BE. In a pilot RCT involving 21 children with BE, the program significantly improved FMS proficiency, with a 21% increase in locomotion skills and a 31% increase in object control. The effect sizes associated with these improvements were, by convention, large (Cohen's $d \geq 1.2$). The program also had a moderate positive effect on aerobic fitness (Cohen's $d = 0.5$) [21]. We now propose to expand this program to a large multi-center RCT to evaluate the efficacy of our exercise program in reducing the frequency of acute exacerbations of BE. Exacerbation frequency is the only known risk factor for lung function decline in children with BE [22]. Reducing the frequency of exacerbations during childhood through therapeutic exercise may be an important clinical management strategy for preventing future decline in lung function and respiratory morbidity later in life.

Aims of the Study {7}

This multi-center RCT is designed to answer the primary research question: In children with BE, does a novel eight-week therapeutic exercise program (compared to wait-list controls) decrease the frequency of exacerbations? The primary hypothesis is that the proportion of children with no exacerbations over 12 months will be significantly higher in children receiving the eight-week therapeutic exercise program than children in the wait-list control condition.

For policy, we will also (a) include a cost-effectiveness evaluation, and (b) assess the program's impact on FMS proficiency, habitual PA, aerobic fitness, HRQoL, and lung function. Our secondary hypothesis is that our specifically designed program for children with BE will be cost-effective and efficacious in improving FMS proficiency, MVPA levels, aerobic fitness (peak VO_2), HRQoL, and lung function (forced expiratory volume in one second, FEV_1). Improvements in these outcomes will play a major role in improving the health and wellbeing of children with BE. Furthermore, by enhancing children's capacity and behavioural capability to engage in health-enhancing PA over the lifespan, the program has strong potential to mitigate the risk of disabling secondary conditions such as obesity, anxiety, and depression.

Trial design {8} {9}

This multi-center, observer-blinded, parallel group (1:1 allocation), RCT will be conducted at the Queensland Children's Hospital (QCH), Gold Cold University Hospital (GCUH) and Royal Darwin Hospital (RDH) in Australia. These hospitals are tertiary settings with dedicated pediatric respiratory services.

Methods: Participants, Interventions And Outcomes

Eligibility criteria {10}

To be eligible for enrolment, participants must be between the ages of six and thirteen years, have a confirmed diagnosis of non-CF BE (by high-resolution chest tomography (HRCT) or if >5 years since the last scan, under the regular care of a pediatric pulmonologist; experienced at least one acute pulmonary exacerbation in the past twelve months; be medically able to participate in exercise, have their parent provide informed consent and not be planning to leave the study catchment area in the 12 months following enrollment. Participants will be excluded if they are unstable medically (as advised by treating pulmonologist); have insufficient cooperation and/or cognitive understanding to perform tasks; have a recent musculoskeletal injury (e.g., muscle strain, sprains, fractures); have underlying chronic illness other than BE (e.g., asthma, CF, neurological or cardiac disorders); are participating in clinical trial of another investigational drug/devise or interventional therapy and are unable to attend sessions or return for follow-up assessments.

Recruitment {15}{24}{26a}

Participants will be recruited from the respiratory clinics at each study site (QCH, GCUH, RDH). On regularly scheduled clinic days, the clinic manager or research nurse will provide an appointment list of patients with a bronchiectasis diagnosis, which includes the patient's age or date of birth. These patients will be approached by research staff before or after their appointment to explain the study and its requirements, gauge interest, and screen for initial eligibility. To assess initial eligibility the families are asked a series of questions that form the inclusion then exclusion criteria. Eligible and interested families will be given a participant information sheet and consent form. Following eligibility screening with the family, the attending physician will confirm the screening questions related to the bronchiectasis diagnosis and suitability for exercise. Parents may request a follow up at a more convenient time or if they would like additional time to consider participation in the study. Written consent may be provided by hard copy form at the time of recruitment or electronically to the study-specific email address. Ethical approval has been granted from the Human Research Ethics Committees of the Children's Health Queensland Hospital and Health Service (HREC/19/QCHQ/56049) and the Northern Territory Department of Health and Menzies School of Health Research (2020-3847) and administratively reviewed by the Queensland University of Technology (1900000821) and the University of Queensland (1900000821). The trial has been prospectively registered with the Australian New Zealand Clinical Trial Registry (ACTRN12619001008112).

