EXPERT REVIEWS

Exercise as part of a cystic fibrosis therapeutic routine

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The role of exercise in cystic fibrosis (CF) is well established, and over the last three decades it has become an important component in the management of all individuals with CF. The role of exercise as a prognostic indicator or therapeutic tool is an important area of research interest in CF care internationally. This article summarizes the currently available evidence regarding exercise capacity in CF, the potential effects of exercise on health outcomes in CF and the challenges faced when trying to incorporate exercise into a CF therapeutic routine, and highlights some methods to facilitate the incorporation of exercise into CF therapeutic routines.

Keywords: cystic fibrosis • exercise • exercise capacity • physiotherapy • therapeutic routine

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Learning objectives

Upon completion of this activity, participants will be able to:

- Analyze factors which limit exercise capacity among patients with CF
- Evaluate benefits of exercise therapy among patients with CF
- Distinguish barriers to exercise therapy among patients with CF
- Assess strategies to promote wider participation in exercise training among patients with CF

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A therapeutic effect is a consequence of any medical intervention. While the term 'therapeutic effect' is most commonly attributed to pharmacological interventions, it can be applied to any treatment approach. Exercise intolerance is an established characteristic of cystic fibrosis (CF) and is dependent on the progression of the disease [1]. Exercise is seen to have the potential to have a therapeutic effect in CF and has therefore become a mainstay of the physiotherapy treatment for CF [2]. Using exercise, either as a prognostic or a therapeutic tool, is an area of renewed interest to clinicians [1]. Judgments of the benefits of exercise on long-term survival in CF to date can only be extrapolated from relatively short-term clinical trials [3]. Despite this, the role of exercise in CF is now well established, and current recommendations are based both on understanding of the physiological mechanisms and clinical reasoning [4]. The purpose of this article is to outline the recent evidence for factors that may contribute to reduced exercise capacity in CF, examine the evidence for attributing improved health outcomes to exercise in CF, discuss the proposed physiological mechanisms and discuss how some of the barriers to exercise in CF might be minimized.

Factors that contribute to a reduction in exercise capacity in CF

A reduction in exercise capacity is a hallmark of CF disease, but the exact mechanisms leading to this impairment remain unclear [1].

Lung function

Decline in lung function is a characteristic of CF, and monitoring and minimizing this decline is central to the clinical management of the disease. However, abnormalities in exercise parameters in early disease and in more stable patients may reflect disease activities that are not detected by spirometry. It has been suggested that the correlation between lung computed tomography abnormalities and exercise limitation is stronger than the correlation between spirometry and exercise limitation [5].

The ventilatory response to exercise in CF differs to that of the healthy individual. As the disease progresses, an increase in dead space [6] necessitates changes in ventilation to maintain adequate alveolar ventilation during exercise. Changes in lung function over time have been shown to correlate with changes in exercise capacity [7,8]. In a longitudinal study of children with CF between 8 and 17 years of age, the rate of decline in aerobic capacity, measured using peak oxygen uptake (VO_{2peak}), in those with a forced expiratory volume in 1 second (FEV_1) of less than 80% predicted was high, but in those with an FEV_1 of greater than 80% predicted VO_{2peak} remained stable [8].

Carbon dioxide (CO_2) retention during exercise testing has also been reported to contribute to a faster rate of decline in FEV_1% in a 3-year study of children with CF between 11 and 15 years of age [9]. Using a maximal exercise test, children who exhibited CO_2 retention (defined as a rise of ≥5 mmHg in end-tidal CO_2 from the first work rate to peak work rate and a failure to reduce end CO_2 after the peak work rate by 3 mmHg by the termination of exercise) had a greater decline in FEV_1% compared with those who did not retain CO_2 [9].

The presence of static hyperinflation – defined as a ratio of residual volume to total lung capacity greater than 30% – in children with mild-to-moderate CF has not been associated with ventilatory constraints during exercise [10]. It is suggested that reduced exercise capacity in individuals with mild-to-moderate hyperinflation, compared with those without hyperinflation, may be explained by preliminary inspiratory muscle fatigue as a result of increased work of breathing, gas trapping and ventilation/perfusion mismatch [10].

