FONTYS UNIVERSITY OF APPLIED SCIENCES
DEPARTMENT OF PHYSIOTHERAPY

The effect of an aerobic exercise program on pulmonary function for children with cystic fibrosis.

What is the effect of an aerobic exercise program on pulmonary function for children and adolescents suffering from cystic fibrosis? Measured in forced vital capacity and forced expiratory volume in one second.

- *A Literature Review*

Martine Solberg Olsen [a]*

[a] *Department of Physiotherapy, English Stream 4A, Fontys University of Applied Sciences, Eindhoven, the Netherlands*
** Corresponding author. E-mail address: solmartine@hotmail.com*

General information	
Name of the project	What is the effect of an aerobic exercise program on pulmonary function for children and adolescents suffering from cystic fibrosis? Measured in forced vital capacity and forced expiratory volume in one second.
Student information	Student: Martine Solberg Olsen. Student number: 2147578 E-mail: solmartine@hotmail.com Telephone: (0047) 91857351 ES4A, Physiotherapy English Stream.
Responsible parties	Fontys University of Applied Sciences Physiotherapy Department, English Stream. Ds. Th. Fliednerstraat 2 5631 BN Eindhoven
Thesis supervisor	Marc Schmitz E-mail: m.schmitz@fontys.nl Telephone: 06 34876387
Thesis coordinator	Chris Burtin E-mail: c.burtin@fontys.nl Telephone: 08 85089866
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Preface

Writing a bachelor thesis is one of the hardest things that I have ever had to do, but it is however, one of the greatest learning experiences that I have been through. It has taken me from thinking like a student, to a professional within my field. Writing a thesis requires patience, structure, an open mind, as well as the ability to fail repeatedly and yet not give up. I consider the process of writing a bachelor thesis as an ongoing learning experience, in which you will not understand everything until after you are done. Hard work, dedication and a lot of inner motivation is some of the key terms that comes to mind upon finishing the thesis; these terms are also qualities that a good physical therapist should have.

Upon being assigned the topic of children with cystic fibrosis, I met this with a lot of hesitation and frustration. I did not have any previous experience with cystic fibrosis. I had never met a patient who suffered from cystic fibrosis. However, as I progressed with my research, I realized that I was presented with a great opportunity to become familiar with a new topic. I realized that I was writing a thesis on a topic which I initially knew nothing about, so I researched and developed knowledge to become somewhat of an expert on it, or at least the response of exercise on the pulmonary function.

The challenging thing about cystic fibrosis is that the children do not deserve this horrible disease that they were born with. These children are dealt a bad hand from birth on, and this gave me the motivation to improve my knowledge, so that I would hopefully discover something which could improve the life of these children.

The first section of this project includes the abstract, which is a summary of my research. includes a description of the problem, the steps that I took to encounter the problem, and the outcome of the research, presented as results. In my discussion part, I am debating, and discussing the findings, as well as the limitations within the studies which I researched, and the limitations of my own research. Recommendations for future research and the conclusion for this research can be found at the very end of this paper. Attached is an overview of the literature which was used to conduct the research, assessment of the quality of the included studies.

With some help from fellow students and thesis advisor, reviewing my paper and helping me find my way through this process. I can finally present to you my bachelor thesis; on the effect of an aerobic training program for children and adolescents suffering from cystic fibrosis. The effect of the intervention is measured on pulmonary function, by measurements of forced vital capacity, and forced expiratory volume in one second.

Martine Solberg Olsen, May, 2013.

Student at Fontys University of Applied Sciences. Graduation class of 2013.

Abstract

Introduction: Cystic fibrosis is a life-limiting, inherited multi-organ disorder affecting Caucasians in the world today. The respiratory system is most often involved, which results in a limited life-span and decreased quality of life. Exercise is an important part of the therapy for cystic fibrosis; therefore the aim of this research was to determine the effect of aerobic exercise therapy on pulmonary function in children and adolescents suffering from cystic fibrosis.

Method: An electronic search was performed in Pub Med, The Cochrane Library and Physiotherapy Evidence Database. The databases were consulted using the search terms; cystic fibrosis, aerobic exercise program and pulmonary function with a combination and variation of the search terms. Included in this research were studies with children and adolescents with a confirmed diagnosis of cystic fibrosis, younger than 20 years old; participating in an aerobic exercise program, for a minimum of 12 days. Only studies which reported outcome measures on pulmonary function were included.

Results: The electronic search resulted in 10 studies which met the set inclusion and exclusion criteria. The majority of the included studies reported significant findings in the change of pulmonary function. There is moderate and limited evidence to support that an aerobic exercise program is effective for improvements in pulmonary function. All of the included studies resulted in improvements, or delayed the progression of the disease and its negative effect on the pulmonary function.

Conclusion: An aerobic exercise program should remain an important part of the therapy program for children suffering from cystic fibrosis, because evidence shows that an aerobic exercise program does have a positive effect on pulmonary function for children suffering from cystic fibrosis.

Key Words: Cystic fibrosis, children, adolescents, aerobic exercise therapy, pulmonary function.

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Introduction

Cystic fibrosis (CF) is one of the most common life-limiting, inherited disorders affecting Caucasians in the world today. In 2011 it was estimated that the incidence of CF in the world was 80 000 affected children and adolescents.[1] The disease is due to a defective gene, and the protein of this particular gene.[2] The defect gene causes problems in several organs. The main problems occur in the respiratory system, with irreversible loss of lung function, often with involvement of the digestive system.[3-5] Respiratory disease has been responsible for the highest mortality rate in the younger CF population, this is mainly due to respiratory infections.[2]

Since there is no curative treatment for this disorder, the early detection of the disorder is crucial for the development of the illness, and the proper treatment may delay or prevent irreversible damage.[6] For this reason, it is important for the first line of health care workers to be familiar with the symptoms, and the treatment of the disorder.[6]

In the past, children suffering from CF were not expected to live until school-age, but nowadays CF patients can live until the age of 30-40.[1] This increased life expectancy is due to developments which have been made within the medical field. These developments includes the newborn screening, early detection of the symptoms, which leads to an early diagnosis of the disorder, as well as the improvements in the pharmacological management.[7]

The current treatment for CF is mainly aimed towards preventing the patients from becoming inactive, and unable to carry out activities of daily life. This is done by actively including the patients in supervised exercise programs, and by managing symptoms with pharmacological therapy.[7, 8] The physical treatment is also focused on symptom management with mucociliary clearance, by passive chest therapy and breathing therapy. Prevention of physical deformities, education and instructions about the disease is also an important part of the management of CF.[4, 9]

Adopting a more active treatment approach for CF patients leads to; improvements of the quality of life, decrease the use of medications, and increase participation in sports and activities.[10] The active approach also decreases the progression of the disease and results in less frequent respiratory infections.[11] The active approach is better for the development, function and general wellbeing of the children, but also a treatment option which is not very costly for society. It is also safer and less aggressive than pharmacological therapy.[1, 11]

Exercise is beneficial and important for CF patients, and the results are promising when following a supervised exercise program.[12] Current exercise programs are focused on aerobic exercise, anaerobic exercise, strength training, breathing techniques, or a combination of these, with a variety in the supervision and intensity.[13]

Aerobic exercise was decided on as the focus of this study, because it is considered to be the most beneficial, and safest exercise intervention for children and adolescents suffering from CF.[4, 14, 15]

For individuals who suffer from CF, the pulmonary function decline is estimated at an annual rate of 2-3%.[16] Recently it has been indicated that CF children with a high aerobic fitness, experience slower deterioration in lung function and greater survival rates than those with lower fitness levels.[9, 12, 17] A study conducted by de Jong et al,[18] showed that there is in fact a comparable correlation between the aerobic exercise capacity of individuals with CF, and the pulmonary function.