Randomisation, allocation and blinding {16a}{16b}{16c}{17a}

At the completion of baseline assessments, participants will be centrally randomized to the therapeutic exercise program or wait-list control using the database randomization module in REDCap (Vanderbilt University, Nashville, USA). Treatment allocation will be computer-generated, stratified by site (permuted blocks), concealed and supervised by an independent statistician. At enrolment each child is assigned to the next treatment on the stratified list. Trained assessors blinded to group allocation will collect, process, and analyse primary and secondary outcome data at each study site. Within an exercise intervention, it is

not possible to blind either instructor or participant; however, project staff delivering the therapeutic exercise program will not take part in outcome assessments.

Interventions

Therapeutic Exercise Group {11a}{11c}{18b}

Children allocated to the intervention will receive the therapeutic exercise program delivered by an accredited exercise physiologist or physiotherapist. The program will include eight, 60-minute weekly sessions supplemented by a home-based program (two sessions per week for eight weeks, approximately twenty minutes per session). This program was designed from the feasibility pilot trial [21]. Group sessions of up to six children, will be conducted in community venues at different times and locations to accommodate family schedules. Siblings and friends are able to attend if space permits. During group sessions, the children will participate in a warm-up, a circuit of six independent games targeting fundamental movement skills and cardiovascular fitness followed by a group game then cool down. Table 1 includes examples of the games categorised into the targeted skills. The games alternate from higher to lower intensity and can be modified to match each child's abilities. Children track completed sessions in a 'Games Passport' where they can collect stickers to track their sessions. The home program is based on games from the group sessions. Parents receive a manual that details the home sessions and strategies to complete these. Each week the child will choose two new activities from the manual to complete with their parent at home. Parents document the number of home sessions completed each week on a chart and an accompanying perceived exertion metric (OMNI score)[23]. The chart is reviewed by the instructor at the next weekly session.

Wait-list control group {11d}{18b}

The wait-list control group will receive usual care, which in the target patient group, is currently limited to little or no prescribed exercise therapy. Children allocated to the wait-list control group will be offered the exercise program at the conclusion of their 12-month follow-up period.

Fidelity of training instructors {11c}{18a}{27}

Prior to leading group sessions, instructors will complete 12-hours of comprehensive training led by the exercise physiology and physiotherapy study investigators. Each instructor will review the intervention manual, standard operating procedures and watch videos demonstrating the setup, instructions, modifications and basic movements for each component of the session. Training will start with observation of the games with a focus on feedback and reflection. It will progress to leading full sessions with real participants, including the rehearsal of scripts developed for the home program and tracking. For quality assurance and program fidelity, heart rate data from a sensor will be collected from a sample of sessions and instructors will complete an essential element checklist after each session. The checklist will include comments about the games completed in the session, and confirmation that home session data were collected. Once the intervention has commenced the lead exercise physiologist or

physiotherapist will intermittently visit each community venue to ensure the intervention is being delivered as outlined in the study materials and training sessions.

Assessment of primary and secondary outcomes {12}{18a}{19}{27}

All measures will be recorded at baseline (T_1), immediately post intervention (T_2), six (T_3) and twelve months (T_4) post baseline by trained assessors blinded to the group allocation (See Figure 1). All assessors will be required to meet predetermined inter- and intra-observer reliability standards for each outcome. All data collected will be recorded using standardized data entry forms created in REDCap. Baseline data collection from parents will include demographics (age, gender, parental age, parental education household income and family structure) and medical information (duration and type of cough, current medications, frequency of doctor visits). Anthropometric characteristics (height, weight, body mass index (BMI), BMI z-score) lung function (FEV 1.0), current medication and relevant medical history from the electronic medical record.

Primary outcome {12}

Pulmonary exacerbation will be defined as treatment with antibiotics for any of the following: increased wet cough, dyspnea, increased sputum volume or colour intensity, new chest examination or radiographic findings, deterioration in FEV_1 percentage by more than 10%, or hemoptysis [24]. Wet cough must be present.

Secondary Outcome Measures {12}

Aerobic fitness

Aerobic fitness will be assessed with a modified shuttle test (MST). The participants move back and forth over a 10m course at an increasingly faster pace as guided by an audible tone. The test stops when the child is unable to reach the marker by the tone. The assessor will ask the child to rate their perceived exertion using the OMNI scale. The total distance, number of laps and OMNI score will be recorded [25, 26]. The MST has been validated in children with chronic respiratory conditions [25-28].