Longer term exercise programs (>1 year), both in children [11] and adults [12] with CF, have been reported to result in a significantly lower annual decline in forced vital capacity than in control groups receiving usual care. It has been shown that fitness can be maintained in the long term, despite deterioration in lung function [12]. However, as more evidence emerges, it seems clear that the relationship between lung function and exercise may only become significant with severe disease and that respiratory factors do not limit maximal symptom-limited exercise in individuals with mild-to-moderate CF lung disease [13,14].

Nutrition

The ability to exercise is determined mainly by pulmonary function and nutritional status [7,15]. Longitudinal changes in nutritional status in CF have been shown to correlate with changes in exercise capacity [7]. Patients with CF have also been shown to have a resting energy expenditure that is 10–30% higher than that predicted compared with controls [16]. The mechanisms leading to this increase may include the energetic cost of breathing, the systemic effects of chronic pulmonary inflammation, malnutrition and the genetic defect underlying CF [16]. In addition, the energetic cost of physical activity has been shown to be higher in adult CF patients when compared with controls [17].

It has been suggested that a high sweat rate and high concentrations of sodium and chloride in CF sweat may significantly reduce serum osmolality, and that this low osmolality in body fluids may deprive individuals with CF of a thirst stimulus, exacerbating normal dehydration during combined exercise and heat stress [18]. Fluid and electrolyte replacements are essential considerations when undertaking airway clearance techniques and exercise therapies for CF. This is of particular importance when exercising in warmer weather.

The presence of CF-related diabetes (CFRD) is another important factor that should be taken into consideration when implementing an exercise program. A reduction in glycosylated hemoglobin (used as a surrogate for glucose control) has been shown to improve with exercise interventions in non-CF diabetic patients [19]. Optimal glucose control during exercise is important to maintain adequate muscle glycogen levels and to avoid exercise-induced hypoglycemia, both of which can contribute to early fatigue and reduced exercise capacity.

The importance of fat-free mass (FFM) as a component of body composition in CF, and its role in exercise capacity, has been highlighted in children with CF [7]. Muscle mass is the largest constituent of FFM and is a critical determinant of aerobic capacity. Nutritional deficiencies can lead to muscle wasting and in the long term, FFM may be important for maintaining exercise capacity [7].

It is clear that there is a specific need to monitor and tailor nutrition in all individuals with CF who are undertaking an exercise program, or when changing the intensity of an exercise program. Adequate nutrition and hydration are essential to allow safe and effective exercise to be undertaken. The importance of the development of FFM and the impact of exercise on CFRD are also essential dietary considerations. Further research is required to fully elucidate these important considerations.

Muscle dysfunction

Debate remains as to whether exercise limitation in CF is caused by the inability of the cardiorespiratory system to meet metabolic demands or intrinsic abnormalities in the muscle itself [20]. There is evidence to suggest that abnormal anaerobic metabolism [21] and decreased maximal muscle strength and power occur in CF [22,23]. Evidence of skeletal muscle dysfunction in children with mild-to-moderate CF and normal nutritional status has been reported [22,24]. These reductions have been attributed to abnormalities in muscle size, associated with diminished work capacity and an increased oxygen cost of exercise [22]. However, one study reported the muscle cross-sectional area to be only slightly smaller in children with CF than in control subjects, leading to the hypothesis that muscle size alone cannot account for the impairment of VO_{2peak} observed in the CF group [24]. Although physical inactivity is reported as being a significant contributing factor to exercise intolerance and reduced skeletal muscle force in adults with CF, it has been suggested that the limitations in muscle force observed are in excess to that expected from physical inactivity alone [25]. Abnormalities in muscle bioenergetic pathways, both during rest and during short bouts of high-intensity exercise in adolescent patients with CF, not observed in other respiratory disease or healthy controls, have recently been reported and may account for these discrepancies [20].