It has been suggested that a limitation in the exercise capacity is directly related to the pulmonary function.[19, 20] The deterioration of the pulmonary function still remains one of the main problems of CF. Physical fitness is affected by lung function and the severity of the disease, increasing the exercise capacity could be a key in preventing these deteriorations.[18]

This provides a good basis for further investigation into the effect of aerobic exercises on pulmonary function. There are several objective measurements of pulmonary function; amongst these are the forced expiration volume in 1 second (FEV_1) and forced volume capacity (FVC). The measurements of FEV_1 and FVC as percentage of predicted outcome for height and age are considered to be good indicators for the pulmonary function.[21] This is measured with a standardized spirometer.[22] Higher values represent better pulmonary function.[17, 23, 24]

Research on the topic of CF is evolving due to the adaption of a more active therapy approach. Research which establishes evidence to include exercise as an essential part of the treatment program for children suffering from CF is much needed. This is to maximize adherence to prescribed programs, and to reduce the pharmacological therapy.[10] The effect of an aerobic exercise program on pulmonary function for children with CF is still inconclusive.[16, 25]

"What is the effect of aerobic exercise therapy on pulmonary function index measured in forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC), in children and adolescents suffering from cystic fibrosis"?

Method

Databases and search terms

An electronic search was performed in Pub Med, The Cochrane Library and Physiotherapy Evidence Database (PEDro). The databases were consulted using the search term; "cystic fibrosis" with a combination of the search terms, which can be found in (table 1).

Table 1, search terms.

	And/or	*And/or*	*And/or*
Cystic Fibrosis	Children	Exercise therapy	Pulmonary function
	Adolescents	Aerobic exercise	
		Aerobic training	

Inclusion and exclusion criteria

Only Randomized Controlled Trials (RCT) or Clinical Trials (CT) was included in this review, the inclusion and exclusion criteria for the studies can be found in (table 2). This search was not limited by the date of the publication.

Table 2, inclusion/exclusion criteria

Inclusion Criteria;	**Exclusion Criteria;**
Study population of children or adolescents diagnosed with cystic fibrosis according to the golden standard,[26] independent of the severity of the disorder.	Subjects with additional co-morbidities which are not related to cystic fibrosis.
An aerobic exercise intervention, including the full program description.	Studies which included exercise and a co-intervention of additional medications other than the current prescription.
Reported outcome measures on pulmonary index function as FEV_1 and/or FVC.	A study population of patients older than 20 years.
Only articles in which the full text is available in English.	Studies in which the exercise program lasted for less than 12 days.

FEV_1= Forced expiration volume in one second, FVC= Forced vital capacity.

Selection procedure

One researcher was responsible for the selection procedure, by screening all the titles which were the result of the initial search. The articles were excluded if they did not appear to have a correlation with the topic in question. If there were any doubts about an article based on the title, then a screen of the abstract followed. The articles which correlate with the topic, or if there were uncertainties, the full text was acquired, and screened. An investigation of the references was conducted, to search for other studies which might be of interest. If then, the article met the set inclusion and exclusion criteria, the article were included in this literature review. The selection procedure is represented in a flowchart, with the number of studies discovered for each section of the selection procedure. The flowchart of the selection procedure, with the identified number of studies can be found in (figure 1) of the results section.

Data extraction

After collecting the data from all of the included studies, the data was put in a table for analysis. The data extraction table can be found in the results section, with a description of the included studies and the reported outcome (table 4).

Quality assessment

To assess the methodological quality of the studies and for bias, the PEDro scale, were applied to all of the randomized controlled trials, and the clinical trials which met the set criteria. The items with a full description can be found in (appendix I). The overview of the methodological quality of the included studies can be found in (table 3) of the results section.

A best evidence synthesis, assessing the methodological quality of the findings was conducted to come to an overall conclusion based on the findings of the included studies. The result of the best evidence synthesis can be found for the outcome measure FVC in (appendix II in table 4), and FEV_1 in (appendix II in table 5). The full description of the best evidence synthesis, with the criteria for classification of the methodological quality can be found in the appendices (appendix III).

Results

The research was performed between April 5th, and April 9th of 2013, by one researcher. The electronic databases were consulted by applying a combination of search terms, as previously described in the method section.

The initial search of the databases resulted in 148 articles. First the search was limited to trials only, and the duplicates were removed. After a thorough screening of the title, abstract, language and the full text, 38 articles were retrieved for manual screening. After applying the inclusion and exclusion criteria, a total of 10 studies were included in this literature review. The majority of the excluded studies also included a study population of subjects older than 20 years old or there were no exercise program included. The search and selection procedure can be found in (figure 1). The search of the references of the included studies did not lead to the inclusion of additional articles.

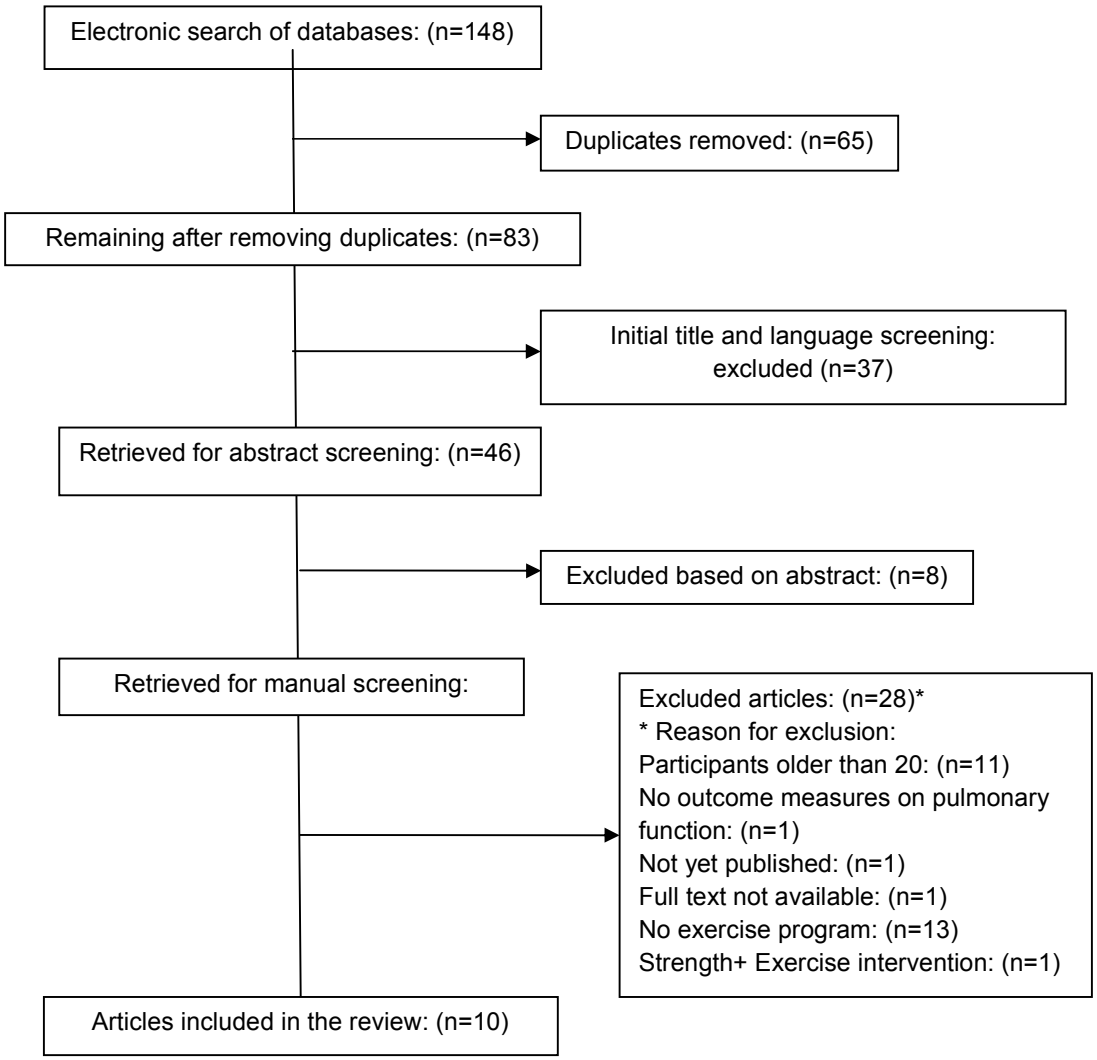


Figure 1. Flowchart, selection procedure. N= Number of studies.