Fundamental Movement Skill Proficiency

The Test of Gross Motor Development 2nd Edition (TGMD-2) will be used to measure movement competency relative to 12 FMS's subdivided into two subscales: locomotor and object control (ball) skills [29]. The TGMD-2 is a valid and reliable measure of FMS proficiency in children. The TGMD-2 is widely used internationally in typically developing children [30, 31] and children with chronic health conditions [32-34]. Test-retest reliability intraclass correlation coefficient (ICC's) are high for the locomotor and ball skills (ICC = 0.92-0.96), and total TGMD-2 (ICC = 0.77-0.98) score [35].

Habitual physical activity

HPA will be assessed with an ActiGraph GT3X+ accelerometer (ActiGraph Corporation, Pensacola, FL, USA), worn on the child's non-dominant wrist for seven consecutive days, except for bathing and water-based activities. The accelerometers will be initialised and downloaded with the ActiLife software (Version 6.14.4). Raw accelerometer data (sampling frequency = 30 Hz) will be downloaded and processed into physical activity metrics using a random forest physical activity classification algorithm specifically developed for children [36, 37]. This validated algorithm uses features extracted from the raw tri-axial acceleration signal (15 second windows) to quantify daily time spent in sedentary activities (sitting or lying down), light- intensity activities and games (slow walking/pottering about, standing, standing arts and crafts), walking, running, and moderate-to-vigorous intensity activities and games (active games with balls, dance). When applied to new data, recognition accuracy was 99.5% for sedentary activities, 92.6% for light-intensity activities and games, 88.0% for moderate-to-vigorous intensity activities and game, 93.2% for walking, and 91.5% for running. Overall classification accuracy was 93.6% [36, 37]. Daily MVPA will be calculated by summing daily time spent in walking, running, and moderate-to-vigorous activities and games. Non-wear periods will be identified by summing the 15 second windows in which the standard deviation of the acceleration signal vector magnitude was < 13 mg for > = 30 consecutive minutes [38]. The child's accelerometer data will be included in the analyses if they had ≥ 3 days in which wear time is 14 hours or longer.

Perceived movement competence

The Pictorial Scale of Perceived Movement Skill Competence (PMSC) is a valid and reliable tool that assesses the fundamental movement skill competence perceptions of young children [39-41]. The pictorial instrument depicts 12 skills, takes a short time to administer and has appropriate ICC's (0.76-0.84) [40].

Health-related Quality of Life

Parents will complete the Core Scales of the Pediatric Quality of Life Inventory (PedsQL^{TM}) and the Chronic Cough QoL (CCQoL) questionnaires [42, 43]. Children will respond to the child-reported PedsQL and the child reported cough specific QoL (if aged >7 years). The PedsQL^{TM} is an efficient multidimensional tool that has 23 items. The items address the domains of Physical Functioning, Emotional Functioning, Social Functioning, and School Functioning. The PedsQL^{TM} has been used in multiple paediatric BE populations with a high internal consistency (ICC=0.88 child, 0.90 parent report) [19, 42]. The CCQoL short form has eight questions and is a reliable, valid instrument to assess chronic cough in children [43].

Lung function – Spirometry

This will be performed by a pediatric respiratory scientist using standard protocols as described by the Thoracic Society of Australia and New Zealand [44].

Economic Evaluation

The within-trial cost-effectiveness analysis and cost-utility analysis will be completed by a health economist to determine whether therapeutic exercise represents 'value for money' compared to usual care over a 12-month period from a healthcare provider perspective. Intervention costs will be determined from the project financial records, including costs associated with therapist training and staff time to deliver programs. Pulmonary exacerbation costs (antibiotic treatment and time of clinical staff) will be taken from the Australian Pharmaceutical Benefits Scheme and the appropriate clinical award wage rate. The outcome of interest will be the proportion of children with no exacerbations over 12-months for the cost-effectiveness analysis, and HRQoL (measured using PedsQL^{TM}) for the cost-utility analysis.