Children with CF have been shown to have a slower phosphocreatine recovery time, which suggests impaired aerobic oxidative metabolism and a lower VO_{2peak} following cardiopulmonary exercise testing [14,20], indicating that the greater the aerobic fitness of a patient, the faster the rate of recovery [13,20]. These results identify the need to assess the recovery from exercise in CF individuals as well as measuring peak exercise capacity, as a high aerobic capacity combined with short recovery are most likely to represent good exercise tolerance [13]. Slowed oxygen uptake kinetics in individuals aged between 10 and 33 years with CF compared with healthy controls have also been reported [26]. Oxygen uptake kinetics is a measure of the ability of an individual's cardiorespiratory system to adapt to changes in work rate and metabolic demand. Impaired oxygen delivery may partially explain this reduction [26].

Genotype

A reduction in anaerobic exercise capacity in individuals with mild CF mutations has been reported [27]. Another study, however, failed to show any association between genotype and VO_{2peak} [28]. In addition, no differences in lung function have been reported between the classes of mutation, and therefore, the relationship between genotype and fitness remains unclear [27]. It has recently been reported that CFTR is expressed at the sarcoplasmic reticulum of skeletal muscle, which may partly explain the role the genotype may have as a potential determinant of exercise capacity in patients with CF [29].

Habitual activity

Physical activity refers to any body movement produced by skeletal muscle and occurs in a variety of forms such as free play, exercise and organized sports [30]. Exercise training, however, can be defined as regular participation in vigorous physical activity to improve physical performance, cardiovascular function and muscle strength, or a combination of all three [30]. Exercise is an important aspect of the growth and general wellbeing of all children [31]. Yet, even in children without CF, it is well documented that recommended guidelines are often not met, with an estimated three out of ten boys and four

out of ten girls not undertaking the recommended 60 min of moderate-to-vigorous-intensity exercise each day [32,33].

In disease states, a negative-feedback loop can be created where reduced exercise capacity levels result in reduced habitual activity, leading to reduced participation in sport, thereby further reducing exercise capacity [30–35]. The total level of habitual activity in CF children has been reported to be comparable to that of their healthy peers, but the type of activity undertaken has been found to be less vigorous [36,37].

Gender

Gender differences in habitual physical activity have been reported [38]. Even in healthy populations, parents and teachers have been shown to have lower physical activity expectations for girls than for boys. However, it has been reported that gender differences in habitual activity are only evident after the onset of puberty, with girls being significantly less active than their male counterparts, a similar finding both in CF patients and in the healthy population [39]. This is supported by a study reporting that more CF males than CF females are engaged in sports clubs [40]. Importantly, CF females categorized as 'low activity' have been reported to have a significantly greater annual decline in lung function than their 'high activity' female peers [41], which further highlights the potential impact of reduced exercise capacity on outcome. A gender gap in survival rates with young CF females (<20 years of age) being significantly more likely to die than males of the same age has been reported [42], although more recently this gap seems to be less apparent [43].

Psychosocial influences

The reduced levels of vigorous physical activity undertaken by children with CF may also be attributed to psychosocial influences. In healthy children, parents' perceptions of their child's moderate-to-vigorous physical activity competency have been shown to be related to the child's actual participation in moderate-to-vigorous physical activities. Parents of children with CF frequently express concerns about their child's participation in vigorous play or sports, and teachers and sports coaches are often reluctant to allow participation in vigorous sports [37]. Illness and the burden of treatment may undermine and deter individuals with CF from exercising, leading to deconditioning and impaired exercise performance [13]. However, the perception of exercise by CF individuals and their families and carers as a therapy for CF has been reported to be more positive compared with other treatments, as exercise is focused on health promotion rather than management of their chronic illness [44].

Proposed physiological effects of exercise on mucociliary clearance in CF

Although CF is a multisystem disorder, lung disease remains the main cause of morbidity and mortality. Abnormalities in airway surface liquid and mucociliary clearance lead to recurrent infection, inflammation and airway obstruction. Exercise is thought to enhance mucociliary clearance by a number of physiological pathways, and this potential positive effect may provide further justification for the inclusion of exercise in a CF therapeutic regimen.

Airflow effects

An increase in ventilation and the generation of a peak expiratory flow bias [45] during exercise may facilitate the movement of mucus from the periphery of the lung to the oropharynx [46]. There is also potential for shear forces, combined with body movement during exercise, to reduce mucus viscoelasticity and facilitate enhanced mucociliary clearance [47].