Methodological quality assessment

Included in this study are three randomized controlled trials with a PEDro score above five (5/10). The scores of the clinical trials ranged from three to six (3/10-6/10). The result of the methodological quality assessment, according to the PEDro scale of the included studies can be found in (table 3).

A description of the items of the PEDro scale criteria can be found in (appendix I).

Table 3. Results of the methodological assessment.

	Eligibility	Randomized	Concealed allocation	Baseline comparability	Blinding of subjects	Blinding of therapist	Blinding of assessor	Outcome measurements	Intention to treat analysis	Between group comparisons	Point estimates and variability	Total score	Study design
Cerny, 1989.[27]	Y	Y	N	N	N	N	N	Y	N	Y	Y	4/10	CT
Gruber et al, 2008.[28]	Y	N	N	Y	N	N	Y	Y	Y	N	Y	5/10	CT
Gulmans et al, 1999.[29]	Y	N	N	N	N	N	N	Y	Y	N	Y	3/10	CT
Orenstein et al, 2004.[30]	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	7/10	RCT
Paranjape et al, 2012.[31]	Y	N	N	N	N	N	N	Y	N	Y	Y	4/10	CT
Selvadurai et al., 2002.[32]	Y	Y	Y	Y	N	N	N	N	N	Y	Y	5/10	RCT
Stanghelle et al, 1988.[33]	Y	N	N	Y	N	N	N	N	N	Y	Y	4/10	CT
Walker et al, 2000.[34]	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6/10	RCT
Zach et al, 1981.[35]	Y	N	N	N	N	N	Y	Y	Y	N	Y	4/10	CT
Zach et al, 1982.[36]	Y	N	N	Y	N	N	Y	Y	Y	N	Y	5/10	CT

Y= Yes, N=No, RCT=Randomized controlled trial, CT= Clinical trial.

Description of results

Of the 38 studies which were identified, 10 studies met the inclusion criteria; Cerny,[27] Gruber et al,[28] Gulmans et al,[29] Orenstein et al,[30] Paranjape et al,[31] Selvadurai et al,[32] Stanghelle et al,[33] Walker et al,[34] Zach et al,[35] Zach et al.[36] All of the included studies assessed the effect of an aerobic exercise program on children suffering from CF. All the included studies evaluated the effect of one or several therapy programs.

The baseline measurements and outcome measurement on pulmonary function, of a total of 471 subjects were included in this review. The age of the participants ranged from 2-20 years old and the duration of the studies ranged from 13 days to 36 months. The duration of the majority of the studies was six weeks or longer.

Table 4, Study characteristics						
Authors, year of publication	**Subjects, age range**	**Intervention, intensity**	**Study duration**	**Baseline measures***	**Outcome measures***	**Results reported by authors**
Cerny, 1989.[27]	N=9 Age 10-20.	15-20 minutes, 2 times per day. Cycle ergometer at 45-65% of the HRR.	13 days	FVC: 68% FEV_1: 45%	FVC: 80% P<0.01 FEV_1: 54% P<0.01	The FVC and FEV_1 improved significantly for the exercise group.
Gruber et al. 2008.[28]	N=286 Age 6-18.	45 minutes 5x/week. Aerobic exercises. Intensity: NR.	Mean of 1 to 1,5 months	FVC: 87,3% SD:8,6 FEV_1: 85,7% SD:21,1	FVC: 89,6% SD:16,6 P<0.05 FEV_1: 82,7%. SD:22,3 P<0 .05	There were significant gains in lung function parameters FEV_1 and FVC at the end of the rehabilitation course.
Gulmans et al. 1999.[29]	N=14 Age 10-16.	20 minutes. 5x/week. Cycle ergo meter at 70-80% of predicted $HR_{max.}$	6 months	FVC:75,8% SD:14,7 FEV_1: 58,1% SD:15,5	FVC:76,6% SD; 14,8 P=NS FEV_1: 59,2% SD:15,9 P=NS	No significant difference in FVC or FEV_1.
Orenstein et al. 2004.[30]	N=25 Age 8-18.	30 minutes 3x/week. Stair stepping at 70% of predicted $HR_{max.}$	12 months	FVC: NR FEV_1: 91,51% SD:18,34	FVC: NR FEV_1: 90.32% SD:17,92 P< 0.558	Decrease in the means of FEV_1 during the first 6 months, followed by an increase from 6 to 12 months, but these changes did not reach significance.
Paranjape et al. 2012.[31]	N=59 Age 6-16.	20-30 minutes 5x/week. At-home aerobic exercises of vigorous intensity.	2 months	FVC: NR FEV_1:100% SD:(52-132)	FVC: NR FEV_1:104% SD:(41-130) P< 0,50	Changes in FEV_1 were not statistically significant.
Selvadurai et al. 2002.[32]	N=22 Age 11-15.	30 minutes 5x/week. Treadmill or cycle ergometer at 70% peak HR.	Mean of 18 days	FVC: 70,7% SD:17,2 FEV_1; 56,8%. SD: 17.9.	FVC: 73,04% SD:4,62 P:NS FEV_1: 63,34% SD:7,76 P<0.05	Significant improvements in FEV_1. No significant change in FVC.
Stanghelle et al, 1988.[33]	N=6 Age 10-13,5	17 minutes 7x/week. Jumping on a trampoline at 70% of $HR_{max.}$	2 months	FVC:89% SD:(74-106) FEV_1; 83,66% SD: (45-113)	FVC: 90,5% SD:18 P<0.05 FEV_1; 82,17% SD:20 P:NS	FVC showed significant improvements. No significant improvement in FEV_1.

Walker et al, 2000.[34]	N=30 Age 7-19.	20 minutes min 3x/week. Optional aerobic exercises at 70-80% of predicted $HR_{max.}$	36 months.	FVC; 92,6% SD: 15,7. FEV_1: 89.2% SD: 19,5.	FVC:92,35% SD:2.81 P<0.02 FEV_1:87,74% SD:3,55 P<0.07	Significant values were discovered for FVC, insignificant findings for $FEV_{1.}$
Zach et al, 1981.[35]	N=10 Age 6-18.	1 hour of swimming. Intensity: NR	2 months	FVC: 88% SD; 15 FEV_1: 82% SD; 24	FVC:95% SD:15 P<0.05 FEV_1:90% SD:23 P<0.05	Significant improvements in FVC and $FEV_{1.}$
Zach et al, 1982.[36]	N=10 Age 2-16.	1 hour of swimming and diving once a day. +Jogging and hiking every day. Intensive programme.	17 days.	FVC: 88% SD:14 FEV_1: 70.6% SD:21	FVC: 93.8% SD:13 P<0.05 FEV_1: 79.2% SD:22 P<0.01	Significant improvements in FVC and $FEV_{1.}$

** = % of predicted value, FEV_1= Forced expiratory volume in one second, FVC= Forced vital capacity, SD = Standard deviation, N= Number of subjects, NR=Not reported, HRR= Peak exercise heart rate minus resting heart rate, HR_{max}= Heart rate maximum, x=Times per week, peakHR= Peak heart rate.*

Reported outcome on pulmonary function

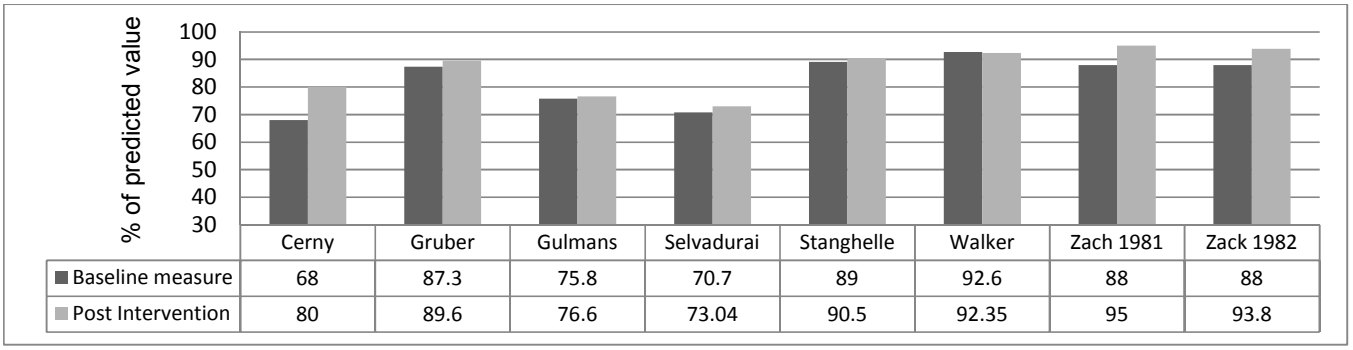
All of the included studies reported outcome of FEV_1 % of predicted outcome for height and age on pulmonary function, measured by a spirometer according to similar standards.[21]

Two of the studies, [30,31] did not report outcome on FVC percentage. The percentage of FVC at baseline, and measurements of the last day of exercise training can be found in (figure 2). The baseline measurements and the measurements of the last day of exercise training, reported as predicted percentage of FEV_1 can be found in found in (figure 3). The outcome measurements on pulmonary function are presented in percentage of the predicted value for age and height.[22] Significance was accepted at the P<0.05 level.