Statistical Analysis {20a}{20b}

The statistical analyses will follow standard principles for RCTs using two group comparisons including all participants on an intention-to-treat basis. For the primary aim, a binary regression model with a suitably chosen link function (e.g., logistic) will be used where the target variable is whether or not an exacerbation occurred over the 12-month study period for each subject. The main covariate of interest is the treatment group (exercise vs. wait-list control). Other covariates potentially influencing the target variable such as age and sex will be considered. Between-group differences on secondary outcomes - aerobic fitness (Peak VO2), habitual PA (objectively measured MVPA), HRQoL (PedsQL), and lung function (FEV_1) will be tested immediately post intervention, at 6-months follow-up, and 12-months follow-up using linear regression with treatment group (exercise vs. wait-list control) as the main effect and baseline measures of the respective outcome, along with other potential confounders (e.g., age, sex), as covariates.

Sample Size and Power {14}

The BREATH trial is designed to detect a significant group difference in the proportion of children with no exacerbations over 12-months. Based on a long-term azithromycin for children with non- CF-BE RCT [24], we assume that 20% of children allocated to the wait-list control condition will not experience an exacerbation over the 12-month study period. Based on the results of an exercise training RCT conducted in 55 adults with BE [13], we expect our therapeutic exercise program to double the proportion of children with no exacerbations over 12-months from 20% to 40%. For 80% power and a 2-tailed alpha of 0.05, a sample size of 79 children per group (N=158) is required to detect a 20% difference between groups. To account for 10% attrition, a total of 174 children will be enrolled.

Discussion

Pediatric BE is a significant contributor to global mortality, morbidity and health-care utilization yet there is a paucity of research on non-pharmaceutical interventions that aim to improve HRQoL and impact disease progression for this population [1-3, 6]. It has been established that children with BE have delayed FMS proficiency leading to insufficient physical activity for health benefit [19]. A pilot RCT involving 21 children with BE demonstrated that a therapeutic exercise program significantly improved FMS

proficiency and aerobic fitness [21]. There is a need to expand this program to a large multi-center RCT to evaluate the efficacy of an exercise program in reducing the frequency of acute exacerbations of BE. This multi-center RCT will establish and test a highly scalable, therapeutic exercise program to reduce the proportion of children with no exacerbations of BE over 12-months and improve movement competency, HRQoL, and exercise capacity.

Improvements in these outcomes are likely to have an immediate positive impact on physical functioning, quality of life and future health. BE exacerbation is the only known risk factor for lung function decline in this patient group. Thus, reducing the frequency of exacerbations during childhood through therapeutic exercise may be an important clinical management strategy for preventing future decline in lung function and respiratory morbidity later in life. The age range is derived from the pilot project to include children developmentally interested in games and play and able to independently follow cues from the instructors. The games sessions will be led by registered exercise health professionals who have completed BREATH specific training.

This RCT is significant because it is the first fully powered RCT to test the effects of a therapeutic exercise program to prevent exacerbations and improve FMS proficiency, fitness, and HRQoL in children with BE. By implementing a developmentally appropriate, play-based exercise program tailored to the individual needs of children with BE, the results have the potential for a major paradigm shift in the way in which therapeutic exercise is prescribed and implemented in children with chronic respiratory conditions. The exercise program can be readily translated. It does not require expensive equipment and can be delivered in variety of settings, including the participant's home. The program of research has strong potential for translation to other paediatric patient groups with similar needs for exercise therapy, including those with obesity, childhood cancers, and neurological conditions such as cerebral palsy. While exercise is well recognised to be universally beneficial, this RCT is required because it will provide long overdue Level 1 evidence regarding the efficacy and cost-effectiveness of tailored therapeutic exercise programs for children with BE.

Trial Status

Recruitment commenced at all sites in early 2021.

Abbreviations

BE: Bronchiectasis; BMI: body mass index; BREATH: Bronchiectasis Exercise as Therapy; CCQoL: Chronic Cough QoL; CF: cystic fibrosis; CSLD: chronic suppurative lung disease; FEV1: forced expiratory volume in one second; FMS: fundamental movement skill; FVC: forced vital capacity; GCUH: Gold Cold University Hospital; HRQoL: health related quality of life; ICC: intraclass correlation coefficient; MST: modified shuttle test; MVPA: moderate-to-vigorous intensity physical activity; N: number; PA: physical activity; PedsQL^{TM}: Core Scales of the Pediatric Quality of Life Inventory; PMSC: The Pictorial Scale of Perceived Movement Skill Competence; QCH: Queensland Children's Hospital; QOL: Quality of life; RCT: randomized

controlled trial; RDH: Royal Darwin Hospital; SD: standard deviation; TGMD-2: Test of Gross Motor Development 2nd Edition;

Declarations

Authors' contributions {5d}{31b}

ST conceived the study, its design and coordination, KO'G, IM, VG, GMc and ABC supported the design and submission to National Health and Medical Research Council, CD oversaw the analysis plan, TL oversaw the economic analysis plan, EB and TJ participated in the development of the intervention, TJ will assist with the recruitment, assessment and intervention. All authors read and approved the final manuscript.