Ion transport effects

Exercise training has been shown to improve fluid balance and retention of serum electrolytes in healthy individuals [18,48,49]. This may be a result of plasma volume expansion, which is characteristic of exercise, but may also be due to a direct effect on ion regulation in the sweat glands themselves [18]. Both maximal and submaximal bouts of exercise have the potential to decrease reabsorptive ion transport, and the level to which this is reduced may depend on the level of exercise intensity [49].

Evidence for the therapeutic effects of exercise in CF

The specific therapeutic effects of exercise in CF continue to be investigated. Both children and adults with CF have been shown to have the ability to increase exercise capacity with exercise training, regardless of disease severity [12,50–53].

An association between aerobic capacity and survival in CF was first reported in 1992, with the demonstration of a significant correlation between aerobic fitness (VO_{2peak}) and 8-year survival (which remained intact after adjustment for other predictor variables such as age, sex, lung function, nutritional status and bacterial colonization) [54]. An association between changes in exercise capacity measured by VO_{2peak} and survival has also been reported in a study of 28 children with CF between 8 and 17 years of age [8]. It is therefore suggested that VO_{2peak} could be used as an independent predictor of survival, but as yet there are no longitudinal data to support this hypothesis.

Regular exercise also has the potential both in the short [40,50,55] and long term [11,12,41] to slow the annual rate of decline in lung function [12,50–53].

Exercise ability may also be an important determinant of quality of life in CF [56]. An association between higher exercise capacity and better quality of life was reported in a study of a small group of children and adolescents with CF [56]. Exercise training in the out patient setting has been shown to result in benefits in quality of life for children, which was maintained at 2-year follow-up [53]. Improved body image following an exercise training program may also improve the perception of quality of life [57].

Inadequate bone mineral accrual during growth and accelerated loss of bone mineralization during childhood have important consequences in adult CF patients. Bone mineral density (BMD) has been shown to be lower in CF patients (age 6–49 years), with normal anthropometric status at all ages, than in the healthy population [58]. Exercise has been shown to maintain or increase BMD in non-CF populations [59], and a correlation between

activity levels and BMD in adolescents and adults with CF has been reported [60,61]. A strong correlation has been demonstrated between the duration and intensity of daily physical activity and BMD in older adolescents and adults with CF, measured using portable activity monitors [62]. However, to date, there has been no controlled interventional trial of the effects of exercise on bone mineral accrual [59,63] and there is still little evidence for the direct therapeutic effects of exercise on BMD in CF. It is generally accepted, however, that increases in exercise levels in children are likely to improve the potential to maximize peak bone mass, thereby reducing future risk of low BMD [59] and its consequences.

The incidence of CFRD is reported as being 2% in children, 19% in adolescents and 40–50% in adults [64]. The reasons for the development of CFRD are mainly attributed to insulin deficiency and, based on the available data, insulin is the only recommended treatment [65]. Current opinions surrounding the benefits of exercise for CFRD are predominantly based on clinical reasoning. A recent systematic review investigated the effects of habitual activity versus structured exercise training (aerobic training, resistance training or a combination of both) in non-CF patients with Type 2 diabetes. A greater reduction in glycosylated hemoglobin levels was reported in the group who undertook the structured exercise training [19]. In the USA, a recent position statement has stated that individuals with CFRD should undertake regular aerobic exercise [65]. However, further research is required to fully establish the physiological effects of exercise on CFRD specifically.

The role of exercise in CF therapeutic routines

Historically, airway clearance techniques were the mainstay of physiotherapy treatment, and exercise was considered 'harmful' [2]. In the last three decades, however, exercise has become a focus of interest in the management of CF.

Research investigating the effects of exercise in CF began in the 1970s with the studies by Godfrey and Mearns, who investigated the physiological responses of individuals with CF to exercise [6]. Early studies showed that exercise training programs and exercise could be used to improve ventilation and help clear respiratory mucus [66]. The safety of exercise in CF was first documented in the early 1980s [67]. Exercise now plays an integral role in the physiotherapy treatment of individuals with CF, and one of the greatest developments in physiotherapy for CF is that exercise is now seen as 'medicine' [18] and for some individuals is established as normal part of life rather than an increase in treatment burden [68].