The mean baseline measurements for FVC of the included studies ranged from 68%, by Cerny et al,[27] to 92,6%, by Walker et al,[34] of predicted outcome. The mean change in percentage of FVC from baseline to post intervention ranged from the lowest at -0,25%,[34] change to 12%,[27] change in predicted FVC. Six of the included studies reported statistical significant improvements in the FVC.[27, 28, 33-36] Three studies reported statistical insignificant results on FVC.[29, 30, 32]

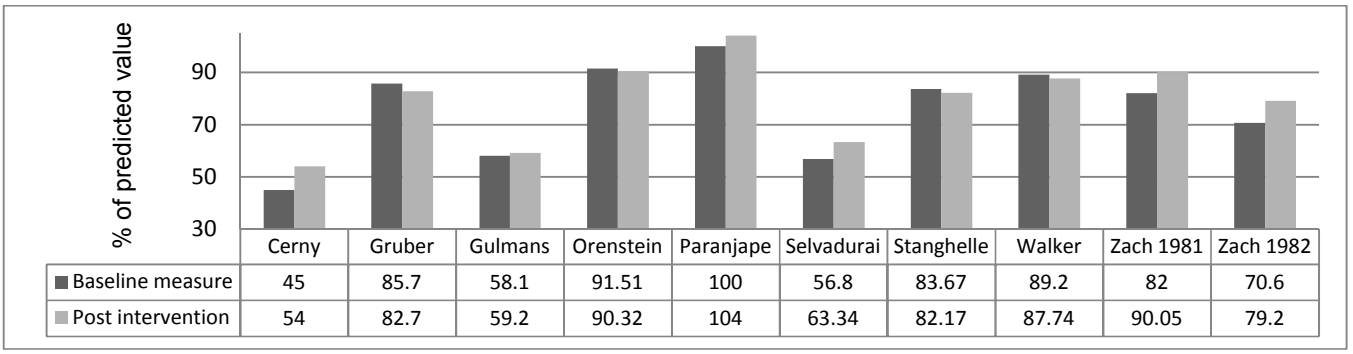
The mean of the baseline measurements for FEV_1 of the included studies ranged from 45%,[27] of predicted outcome to 100% of predicted outcome.[31] The mean in percentage from baseline to after the intervention ranged from the lowest at -3%,[28] change to 9%,[27] change in $FEV_{1.}$ Six of the included

studies reported statistical significant improvements in the pulmonary function measured by FEV_1.[27,28,32,34,35,36] Four studies reported statistical insignificant findings in the change of FEV_1, after the exercise program.[29,30,31,33]



	Cerny	Gruber	Gulmans	Selvadurai	Stanghelle	Walker	Zach 1981	Zack 1982
Baseline measure	68	87.3	75.8	70.7	89	92.6	88	88
Post Intervention	80	89.6	76.6	73.04	90.5	92.35	95	93.8

Figure 2, Forced vital capacity (FVC).



	Cerny	Gruber	Gulmans	Orenstein	Paranjape	Selvadurai	Stanghelle	Walker	Zach 1981	Zach 1982
Baseline measure	45	85.7	58.1	91.51	100	56.8	83.67	89.2	82	70.6
Post intervention	54	82.7	59.2	90.32	104	63.34	82.17	87.74	90.05	79.2

Figure 3, Forced expiration volume in one second. (FEV_1)

Exercise program description

Four of the exercise programs consisted of a choice of different aerobic exercise activities, such as running, swimming, cycling and soccer.[28, 31, 34] Three of the exercise programs used an ergometer bike, or treadmill, with the intensity progressed to 70-80% of predicted $HR_{max.}$[27, 29, 32] One of the studies included an exercise program consisting of a stair stepping machine,[30] one study used a trampoline,[33] and two studies used a swimming program as the intervention.[35, 36]

Discussion

The aim of this research was to determine the effect of an aerobic exercise program on pulmonary function, for children suffering from CF. The purpose of this research was to improve the treatment of patients with CF; which could eventually increase the life expectancy, and prevent declinations in pulmonary function. The results extracted from the included studies, establishes that an aerobic exercise program does in fact influence the pulmonary function. The majority of the studies included in this literature review, reported a positive outcome on pulmonary function after a period of an aerobic exercise program. The outcome was however not statistical significant in all of the included studies, but the findings present some insight into the increased survival rate, due to the measurements on pulmonary function.[37] Five of the included studies reported statistical significant findings in the change of FVC and FEV_1 as percentage of predicted value for age and height, after a period of an aerobic exercise program.[27, 28, 34-36]

The studies included in this review had similarities and differences in their study designs in regards to the number of included subjects, and the inclusion criteria for the subjects. The exercise programs also varied in intensity, duration, and choice of equipment, instructions and supervision. All of these factors could contribute to the variety of the outcome on pulmonary function which was discovered in this study. The similarities and differences of the included studies will be discussed, and the possible reasons for the variety in the outcome will be accounted for.

Interpretation of the results

The intensity and supervision of the included studies varied from a rigorous routine with several training sessions per day, which were supervised by specialized physical therapist, to in-home exercise routine which only encouraged the subjects to exercise. One study explored the effect of a very intense and rigid exercise program, which involved several swimming, jogging and activity sessions per day.[36] This intensive exercise routine resulted in statistical significant outcomes on pulmonary function. While other studies let the children decide the intensity themselves,[31, 34] which could be one of the reasons for the statistical insignificant findings on pulmonary function.

Three of the studies included an exercise program with a wide variety of exercises, one of these reported statistical significant effects on the pulmonary function.[28] One resulted in statistical insignificant results,[31] and one detected statistical significant results on FVC only.[34] The statistical significant findings are thought to be attributed to higher adherence to the program, motivation for performance and perceived competence of the children, which is consistent with the literature on the topic of adherence for children with chronic disorders.[15, 38] The free choice of exercise was also meant to make the therapy more enjoyable and easier to implement into the subjects daily routine, which could make it more feasible to commit to over a long period of time.[15] Four of the included studies are

considered relevant for clinical practice, because they assessed the effect of a home exercise program which is easy for the patients to implement into their daily life.[28, 31, 34, 36]

According to Paranjape et al,[31] a small sample size could be the reason for the lack of detection in significant changes. However, six of the included studies with a small sample size, (less than 60 subjects) reported significant changes in one or both of the parameters of pulmonary function.[32-36, 39] Only three of the included studies with a small sample size reported insignificant results.[29-31] In this study it is therefore not possible to state with absolute confidence that a small sample size can account for the insignificant findings. There are however indications which can lead us to believe that a larger sample size might detect statistical significant findings, because Gruber et al,[28] included in their study a large sample size (286 subject) which resulted in statistical significant findings.