Author details

[1]Queensland University of Technology, Brisbane, QLD, Australia. [2]Queensland Children's Hospital, Brisbane, QLD, Australia. [3]Gold Coast University Hospital, Gold Coast, QLD, Australia. [4]The University of Queensland, Brisbane, QLD, Australia. [5]Menzies School of Health Research, Darwin, NT, Australia. [6]George Institute for Global Health, Sydney, NSW, Australia. [7]Griffith University, QLD, Australia.

Funding {4}

National Health and Medical Research Council

Competing interests {28}

The authors declare that they have no competing interests

References

1. Chang AB, Redding GJ, Everard ML. Chronic wet cough: Protracted bronchitis, chronic suppurative lung disease and bronchiectasis. Pediatric Pulmonology. 2008;43(6):519-31.

2. Kapur N, Masters IB, Newcombe P, Chang AB. The burden of disease in pediatric non-cystic fibrosis bronchiectasis. Chest. 2012;141(4):1018-24.

3. Wurzel DF, Chang AB. An update on pediatric bronchiectasis. Expert Review of Respiratory Medicine. 2017;11(7):517-32.

4. Chang AB, Bush A, Grimwood K. Bronchiectasis in children: diagnosis and treatment. Lancet. 2018;392(10150):866-79.

5. Goyal V, Grimwood K, Marchant JM, Masters IB, Chang AB. Paediatric chronic suppurative lung disease: clinical characteristics and outcomes. Eur J Pediatr. 2016;175(8):1077-84.

6. O'Grady KF, Grimwood K. The likelihood of preventing respiratory exacerbations in children and adolescents with either chronic suppurative lung disease or bronchiectasis. Frontiers in Pediatrics. 2017;5:58.

7. McCallum GB, Binks MJ. The Epidemiology of Chronic Suppurative Lung Disease and Bronchiectasis in Children and Adolescents. Front Pediatr. 2017;5:27.

8. Hall KK, Chang AB, Anderson J, Arnold D, Goyal V, Dunbar M, et al. The Incidence and Short-term Outcomes of Acute Respiratory Illness with Cough in Children from a Socioeconomically Disadvantaged Urban Community in Australia: A Community-Based Prospective Cohort Study. Frontiers in Pediatrics. 2017;5:228.

9. Chang AB, Bell SC, Torzillo PJ, King PT, Maguire GP, Byrnes CA, et al. Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand Thoracic Society of Australia and New Zealand guidelines. Med J Aust. 2015;202(3):130.

10. Chang AB, Bell SC, Torzillo PJ, King PT, Maguire GP, Byrnes CA, et al. Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand Thoracic Society of Australia and New Zealand guidelines. Med J Aust. 2015;202(3):130.

11. Lee AL, Gordon CS, Osadnik CR. Exercise training for bronchiectasis. Cochrane Database Syst Rev. 2021(4).

12. Joschtel B, Gomersall SR, Tweedy S, Petsky H, Chang AB, Trost SG. Effects of exercise training on physical and psychosocial health in children with chronic respiratory disease: a systematic review and meta-analysis. BMJ Open Sport and Exercise Medicine. 2018;4(1):e000409.

13. Lee AL, Hill CJ, Cecins N, Jenkins S, McDonald CF, Burge AT, et al. The short and long term effects of exercise training in non-cystic fibrosis bronchiectasis--a randomised controlled trial. Respiratory Research. 2014;15:44.

14. Niksarlioglu E, Uysal M, Camsari G. Obesity and related factors in bronchiectasis. European Respiratory Journal. 2017;50(suppl 61):PA3586.

15. Joschtel B, Gomersall SR, Tweedy S, Petsky H, Chang AB, Trost SG. Objectively measured physical activity and sedentary behaviour in children with bronchiectasis: a cross-sectional study. BMC Pulm Med. 2019;19(1):7.