Early diagnosis, in particular, the introduction of newborn screening (2007 in the UK) and emerging new therapies are resulting in a changing cohort of pediatric CF patients. Early intervention, both for prophylactic purposes and for the treatment of infection, aims to prevent the onset and progression of the disease process. Physiotherapy management of these infants, particularly those who are 'asymptomatic', has needed to adapt to a more dynamic 'treatment' approach [69]. In some centers, the focus of physiotherapy treatment in the asymptomatic infant and toddler is now focused on daily structured physical activity and exercise, with the addition of an airway clearance component when required [70]. This treatment approach begins from the time of diagnosis and is in contrast to the historical formal prescription of twice-daily postural drainage and percussion. Physiotherapy regimens for CF should be individualized and incorporate a variety of components, which change over time depending on age and clinical status.

Incorporating exercise into the CF physiotherapy routine

It has been suggested that exercise alone can be used as an airway clearance technique; however, the evidence to support this is limited [66]. Traditionally, it has been suggested that exercise should be complimentary and not exclusive to airway clearance, but these suggestions are based on data from adult studies in the early 1990s [71,72]. A systematic review has also concluded that the addition of exercise to chest physiotherapy significantly improves lung function compared with chest physiotherapy alone [63]. Extrapolating these suggestions to the 'modern' pediatric CF cohort of patients must be carefully considered, as appropriate and effective exercise training alone may indeed prove sufficient for some CF individuals.

Risks

The risks associated with exercise in CF remain a concern to some clinicians and individuals involved in CF care. The incidence of exercise-related serious adverse events was less than 1% in a survey of German CF centers [73]. It has been reported that clinically significant exercise induced desaturation in children with CF (defined as a fall in oxygen saturation during exercise of >4% from baseline) [74] may lead to a reduction in exercise capacity [75]. A recent retrospective review of 75 adult CF patients exercise test data reported that 23% of patients demonstrated a drop in oxygen saturation below 90% during maximal exercise, which is defined as exercise induced hypoxemia [76]. It is essential that potential risks [30] to CF individuals are recognized and identified using appropriate and timely exercise testing to allow safe and effective exercise training to be undertaken.

Burden of 'treatment'

Despite the modern ongoing transition of exercise as a normal part of life rather than as a medical intervention, it is important to remember that for many individuals with CF, the daily treatment-related burden remains high. A survey in the USA reported that adults with CF spend a mean of 108 min per day on a wide range of CF therapies, including taking medications (50 min), undertaking airway clearance physiotherapy (29 min) and exercise (29 min), regardless of age or disease severity [77]. Self-reported adherence to exercise programs in adults with CF has been reported to be as low as 24% [78]. In addition, unique complications, which continue to emerge as longevity improves, make the burden of physiotherapy treatment for some individuals considerably greater [2].

Modern 'culture'

Both in health and disease, several barriers exist to participation in regular physical activity. In the pediatric population in particular, there is an ever-increasing amount of time spent watching television, using computers and gaming consoles [34]. Social factors that are known to influence willingness to participate in regular activity include social support, perception of competency, self-esteem, enjoyment of the activity and factors associated with the patient's behavior, which include patient motivation, choice and accessibility to facilities. In CF, the emphasis should be placed on how exercise can modulate the disease process and ways in which exercise can be performed and promoted [35]. Minimizing the perceived barriers to exercise in CF and optimizing motivators is likely to influence the success of any program [79].

Parental involvement

Parents play a particularly important role in influencing a young child's physical activity patterns. Parents can influence children to become active through four mechanisms applied either individually or in combination [80,81]:

- Simple parental encouragement can reduce sedentary time and increase physical activity;
- Direct parental involvement and active family participation in physical activities;
- Parental facilitation by providing appropriate equipment, access to programs and facilities;
- The role model offered by an active parent through participation in exercise.