The studies included subjects with a varying levels of impairments in the pulmonary function; Gulmans et al,[29] only included subjects with an FEV_1 lower than 90% of predicted values for height and age, this resulted in insignificant findings on pulmonary function. Walker et al,[34] included mainly subjects with mild and moderate impairments in their pulmonary function, which only resulted in significant findings on FVC. Paranjape et al,[31] included subjects with mild impairments, (median FEV_1 of more than 90% of predicted value), did not discover significant findings in pulmonary function. The variation in the inclusion criteria could affect the outcome, because in the study by Stanghelle et al,[33] the two most affected participants in the study, showed a more marked improvement on pulmonary function, compared to those with less severe impairments in pulmonary function. These findings indicate that subjects with severe impairments of pulmonary function, benefits greatly from an exercise program. There was however no direct correlation between the initial impairment in pulmonary function of the subjects, and the effect of an aerobic exercise program.

Orenstein et al,[30] excluded subjects which were already exercising on a regular basis. By only including subjects who were not already exercising on a regular basis, it could mean that they were not motivated to exercise, which could be an explanation for the insignificant findings. Zach et al,[35, 36] only included children with stable clinical conditions in both of their studies, this could be one reason for the significant findings in both of the studies.

Stanghelle et al,[33] included subjects which also suffered from pancreatic achylia, while Gulmans et al,[29] excluded subjects which had other co-morbidities, or CF related symptoms. Neither of these studies resulted in significant changes on pulmonary function. This leads the author to believe that the inclusion of subjects with or without CF related symptoms cannot account for the insignificant findings.

Several of the included studies chose for the participants to continue with the pharmacological treatment, which also included corticosteroids. Nikolaizik et al,[40] demonstrated in their study that inhaled corticosteroids improved FEV_1. Two of the studies [30,34] instructed the patients to continue with their normal therapy regimen, which consisted of corticosteroids. Neither of these studies produced significant results on either parameter of pulmonary function. Therefore it is not possible to establish the role of the corticosteroids on pulmonary function in this research.

In addition to an aerobic exercise program, the study conducted by Cerny et al,[27] included daily bronchial drainage treatment, this could account for the improvements in pulmonary function. A previous study conducted by Desmond et al,[41] established that one single bronchial drainage treatment per day, produced significant improvements on pulmonary function.

The studies included in this review included an exercise program which lasted from 13 days to 3 years. The short duration of some of the included studies, could also have been one of the reasons for the statistical insignificant outcome. This is because it has been established that permanent changes in pulmonary function is only seen after 12 months of intervention in children with CF.[16, 42] However, Walker et al,[34] debated that three weeks of exercise intervention should be sufficient to produce changes on pulmonary function. There was no direct correlation established for the duration of the exercise program with regards to the outcome. This is also believed to be attributed to the poor adherence to treatment which is seen in children and adolescents suffering from chronic disorders, because of the problems and complications accompanying CF.[43]

Clinical relevance

The clinical relevance of the study with the intensive exercise program,[36] for the purpose of this study can be debated, because it is not feasible for children with CF, and their families to maintain such a high level of activity on a daily basis. It is however beneficial to understand the effect of maintaining a certain intensity and high levels of activity.

There could not be detected any direct correlation with regards to setting, exercise frequency, choice of equipment, instructions and supervision, or the differences in the age of the subjects in the included studies. It was however noted that the studies in which the exercise programs included a swimming component produced significant results on pulmonary function.[28, 35, 36] A swimming program also promotes mucus clearance.

All of the included studies in which the training session lasted for more than 45 minutes per day, resulted in a significant outcome on both parameters for pulmonary function.[27, 28, 35, 36] The studies, in which the training session lasted for 30 minutes or less per day, resulted in statistical insignificant outcome on both of the parameters for pulmonary function.[29-31] However, the results of the FVC only, did reach statistical significance for two of the included studies.[33, 34] One study found statistical significant changes in FEV_1 after a period of an aerobic exercise program.[32] Therefore it is recommended that the training session should last for 45 minutes or longer per day, to achieve true changes on the pulmonary function.

One limitation of an exercise program in the treatment of CF is that it is only possible to carry out when the children are in a stable period. The outcome of this literature review seems to be most applicable for the physical therapist working with children in an out-patient clinic, instructing, supervising and educating the children and their families. It should however be noted that two of the included studies

investigated the effect of an exercise program in a hospital setting[27, 32], which resulted in promising findings on pulmonary function.

Comparability of the included studies

There are few contraindications for an exercise program for children with CF, when the program is designed and supervised by professionals. The included studies in this review included supervision, and program designs which were appropriate for children and adaptations were made when necessary. It was not reported by any of the studies that the exercise program presented any complications for the subjects, or their families.

In three of the included studies, there were no dropouts reported.[27, 28, 32] Due to physical deteriorations, one subject per study dropped out from the studies by; Gulmans et al,[29] Stanghelle et al,[33] and Zach et al.[35] There were seven subject who dropped out of the study by Orenstein et al,[30] the authors did not list a reason for the dropout. Six subjects dropped out from the study by Paranjape et al,[31] due to unrelated illness or injury. Four subjects dropped out from the study by Walker et al,[34] due to unforeseen circumstances. Two subjects were excluded from the study by Zach et al,[36] because of insufficient cooperation because of young age. The number of dropouts in the studies, are considered to be low, neither of the studies reported the exercise program as the reason for the dropouts.

All of the included studies diagnosed the subjects according to the same criteria,[26] and a spirometer was used to assess the pulmonary function for all the included studies.[22] The spirometers were of similar types, and used according to similar protocols.[21] This ensured that the studies were comparable at baseline and after the exercise intervention.

Limitations of the included studies

Since there was no co-intervention assessed in this study, the results in the improvements on pulmonary function cannot be stated with absolute confidence. The choice of an aerobic exercise program was based on literature showing that aerobic exercises is beneficial, safe, and has several positive outcomes for children with CF.[11-13, 44] However, several studies have established statistical significant improvements in pulmonary function, with other types of training than aerobic training as the main intervention.[32, 45]

The methodological quality of the majority of the included studies is considered to be moderate, while some were of good quality and poor quality, as demonstrated in (table 2) of the results section. Neither of the studies reported blinding of the subjects or therapist, which is recommended to decrease the risk of bias.[46] Unfortunately acquiring all of the RCT's which have been conducted on this topic was not possible, because the articles either had not been published,[47] or the article could not be retrieved.[48]

As demonstrated in, (appendix II) there is only moderate and limited evidence to establish the effect of an aerobic exercise program for children with CF on pulmonary function. It is possible that by including all of the research which is conducted on the topic of CF, the outcome of this research would have been affected. The outcome of those studies is unknown to the researcher, so this cannot be established.

Several of the studies also included other forms of training, compared the aerobic exercise therapy to a control group, or another intervention group. Outcome measurements on pulmonary function were generally not the primary outcome measurement which was researched. Six of the included studies,[27-31, 36] did therefore not discuss the reason for the insignificant or significant changes on pulmonary function, which is considered a limitation for the purpose of this review.

Strengths and limitations of this review

Limitations of this research are that it was conducted over a short period of time, with only one inexperienced researcher compiling, and assessing all of the relevant studies. This is considered a limitation because it did not meet the recommendations by van Tulder et al.[49] Stating that at least two researchers should be responsible for the application of the inclusion criteria, this is to ensure the quality of the research. This article has been revised several times, by different researchers. This does however not necessarily mean that the content of this article has been revised methodically, which is another limitation of this study.

The researchers revising this article did not acquire all of the relevant information and knowledge to provide critical feedback, which is another limitation of this study. The validity of research is a topic of discussion for any article with research conducted by only one researcher. Another limitation of this study was the set parameters of the language restrictions, only including studies published in English.

Even though this study was conducted by only one researcher, a strong point of this study is that when the researcher was in doubt about a study, or the outcome, a second or third researcher was consulted. The advantage of consulting with another researcher is that this researcher might have a more objective or different point of view, which increases the validity of this study. Another strong point of this study with respect to the methodological quality of the included studies, is that a second or third assessor confirmed the PEDro score, as recommended by van Tulder et al.[49]

The method used to acquire all of the relevant articles was according to recommendations.[50] The databases used for the research are considered to be some of the most comprehensive databases within the field of physical therapy.[51]

Conclusion

The results analyzed in this literature review demonstrates that an aerobic exercise program has a positive effect on pulmonary function for children suffering from CF. The majority of the included studies reported a statistical significant outcome in improvements on pulmonary function. In those studies which did not show significant improvements in pulmonary function, it was established that an aerobic exercise program reduced the rate of declination in pulmonary function.