16. Lubans DR, Morgan PJ, Cliff DP, Barnett LM, Okely AD. Fundamental movement skills in children and adolescents: review of associated health benefits. Sports Med. 2010;40(12):1019-35.

17. Robinson LE, Stodden DF, Barnett LM, Lopes VP, Logan SW, Rodrigues LP, et al. Motor Competence and its Effect on Positive Developmental Trajectories of Health. Sports Med. 2015(1179-2035 (Electronic)).

18. Barnett LM, van Beurden E, Morgan PJ, Brooks LO, Beard JR. Childhood motor skill proficiency as a predictor of adolescent physical activity. J Adolesc Health. 2009;44(3):252-9.

19. Joschtel B, Gomersall S, Trost SG. Fundamental movement skills among children with non-CF bronchiectasis. Journal of Science and Medicine in Sport. 2017;20:e63.

20. Joschtel B, Gomersall S, Tweedy S, Petsky H, Chang AB, Trost SG. Fundamental Movement Skill Proficiency and Objectively Measured Physical Activity in Children with Bronchiectasis: A Cross-Sectional Study. Research Square; 2020.

21. Joschtel B, Gomersall S, Tweedy S, Petsky H, Chang A, Trost SG. Effects Of A Therapeutic Exercise Program In Children With Non-cf Bronchiectasis. Med Sci Sports Exerc. 2018;50.

22. Kapur N, Masters IB, Chang AB. Exacerbations in noncystic fibrosis bronchiectasis: Clinical features and investigations. Respir Med. 2009;103(11):1681-7.

23. Rice KR, Gammon C, Pfieffer K, Trost SG. Age related differences in the validity of the OMNI perceived exertion scale during lifestyle activities. Pediatr Exerc Sci. 2015;27(1):95-101.

24. Valery PC, Morris PS, Byrnes CA, Grimwood K, Torzillo PJ, Bauert PA, et al. Long-term azithromycin for Indigenous children with non-cystic-fibrosis bronchiectasis or chronic suppurative lung disease (Bronchiectasis Intervention Study): a multicentre, double-blind, randomised controlled trial. The Lancet Respiratory Medicine. 2013;1(8):610-20.

25. Cox NS, Follett J, McKay KO. Modified shuttle test performance in hospitalized children and adolescents with cystic fibrosis. J Cyst Fibros. 2006;5(3):165-70.

26. Selvadurai HC, Cooper PJ, Meyers N, Blimkie CJ, Smith L, Mellis CM, et al. Validation of shuttle tests in children with cystic fibrosis. Pediatric Pulmonology. 2003;35(2):133-8.

27. Coelho CC, Aquino EdS, Almeida DCd, Oliveira GC, Pinto RdC, Rezende IMO, et al. Análise comparativa e reprodutibilidade do teste de caminhada com carga progressiva (modificado) em crianças normais e em portadoras de fibrose cística %J Jornal Brasileiro de Pneumologia. 2007;33:168-74.

28. del Corral T, Gómez Sánchez Á, López-de-Uralde-Villanueva I. Test-retest reliability, minimal detectable change and minimal clinically important differences in modified shuttle walk test in children and adolescents with cystic fibrosis. Journal of Cystic Fibrosis. 2020;19(3):442-8.

29. Ulrich D. Test of gross motor development (3rd ed.). Austin, TX: Pro-Ed; 2016.

30. Webster EK, Martin CK, Staiano AE. Fundamental motor skills, screen-time, and physical activity in preschoolers. Journal of Sport and Health Science. 2019;8(2):114-21.

31. Williams HG, Pfeiffer KA, Dowda M, Jeter C, Jones S, Pate RR. A Field-Based Testing Protocol for Assessing Gross Motor Skills in Preschool Children: The CHAMPS Motor Skills Protocol (CMSP). Meas Phys Educ Exerc Sci. 2009;13(3):151-65.

32. Capio CM, Sit CHP, Abernethy B. Fundamental movement skills testing in children with cerebral palsy. Disability and Rehabilitation. 2011;33(25-26):2519-28.

33. Schott N, Holfelder B, Mousouli O. Motor skill assessment in children with Down Syndrome: relationship between performance-based and teacher-report measures. Res Dev Disabil. 2014(1873-3379 (Electronic)).