Parents of children with CF perceive fewer benefits of exercise and greater barriers to activity than parents of healthy children, more so in girls than boys [82]. It has also been reported that less than half of the parents of children with CF knew that exercise performance was related to long-term prognosis or that exercise could be beneficial for even the most severely affected child with CF [82]. With the more recent emphasis on inclusion of exercise in therapeutic regimens, one hopes that both families and clinicians are now somewhat better informed.

Education through the ages

When children are young, their parents and carers play a vital role in establishing lifestyle. It is therefore very important to give effective education on exercise from the time of diagnosis so that regular physical activity is incorporated as the norm [70]. Age-appropriate education of children from an early age is also essential to facilitate adherence to exercise throughout childhood, adolescence and adulthood. The principles of exercise training using the FITT principle of frequency, intensity, time and type should be taught and emphasized at all stages and during all interactions in order to facilitate effective and therapeutic exercise participation. It must be remembered, however, that effective interventions are generally those that educate as well as facilitate physical activity by providing opportunities and supportive environments at school, at home and in the community [32]. It is well known that education alone is not sufficient to change behavior and to sustain these behaviors [32].

Alternative options

Clinicians also need to take some responsibility for facilitating participation in exercise and encouraging newer models of care that include involvement in age-appropriate activities alongside their healthy peers. Organizing membership to gym facilities is an area of current interest and may help to encourage adherence to exercise programs' particularly in the pediatric population where gym membership is often seen as a benefit rather than a burden. The evidence to demonstrate the benefits of these different models of care is lacking to date. Important issues such as cross-infection and financial burden must be considered carefully, and further research is required to establish the viability of such programs [44].

Seasonality has been shown to impact the amount of time spent in undertaking habitual activity [38]. It is therefore essential that clinicians recognize this and tailor individual exercise programs to reflect and facilitate the recommended exercise guidelines throughout the year. The type of activities that are recommended should also take into account individual preferences and enjoyment levels. It is essential that alternative activities are encouraged and facilitated, if the traditional forms of gym-based exercise or team-based sports are disliked.

Exercise programs using a gaming console have also received increased attention in the last decade and may offer the potential to meet some of the challenges associated with exercise adherence [83]. A recent Australian report examined the cardiovascular demands produced through the use of a well-known gaming console in comparison to treadmill or cycle ergometer exercise in adults with stable CF [83]. The results showed comparable changes in physiological measurements, and individuals reported greater enjoyment when using the gaming console [83]. The limitations of this study include the fact that measurements were based on one short session of each exercise, and there may have been a novelty effect as participants reported little previous experience using these devices. With the increased usage of activity-based gaming consoles, it is important that 'appropriate' games in terms of intensity in particular are advised and that these interventions should not take the place of more traditional exercise on a regular basis. However, it is well known that enjoyment and perceived competence are important factors to improve adherence, and the use of a gaming console in an appropriate way may be beneficial, although so far there is little evidence to support this.

Ongoing challenges & unmet needs

There are a number of ongoing challenges regarding the incorporation of exercise into a CF therapeutic routine. These challenges are described in the following subsections.

Exercise testing & training guidelines

Exercise testing is underutilized in the CF population [84] and, as a result, individualized and tailored exercise training remains inadequate, despite the ever-increasing evidence base to support its use. A recent survey has reported that only 15.6% of

exercise programs are tailored to the individual [84]. It is essential that annual exercise testing (as a minimum) is undertaken to facilitate appropriate, individualized, safe and effective training programs, and to allow longitudinal monitoring of disease progression.

Management of all individuals with CF should include assessment of fitness, education about the benefits of exercise, exercise advice, monitoring of adherence to exercise and, where appropriate, introduction of strategies to maintain or improve exercise levels regardless of disease severity [65]. Traditionally, exercise-training programs have focused on aerobic activities but as the evidence base increases for the value of anaerobic, strength and interval-type training [51,85,86], exercise programs can be made more varied and enjoyable.

In mild-to-moderate CF lung disease, the current guidelines for physical activity for healthy children and adults are applicable in CF and have been recommended as the basis for exercise advice in CF [65]. With increasing disease severity, a more considered approach to exercise programs is required, incorporating more interval-type training with frequent re-evaluation. Historically, exercise-training regimens for children have been extrapolated from the recommendations for adults [31]. Recently published exercise training guidelines assist CF patients and health professionals to tailor exercise regimes in an appropriate and effective manner to ensure an exercise training effect for all individuals with CF [30].