Recommendations

An aerobic exercise program is considered to be safe, beneficial on exercise parameters, and to slow down the disease progression on pulmonary measurements. It should be noted that exercise regimens for children should include components of fun and involvement of the family. In addition, the program and intensity should include variety, and be adapted to the child, and the child's own interest, to maximize adherence.

This research article provides evidence for including an aerobic exercise program as a part of the therapy for children suffering from CF. It is recommended that the program is designed specifically for the child in question. The exercise program should be easy to follow, and emphasize the importance of maintaining a relative high intensity throughout. It should however be noted that the regular therapy routine should be maintained, and that an exercise program should not replace other types of treatment. It could also be beneficial to combine several aspects of exercise with the aerobic exercise program, like strength, flexibility, breathing and chest therapy.

Further research on the topic should include several different exercise types, to figure out a suitable combination of the different types of exercise therapy. Determining the specific intensity, type of training, and frequency per week is important to achieve optimal results on pulmonary function, exercise parameters and quality of life for children with CF. Studies should also be conducted with the pharmacological treatment, to assess the effect of the medications on the pulmonary function, and the effect of medications on the exercise capacity.

It is recommended that another literature review for children with CF should also include several outcome measures of different parameters, to be able to get a full overview of the effect of the exercise program. It is also recommended to only include new research, to be able to improve the current standards of treatment for children with CF.

Bibliography

1. Cohan-Cymberknoh M, Shoseyov D, Kerem E. Strategies That Increase Life Expectancy and Improve Quality of Life. Am J Respir Crit Care Med. 2011;183:1463-71.

2. Gibson R, Burns J, Ramsey B. Pathophysiology and Management of Pulmonary Infections in Cystic Fibrosis. Am J Respir Crit Care Med. 2003;168 (8):918-51.

3. Ernst M, Johnson M, Stark L. Developmental and Psycological Issues in Cystic Fibrosis. Pediatr Clin North Am. 2011;58(4):865-85.

4. Elbasan B, Tunali N, Duzgun I, Ozcelik U. Effects of Chest Physiotherapy and Aerobic Exercise Training on Physical Fitness in Young Children with Cystic Fibrosis. Ital J Pediatr. 2012;38:2.

5. Shoemaker M, Hurt H, Arndt L. The Evidence Regarding Exercise Training in the Management of Cystic Fibrosis, a Systematic Review. Cardiopulm Phys Ther J. 2008;19(3):75-83.

6. Southern K, Merelle M, Danker-Roelse J, Nagelkerke A. Newborn Screening for Cystic Fibrosis (Review). Cochrane Lib. 2009 (4):1-33.

7. Bell S, Robinson P. Exacerbations in Cystic Fibrosis: 2 Prevention. Thorax. 2007;62:723-31.

8. Peebles, P. Practical Guidelines for Cystic Fibrosis Care. London: Churchill Livingstone; 1998.

9. Philpott J, Houghton K, Luke A. Physical Activity Recommendations for Children with Specific Chronic Health Conditions. Pediatr Child Health. 2010;15(4):213-8.

10. Bradley JM, Moran F. Physical Training for Cystic Fibrosis. Cochrane Database of Syst Rev. 2008 (7):1-55.

11. Rand S, Prasad A. Exercise Improves Lung Function and Habitual Activity in Children with Cystic Fibrosis. Expert rev Respir Med. 2011;6 (3):341-51.

12. Dwyer T, Elkins M, Bye P. The Role of Exercise in Maintaining Health in Cystic Fibrosis. Curr Opin Pulm Med. 2011;17(6):455-60.

13. Rand S, Prasad A. Exercise as Part of a Cystic Fibrosis Therapeutic Routine: The Role of Exercise in Cystic Fibrosis Therapeutic Routines. Expert rev Respir Med. 2012;6(3):1-12.

14. de Jong W, Grevink R, Roorda R, Kaptein A, van der Schans C. Effect of a Home Exercise Training Program in Patients with Cystic Fibrosis. Chest. 1994;105(5):463-8.

15. Prasad A, Cerny F. Factors That Influence Adherence to Exercise and Their Effectiveness: Application to Cystic Fibrosis. Pediatric Pulmonology. 2002;34(1):66-72.

16. Orenstein D, Higgins L. Update on the Role of Exercise in Cystic fibrosis. Curr Opi Pulm Med. 2005 (11):519-23.

17. Hebestreit H, Kieser S, Rudiger S, Schenk T, Junge S, Hebestreit A, et al. Physical Activity Is Independently Related to Aerobic Capacity in Cystic Fibrosis. Eur Respir J. 2006;28:734–9.

18. de Jong W, Grevink R, Mannes G, van Aalderen W, Koeter G, van der Schans P. Relationship between Dyspnoea, Pulmonary Function and Exercise Capacity in Patients with Cystic Fibrosis. Respir Med. 1997 (91):41-6.

19. Marcotte J, Grisdale R, Levison H, Canny G, Coates A. Multiple Factors Limit Exercise Capacity in Cystic Fibrosis. Pediatr Pulm. 1986;2(5):274-81.

20. Lands L, Heigenhauser G, Jones N. Analysis of Factors Limiting Maximal Exercise Performance in Cystic Fibrosis. Clin Sci. 1992 (83):391-7.

21. Vilozni D , Bentur L, Efrati O, Minuskin T, Barak A, Szeinberg A, et al. Spirometry in Early Childhood in Cystic Fibrosis Patients. Chest. 2007;131(2):356-61.

22. Koopman M Zanen P, Kruitwagen CL,van der Ent C, Arets H. Reference Values for Paediatric Pulmonary Function Testing: The Utrecht Dataset. Respiratory Medicine. 2011 1//;105(1):15-23.

23. Chaitra B, Pandurang N, Nagaraja P, Vijay M. Effect of Aerobic Exercise Training on Pulmonary Function Tests: A Pragmatic Randomized Controlled Trial. Int J Pharma Bio Sci. 2011;2(4):455-60.

24. Gandevia B, Hugh-Jones P. Terminology for Measurements of Ventilatory Capacity; a Report to the Thoracic Socity. Thorax. 1957;12(290):290-3.

25. Orenstein D, Franklin B, Doershuk C, Hellerstein H, Germann , Horowitz J, et al. Exercise Conditioning and Cardiopulmonary Fitness in Cystic Fibrosis. The Effects of a Three-Month Supervised Running Program. Chest. 1981;80(4):392-8.

26. Rosenstein BJ, Cutting GR. The Diagnosis of Cystic Fibrosis: A Consensus Statement. Cystic Fibrosis Foundation Consensus Pane. J Pediatr. 1998;132:589-95.

27. Cerny F. Relative Effects of Bronchial Drainage and Exercise for in-Hospital Care of Patients with Cystic Fibrosis. Phys Ther. 1989 (69):633-9.

28. Gruber W, Orenstein D, Braumann K, Hüls G. Health-Related Fitness and Trainability in Children with Cystic Fibrosis. Pediatr Pulm. 2008;43(10):953-64.

29. Gulmans V, de Meer K, Brackel H, Faber J, Berger R, Helders P. Outpatient Exercise Training in Children with Cystic Fibrosis: Physiological Effects, Perceived Competence, and Acceptability. Pediatr Pulm. 1999;28:39-46.

30. Orenstein D, Hovell M, Mulvihill M, Keating K, Hofstetter R, Kelsey S, et al. Strength Vs Aerobic Training in Children with Cystic Fibrosis. Chest. 2004;126:1204-14.

31. Paranjape SM, Barnes LA, Carson KA, von Berg K, Loosen H, Mogayzel P. Exercise Improves Lung Function and Habitual Activity in Children with Cystic Fibrosis. J Cyst Fibro. 2012;11(1):18-23.

32. Selvadurai H, Blimkie C, Meyers N, Mellis C, Cooper P, Van Asperen P. Randomized Controlled Study of in-Hospital Exercise Programs in Children with Cystic Fibrosis. Pediatr pulm. 2002 (33):194-200.