34. Banks L, Rosenthal S, Manlhiot C, Fan C-PS, McKillop A, Longmuir PE, et al. Exercise Capacity and Self-Efficacy are Associated with Moderate-to-Vigorous Intensity Physical Activity in Children with Congenital Heart Disease. Pediatric Cardiology. 2017;38(6):1206-14.

35. Maeng H, Webster EK, Pitchford EA, Ulrich DA. Inter- and Intrarater Reliabilities of the Test of Gross Motor Development-Third Edition Among Experienced TGMD-2 Raters. Adapted physical activity quarterly. 2017;34(4):442-55.

36. Trost SG, M. A, KA. P. A novel two-step algorithm for estimating energy expenditure from wrist accelerometer data in youth. Paper presented at the 5th International Conference on Ambulatory Monitoring of Physical Activity and Movement; Washington DC2017.

37. Chowdhury AK, Tjondronegoro D, Chandran V, Trost SG. Ensemble methods for classification of physical activities from wrist accelerometry. Med Sci Sports Exerc. 2017;49(9):1965-73.

38. Ahmadi M, Nathan N, Sutherland R, Wolfenden L, Trost SG. Non-wear or sleep? Evaluation of five non-wear detection algorithms for raw accelerometer data. Journal of Sports Sciences. 2020;38(1466-447X (Electronic)).

39. Barnett LM, Ridgers ND, Zask A, Salmon J. Face validity and reliability of a pictorial instrument for assessing fundamental movement skill perceived competence in young children. Journal of Science and Medicine in Sport. 2015;18(1):98-102.

40. Barnett LM, Robinson LE, Webster EK, Ridgers ND. Reliability of the Pictorial Scale of Perceived Movement Skill Competence in 2 Diverse Samples of Young Children. Journal of Physical Activity and Health. 2015;12(8):1045-51.

41. Barnett LM, Vazou S, Abbott G, Bowe SJ, Robinson LE, Ridgers ND, et al. Construct validity of the pictorial scale of Perceived Movement Skill Competence. Psychology of Sport and Exercise. 2016;22:294-302.

42. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. Med Care. 2001;39(8):800-

12.

43. Newcombe PA, Sheffield JK, Juniper EF, Petsky HL, Willis C, Chang AB. Validation of a parent-proxy quality of life questionnaire for paediatric chronic cough (PC-QOL). Thorax. 2010;65(9):819-23.

44. Johns DP, Pierce R. Pocket Guide to Spirometry. 3rd edition ed: McGraw-Hill Australia; 2011.

Tables

Table 1 Examples of Games Targeting FMS's and Fitness Parameters

Agility and Coordination
Hoop to Hoop: Set the playing field by placing four hoops in parallel. In the first hoop place 4-8 bean bags. The participant starts on their hands and feet but knees off the ground to form a triangular shape with their body. They pick up a bean bag and throw or place it into the next hoop. They do this with all bean bags then move their body to the next hoop. They repeat this relay until all bean bags are in the last hoop. If they are fast enough they can repeat this process to return to the start.
Balance
Lily Pad Leap: Set the playing field by laying out two lily pads. The child crosses the pond by placing one lily pad in front of the other, stepping onto it, then picking up the lily pad behind to place it in front of themselves.
Kicking
Tower Seize: Create a playing area using cones to mark the boundaries. Each ball is a flaming cannon to be kicked at the enemy's tower fort (goal). The child starts at the furthest from the goal and runs over to a ball before kicking it into the goal. They repeat this until all balls are successfully in the goal.
Strength
Help the Miners: The playing field is set up with a washing basket at one end and a collection of medicine balls spaced 4-6m away. The child heads into the mine to collect the gems. They squat down to pick up the medicine ball then walk back to lift it into the washing basket. The medicine balls further away are heavier and are the more valuable gems.
Strike, Hit, Dribble
Thor's Croquet: Set the playing field to have small hurdles spaced a 2-3m apart from the starting line. The child dribbles a hockey ball with a hockey stick under each hurdle. They need to leap over each hurdle before dribbling the ball with the hockey stick to the next hurdle. If they reach the end they can dribble the ball back to the start and repeat. They may need to run to retrieve their ball if they overshoot their target.
Throwing and Catching
Feed the Monster: Set the playing field by scattering the food toys 1-5m from a washing basket. Place the hungry monster mouth resource on top of the washing basket. The goal is for the child to pick up each piece of food and feed the hungry monster by accurately throwing the food into its mouth. Encourage the child to squat to pick up each item of food.
Group Game
Blob Tag: A modified game of tag. One participant starts as the blob and aims to tag a peer with their hand. Once tagged they join hands to become a bigger blog. The game ends when everyone is part of the blob. Mark clear boundaries for this game to be successful.