Continuing lack of long-term controlled intervention studies

Early exercise intervention studies (home- and hospital-based swimming, cycling and running training programs) reported very promising results [87–89]. The lack of randomized control groups means that these studies fail to account for the changes over time that occur in CF patients as a result of the disease process itself [90]. It is essential that future interventional studies that incorporate controls are long term and take into account the natural progression of the disease in order to establish the benefits of exercise training in the CF population and, in particular, the potential effects on long-term survival.

Expert commentary

Exercise is now seen as an important part of the management of individuals with CF. However, exercise training and testing practices vary considerably both in the UK and internationally. Although the specific therapeutic effects of exercise in CF and the judgments of the benefits of exercise on long-term outcomes in CF are still under investigation, it is reasonable to suggest that exercise has the potential to have a positive effect on physiological parameters and outcome. However, in order for exercise to be routinely seen as 'medicine' for CF, an increase in knowledge, resources and clinical approach is necessary in many centers. It is essential that effective daily exercise and physical activity are established as a routine part of life for all CF individuals from the time of diagnosis. Active facilitation by parents, carers and medical teams is required to ensure that the incorporation of physical activity and exercise continues throughout the lifespan of a CF individual. There are a number of barriers faced by both CF individuals and health professionals when trying to incorporate effective exercise regimes. It is essential that these barriers are taken into consideration and attempts are made to provide alternative and individualized options.

Five-year view

It is difficult to speculate how the field of exercise in CF will evolve over the next 5 years. If exercise continues to be viewed as 'medicine' for CF, it might be anticipated that exercise will be seen as a vital component not only as a therapeutic treatment but also as a prognostic indicator. In order for this to occur, it is essential that a number of practices become routine in CF centers. The following subsections describe these practices.

Formal exercise testing as part of the annual review process

VO_{2peak} testing is the gold-standard exercise test and is viewed as the most precise method of exercise testing [84]. However, it has been reported that most UK centers do not have the resources to measure VO_{2peak} [84]. Although there are a number of field exercise tests available for use in the CF population, many of these tests have significant limitations, particularly in individuals with mild-to-moderate disease severity and in the pediatric population. In an ideal world, annual VO_{2peak} testing for all individuals older than 6 years of age should be undertaken, but this is probably unrealistic, although the introduction of new, more portable gas analysis equipment may facilitate this in centers where laboratory facilities are currently unavailable. Therefore, it is essential that a more appropriate and effective field-based test is developed to take into account the emerging 'fitter' cohort of CF patients. This would allow effective exercise testing that would provide clinically relevant information in the absence of the gold-standard test.

The establishment of a lifestyle incorporating fitness & exercise by newborn screened CF infants

As the newer cohort of newborn screening infants move through childhood and into adulthood, it is anticipated that a positive attitude to exercise will be well established. With appropriate interventions when these children are very young, a behavioral change may occur, so that regular exercise and physical activity is a routine part of daily life.

Increased knowledge of exercise training

Ongoing education of healthcare providers has been identified as an important factor in implementing exercise in clinical practice [91]. It is now well documented that exercise training and testing is underutilized despite standard recommendations and guidelines [84]. It is important that clinicians and medical teams further develop their knowledge of exercise testing and training, as without doing so the establishment of exercise as a therapeutic routine for CF may prove difficult. It is also essential to recognize that simple communication may not be enough, and concerted

action may be needed to facilitate and create environments and conditions that make it easier for individuals with CF to be active both in the hospital and at home.

It is clear that a number of factors need to be taken into account when considering the implementation of a therapeutic exercise regimen for CF individuals. It should always be recognized that therapies are only effective if they are adhered to. Introduction of a new component, although clinically worthwhile, may not be adhered to, particularly where the treatment burden is already high. The perceived physiotherapy-related treatment burden has been reported to depend on how an individual views their treatment in the context of their other daily responsibilities and demands [77]. The importance of placing emphasis on exercise from an early age is therefore essential to facilitate a lifestyle that incorporates exercise and physical activity throughout childhood and into the adult years.