33. Stanghelle JK, Hjeltnes N, Bangstad HJ, Michalsen H. Effect of Daily Short Bout of Trampoline Exercise During 8 Weeks on the Pulmonary Function and the Maximal Oxygen Uptake of Children with Cystic Fibrosis. Int J Sports Med. 1988;9:32-6.

34. Schneiderman-Walker J, Pollock S, Corey M, Wilkes D, Canny G, Pedder L, et al. A Randomized Controlled Trial of a 3-Year Home Exercise Program for Cystic Fibrosis. J Pediatr. 200;136(3):304-10.

35. Zach M, Purrer B, Oberwaldner B. Effect of Swimming on Forced Expiration and Sputum Clearance in Cystic Fibrosis. Lancet. 1981:1201-3.

36. Zach M, Oberwaldner B, Hausler F. Cystic Fibrosis, Physical Exercise Versus Chest Physiotherapy. Arch Dis Child. 1982;57:587-9.

37. Shale DJ. Predicting Survival in Cystic fibrosis. Thorax. 2007;52:309.

38. Smith B, Wood BL. Psychological Factors Affecting Disease Activity in Children and Adolescents with Cystic Fibrosis: Medical Adherence as a Mediator. Curr Opin Pediatr. 2007;19(5):553-8.

39. Cerny F, Pullano T, Cropp G. Cardiorespiratory Adaptations to Exercise in Cystic Fibrosis. Am Rev Respir Dis. 1982;126(2):217-20.

40. Nikolaizik WH, Schöni MH. Pilot Study to Assess the Effect of Inhaled Corticosteroids on Lung Function in Patients with Cystic Fibrosis. J Pediatr. 1996;128(2):271-4.

41. Desmond KJ, Schwenck WF, Thomas E, Beudry P, Coates A. Immediate and Long-Term Effects of Chest Physiotherapy in Patients with Cystic Fibrosis. Paediatr Respir J. 1983;103:538-42.

42. Scmidt A, Jacobsen U, Bregnballe V, Olesen H, Ingemann-Hansen T, Thastum M, et al. Exercise and Quality of Life in Patients with Cystic Fibrosis, a 12-Week Intervention Study. Physiother Theory Pract. 2011;27(8):548-56.

43. DiMatteo R. Variations in Patients' Adherence to Medical Recommendations a Quantitative Review of 50 Years of Research. Medical Care. 2004;42(3):200-9.

44. Nixon P, Orenstein D, Kelsey SF, Doershuk C. The Prognostic Value of Exercise Testing in Patients with Cystic Fibrosis. N England Journal of Medicine. 1992 (327).

45. Moorcroft AJ, Dodd ME, Morris J, Webb. AK. Individualised Unsupervised Exercise Training in Adults with Cystic Fibrosis. Thorax. 2004;59:1074-80.

46. de Morton N. The Pedro Scale Is a Valid Measure of the Methodological Quality of Clinical Trials: A Demographic Study. Aust J Physiother. 2009;55:129-33.

47. Phillips AL, Lee L, Britton LJ, Hoover W, Lowman JD. Efficacy of a Standardised Exercise Protocol in Inpatient Care of Patients with Cystic Fibrosis. Pediatr Pulm. 2008;43:385.

48. Turchetta A, Salerno T, Lucidi V, Libera F, Cutrera R, Bush A. Usefulness of a Program of Hospital-Supervised Physical Training in Patients with Cystic Fibrosis. Pediatr Pulm. 2004 (38):115-8.

49. van Tulder M, Furlan A, Bombardier C, Bouter L. Updated Method Guidelines for Systematic Reviews in the Cochrane Collaboration Back Review Group. Spine. 2003;12(28):1290-9.

50. van der Velde G van Tulder M, Côté P, Hogg-Johnson S, Aker P, Cassidy JD, Carroll L, Guzman J, Haldeman S, Holm L, Hurwitz E, Nordin M, Peloso P. The Sensitivity of Review Results to Methods Used to Appraise and Incorporate Trial Quality into Data Synthesis. Spine. 2007;7(32):796-806.

51. Michaleff Z, Costa L, Moseley A, Maher CG, Elkins MR, Herbert R, et al. Central, Pedro, Pubmed, and Embase Are the Most Comprehensive Databases Indexing Randomized Controlled Trials of Physical Therapy Interventions. Phys Ther. 2011;91(2):190-7.

Appendix I: PEDro scale [46]

1.	Eligibility criteria were specified
2.	Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)
3.	Allocation was concealed
4.	The groups were similar at baseline regarding the most important prognostic indicators
5.	There was blinding of all subjects
6.	There was blinding of all therapists who administered the therapy
7.	There was blinding of all assessors who measured at least one key outcome
8.	Measurements of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups
9.	All subjects for whom outcome measurements were available received the treatment or control condition as allocated, or where this was not the case, data for at least one key outcome were analyzed by "intention to treat"
10.	The results of between-group statistical comparisons are reported for at least one key outcome
11.	The study provides both point measurements and measurements of variability for at least one key outcome

Notes on administration of the PEDro scale:

All criteria Points are only awarded when a criterion is clearly satisfied. If on a literal reading of the trial report it is possible that a criterion was not satisfied, a point should not be awarded for that criterion.

Criterion 1: This criterion is satisfied if the report describes the source of subjects and a list of criteria used to determine who was eligible to participate in the study.*

Criterion 2: A study is considered to have used random allocation if the report states that allocation was random. The precise method of randomization need not be specified. Procedures such as coin-tossing and dice-rolling should be considered random. Quasi-randomization allocation procedures such as allocation by hospital record number or birth date, or alternation, do not satisfy this criterion.

Criterion 3: Concealed allocation means that the person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated to. A point is awarded for these criteria, even if it is not stated that allocation was concealed, when the report states that allocation was by sealed opaque envelopes or that allocation involved contacting the holder of the allocation schedule who was "off-site".

Criterion 4: At a minimum, in studies of therapeutic interventions, the report must describe at least one measure of the severity of the condition being treated and at least one (different) key outcome measure at baseline. The rater must be satisfied that the groups' outcomes would not be expected to differ, on the basis of baseline differences in prognostic variables alone, by a clinically significant amount. This criterion is satisfied even if only baseline data of study completers are presented.

Criteria 4, 7-11: Key outcomes are those outcomes which provide the primary measure of the effectiveness (or lack of effectiveness) of the therapy. In most studies, more than one variable is used as an outcome measure.

Criterion 5-7: Blinding means the person in question (subject, therapist or assessor) did not know which group the subject had been allocated to. In addition, subjects and therapists are only considered to be "blind" if it could be expected that they would have been unable to distinguish between the treatments applied to different groups. In trials in which key outcomes are self-reported (eg, visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind.

Criterion 8: This criterion is only satisfied if the report explicitly states both the number of subjects initially allocated to groups and the number of subjects from whom key outcome measures were obtained. In trials in which outcomes are measured at several points in time, a key outcome must have been measured in more than 85% of subjects at one of those points in time.

Criterion 9: An intention to treat analysis means that, where subjects did not receive treatment (or the control condition) as allocated, and where measures of outcomes were available, the analysis was performed as if subjects received the treatment (or control condition) they were allocated to. This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all subjects received treatment or control conditions as allocated.

Criterion 10: A between-group statistical comparison involves statistical comparison of one group with another. Depending on the design of the study, this may involve comparison of two or more treatments, or comparison of treatment with a control condition. The analysis may be a simple comparison of outcomes measured after the treatment was administered, or a comparison of the change in one group with the change in another (when a factorial analysis of variance has been used to analyze the data, the latter is often reported as a group × time interaction). The comparison may be in the form hypothesis testing (which provides a "p" value, describing the probability that the groups differed only by chance) or in the form of an estimate (for example, the mean or median difference, or a difference in proportions, or number needed to treat, or a relative risk or hazard ratio) and its confidence interval.