Figures

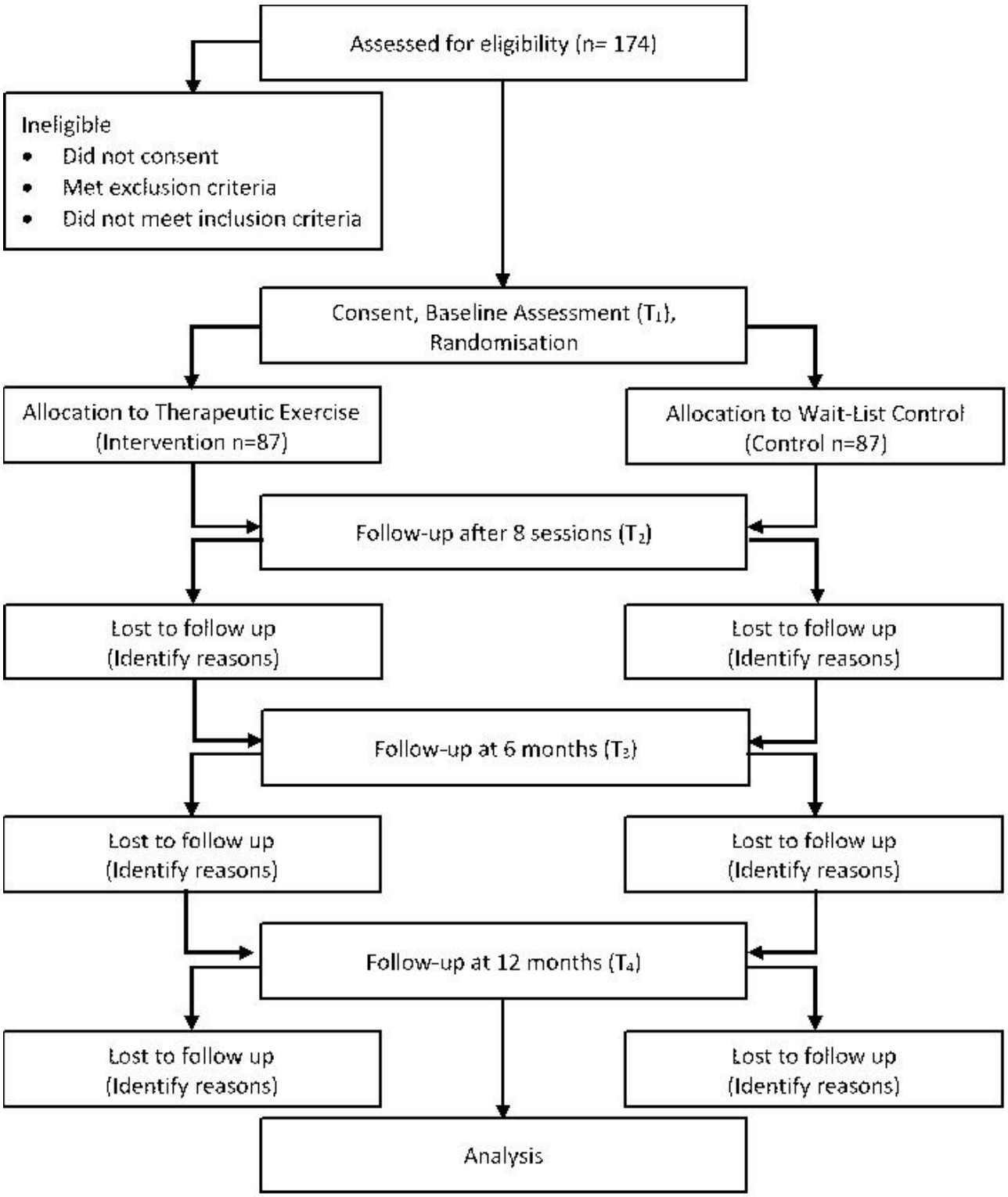

Figure 1

BREATH trial CONSORT flow chart