Conclusion

In conclusion, evidence suggests that exercise is safe, beneficial and has the potential to have a significant effect on outcome for individuals with CF. However, the current practice of exercise testing and exercise prescription in CF centers is highly variable. In order for exercise to become an integral part of the therapeutic clinical management of individuals with CF, it is important that all those involved in CF care view exercise as a 'medicine' for CF. Exercise should be tailored and monitored for each individual using objective outcomes. In order to do this, increased knowledge, resources and a change in clinical approach are necessary.

Key issues

- Exercise is an essential component in the management of individuals with cystic fibrosis (CF).
- There are a number of factors that may contribute to a reduction in exercise capacity in CF, which include abnormal lung function, nutritional status, potential muscle dysfunction, genotype, level of habitual activity, gender and psychosocial influences.
- The specific therapeutic effects of exercise in CF are still under investigation, but a correlation between aerobic fitness and survival, a reduction in the rate of decline in lung function and improvements in quality of life scores have been reported.
- The potential benefits of exercise on bone mineral density and CF-related diabetes need to be established with further research.
- The role of exercise in the CF therapeutic routine has changed considerably since the 1980s, and exercise is now a mainstay component in the daily routine for many individuals with CF, particularly those diagnosed by newborn screening.
- There are many barriers to the incorporation of exercise into a CF therapeutic routine, but these can be reduced by encouraging parental involvement, providing effective age-appropriate education and by facilitating involvement in exercise.
- Although judgments of the benefits of exercise on long-term outcomes in CF are currently extrapolated from relatively short-term clinical trials, it is reasonable to suggest that exercise has the potential to have a positive effect on outcome.
- It is widely accepted that exercise is safe and beneficial for all individuals with CF, but a change in clinical approach is essential in order for an improvement in the current practice of exercise testing and training in CF centers to occur.

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• of interest
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Medscape EDUCATION Exercise as part of a cystic fibrosis therapeutic routine

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Activity Evaluation
Where 1 is strongly disagree and 5 is strongly agree

	1	2	3	4	5
1. The activity supported the learning objectives.					
2. The material was organized clearly for learning to occur.					
3. The content learned from this activity will impact my practice.					
4. The activity was presented objectively and free of commercial bias.					

1. You are seeing an 8-year-old boy with cystic fibrosis (CF), and his parents are concerned that he can only walk short distances before losing his breath.
What should you consider regarding the factors that contribute to a reduction in exercise capacity in CF?

- ☐ **A** CT findings do not correlate with exercise limitations
- ☐ **B** CO_2 retention during exercise is associated with a lower rate of forced expiratory volume in 1 second (FEV_1) decline
- ☐ **C** Patients with CF can expend up to 30% more energy at rest compared with individuals without CF
- ☐ **D** Girls are generally more physically active than boys among children with CF

2. What can you tell this family regarding the therapeutic effects of exercise in CF?

- ☐ **A** Only mild-to-moderate CF responds to exercise
- ☐ **B** There is a correlation between aerobic fitness and survival
- ☐ **C** Randomized trials have found that exercise promotes higher bone mineral density among patients with CF
- ☐ **D** Exercise still has no role in physiotherapy for CF

3. What else should you consider before prescribing an exercise routine for this patient?

- ☐ **A** There is strong evidence that exercise alone is the best means to clear an airway
- ☐ **B** Hypoxemia during exercise occurs in less than 2% of adults with CF
- ☐ **C** Adherence to exercise programs among adults with CF is less than 25%
- ☐ **D** Most parents are fully aware of the benefits of exercise for children with CF

4. What should you tell these parents regarding exercise evaluation and therapy for their son?

- ☐ **A** He should undergo semi-annual treadmill evaluations to measure VO_{2peak}
- ☐ **B** Their participation can reduce his sedentary time and encourage physical activity
- ☐ **C** Exercise therapy should be reserved for children at age 10 and older
- ☐ **D** Exercise should not be viewed as "medicine" for CF