Criterion 11: A point measure is a measure of the size of the treatment effect. The treatment effect may be described as a difference in group outcomes, or as the outcome in (each of) all groups. Measures of variability include standard deviations, standard errors, confidence intervals, interquartile ranges (or other quantile ranges), and ranges. Point measures and/or measures of variability may be provided graphically (for example, SDs may be given as error bars in a Figure) as long as it is clear what is being graphed (for example, as long as it is clear whether error bars represent SDs or SEs). Where outcomes are categorical, this criterion is considered to have been met if the number of subjects in each category is given for each group.

Score is given: 0-10/10.

*Criterion 1 is not awarded points.

Appendix II: Results of the best evidence synthesis

Table 5. Change in FVC.

Author, year.	Quality, method.	Outcome	Evidence level
Cerny, 1989[27]	Moderate quality CT.	Significant	There is moderate evidence to support that the FVC significantly improves after a period of participating in an exercise program, for children suffering from cystic fibrosis.
Gruber et al, 2008[28]	Moderate quality CT	Significant	
Stanghelle et al, 1988[33]	Moderate quality CT	Significant	
Walker et al, 2000[34]	Good quality RCT.	Significant	
Zach et al, 1981[35]	Moderate quality CT	Significant	
Zach et al, 1982[36]	Moderate quality CT	Significant	
Gulmans et al, 1999[29]	Poor quality CT	Insignificant	
Selvadurai et al, 2002[32]	Moderate quality RCT	Insignificant	

RCT= Randomized controlled trial. CT= Clinical trial. FVC= Forced expiration volume.

Table 6. Change in $FEV_{1.}$

Author, year.	Quality, method.	Outcome	Evidence level
Cerny,1989[27]	Moderate quality CT.	Significant	There are indicative findings to support that the changes in FEV_1, is due to an exercise program, for children who suffer from cystic fibrosis.
Gruber et al, 2008[28]	Moderate quality CT	Significant	
Selvadurai et al, 2002[32]	Moderate quality RCT	Significant	
Zach et al, 1981[35]	Moderate quality CT	Significant	
Zach et al, 1982[36]	Moderate quality CT	Significant	
Gulmans et al,1999[29]	Poor quality CT	Insignificant	
Orenstein et al, 2004[30]	Good quality RCT	Insignificant	
Paranjape et al, 2012[31]	Moderate quality CT	Insignificant	
Stanghelle et al,1988[33]	Moderate quality CT.	Insignificant	
Walker et al, 2000[34]	Good quality RCT	Insignificant	

RCT= Randomized controlled trial. CT= Clinical trial. FEV_1= Forced expiration volume in one second.

Appendix III: Best Evidence Synthesis.[49]

Best Evidence Synthesis

Strong evidence	Provided by consistent, statistically significant findings in outcome measures in at least two high quality RCT's #
Moderate Evidence	Provided by consistent statistically significant findings in outcome measures in at least one high quality RCT and at least one low quality RCT or high quality CCT. #
Limited Evidence	Provided by consistent statistically significant findings in outcome measures in at least one high quality RCT # or provided by consistent statistically significant findings in outcome measures in at least two high quality CCT's # (in absence of high quality RCT's)
Indicative Findings	Provided by statistically significant findings in outcome and or process measures in at least one high quality CCT or one low quality RCT # (in absence of high quality RCT's. or provided by consistent
No Evidence	In cases of results of eligible studies that do not meet the criteria for one of the above stated level of evidence, or in case of conflicting results among RCT's and CCT's or in case of no eligible studies.

RCT's= Randomized controlled trials: CCT's= Controlled clinical trials

#if the portion of studies that show evidence is < 50% of the total number of studies within the same category of methodological quality and study design (RCT's and CCT's) we state no evidence.

Appendix IV: Approval of the project plan

Fontys

B4 Assessment form project plan

Name: Martine Olsen Student no:

Date: 12 maart 2013

Title: "What is the effect of aerobic exercise therapy on pulmonary function index, measured in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC), in children and adolescents suffering from cystic fibrosis?"

General	
- The project plan is according to format	yes
- Spelling and language are correct	yes
Problem description and problem definition (introduction)	
- The problem description is sufficiently clearly formulated	yes
- The problem description reflects social and paramedical relevance	yes
A concrete and relevant research question (or questions) can be formulated based on the problem definition, including possible sub questions	yes
Objective	
The objective is:	
- Sufficiently clearly and concretely formulated	yes
- Relevant for a selected target group within the (paramedical) professional practice	yes
- Practically feasible	yes
- Achievable within the set time	yes
Project product	
The project product:	
- Is in line with the problem definition, research question and objective	yes
- Is usable for the selected target group	yes
- Is in line with the client's wishes	yes
- The product requirements are accurately described	yes
Activities/method	
Sufficient insight is given into the type of activities and types of sources for the performance of the research and the realization of the product	yes
Time schedule	
- The time schedule gives a global phasing and time investment for the project as a whole and for the coming weeks an increasingly detailed schedule	yes

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- Important moments are recorded in the table (typographically noticeable)	
(e.g. contact moments, handing-in moments)	yes
- The time schedule gives a global task division of the planned activities	yes

Estimated costs

Clear insight is given in:	
- The costs to be expected concerning money and hours	yes
- The division of these costs (project leader, student, programme)	yes

Literature

- Used and planned literature is specific and mentioned to a sufficient extent	yes
- Relevant and recent literature is referred to	yes
- Literature references, in the text and in the literature list, are made	
according to the Writer's Guide (Wouters 2012)	yes

Comments: DEAR MARTINE. YOU HAVE A GO, BUT PLEASE CHANGE THE COMMENTS JAAP AND I MADE. THESE CHANGED ITEMS WON'T BE CHECKED AGAIN. WE TRUST ON YOU TO DO THIS; IT'S YOUR RESPONSIBILITY. WE THINK THE COMMENTS ARE QUITE CLEAR. CONGRATULATIONS. YOU MAY PROCEED WITH THE PROJECT. JAAP HAS PLACED HIS COMMENTS IN SMALL LITERATUUR. I WILL MAKE MINE IN CAPSLOCK LETTERS IN THE TEXT.

WELL WRITTEN INTRODUCTION

- THE «C» IN YOUR PICO IS : NOT RECEIVING ANY THERAPY?
- THE PICO SHOULD BE REFLECTED IN SEARCH STRATEGY AND IN-EXCLUSION CRITERIA
- I'M NOT HAPPY WITH YOUR DATA EXTRACTION TABLE. PLEASE DOWNLOAD REVIEWS AND SEE HOW THEY DID IT. YOU'LL SEE THAT THE DATA EXTRACTION TABLE HAS MAX. 8 -9 COLLUMS. IN THESE COLLUMS IS WRITEN WHAT YOU HAVE WRITTEN IN YOUR ROWS. SO YOUR HEADINGS (VERTICALLY PRESENTED BELOW) SHOULD BE PRESENTED HORIZONTALLY. ONE COULD CREATE A 100 COLLUMS BUT WE SHOUD STICK TO A MXIMUM OF 8/9. WHAT IS REALLY INTERESTING TO FOCUS ON?

Introduction; Comment: The disease is properly introduced.

Problem definition: The «results» are more or less presented in the problem definition...this seems not very tactical.

The relevant outcome measures are properly introduced.

Pico: The control in the PICO probably is «no intervention»?

3.4 aerobic training; The definition of aerobic training is not very clear...the relation with this research is not very clear...

3.4: The other definitions are clearly defined.

4.3: The search strategy could be a bit more according to the PICO style?

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4.4 : Inclusion criteria are clearly defined. Exclusion criteria as well.
4.7: Quality assessment is clearly described, although the best evidence synthese is better placed under data analysis (and synthesis)
5.1. Project products are clearly described.
The time table is worked out fine, and contains sufficient peer feedback
The references do not seem fully consistent.
In general the method section is described in sufficient details. It gives me sufficient confidence that the student will be able to make it a succes. Therefore a GO

All points under B3.1 up to and including B3.8 must be answered with a 'yes' in order to receive a GO for the project. The supervisor discusses with the student which points need adjustment.

GENERAL: **GO**

Name assessor:

Marc Schmitz
12/3/2013

Jaap Jansen
12/3/2013

Date + Signature