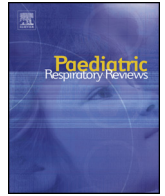




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## Paediatric Respiratory Reviews



Cochrane Corner



## Physical exercise training for cystic fibrosis

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### WHY WAS IT IMPORTANT TO DO THIS COCHRANE REVIEW [1]

Cystic fibrosis (CF) is the most common life-shortening autosomal recessively inherited disease in Caucasian populations [2]. Progressive respiratory disease in CF results in an abnormal ventilatory response to exercise which contributes to dyspnea and is a major limiting factor to exercise tolerance [3]. In addition, a sedentary lifestyle contributes to the progression of physical and functional impairment in CF [4], likely with the consequence of a reduced life expectancy as exercise capacity is linked to survival [5]. Exercise has received growing recognition among researchers and clinicians as treatment for chronic disease including CF lung disease [6,7]. In CF, exercise has the potential to improve airway clearance through a combination of hyperventilation, mechanical vibration, and improved sputum viscoelasticity thereby leading to facilitated and increased sputum expectoration [8,9]. Regular physical exercise improves exercise tolerance and slows progressive pulmonary function decline [4,10].

Until today, much of the knowledge on the effects of physical conditioning in CF originates predominantly from observational or small non-randomized and non-controlled studies. Therefore, a systematic review of evidence from randomised controlled trials (RCTs) on the effects of regular physical exercise training was required to critically evaluate potential beneficial effects on patient-relevant outcomes in CF.

### WHAT COMPARISONS DID WE MAKE IN THIS REVIEW

The primary aim of this review was to assess the effects of physical exercise training on exercise capacity (e.g., peak oxygen consumption -  $VO_{2peak}$ ), pulmonary function (e.g., forced expiratory volume at one second -  $FEV_1$ ), and health-related quality of life

(HRQoL). Secondary outcomes were CF-related mortality, muscle strength and anaerobic capacity, further indices of exercise capacity and pulmonary function, physical activity, body composition, acute exacerbations, bone health, diabetic control, antibiotic use, compliance with exercise training and adverse events related to the exercise intervention or exercise testing as part of the intervention.

The review included RCTs recruiting participants with CF of any age and any degree of disease severity, diagnosed on the basis of clinical criteria and sweat testing or genotype analysis. We included any type of prescribed physical exercise training (aerobic training or anaerobic training or a combination of both training regimens) delivered to individuals with CF compared to usual care. We excluded studies which involved pure respiratory muscle training.

Two authors independently extracted data and assessed the risk of bias for each included study according to the Cochrane risk of bias tool [11].

### WHAT WERE THE FINDINGS OF THIS REVIEW?

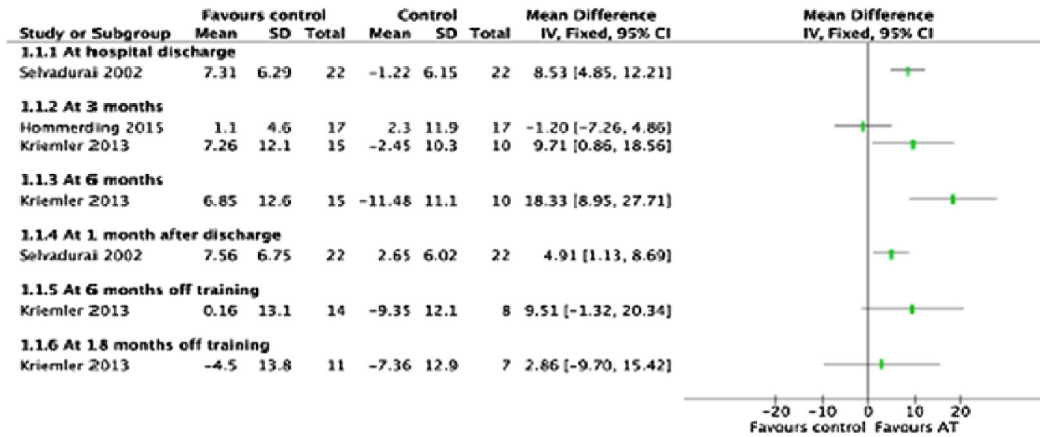
The review included 13 predominantly small parallel group RCTs with a total of 402 participants with a wide range of severity of CF lung disease [12–24]. The study duration ranged from less than one month up to three years; four studies were short-term and recruited hospitalised patients [12,22–24] and the other nine studies were longer term and recruited outpatients [13–21]. There was wide heterogeneity in study designs with seven studies using a supervised training approach; five studies a partially supervised approach and one study an unsupervised training approach.

The overall risk of bias of the 13 included studies was judged as low to moderate, due to a combination of unclear reporting of random sequence generation or allocation concealment (selection bias) and lack of information regarding blinding of outcome assessors. None of the included studies was blinded for group assignment, as it is impossible to blind exercise training. It is unclear if this could cause bias.

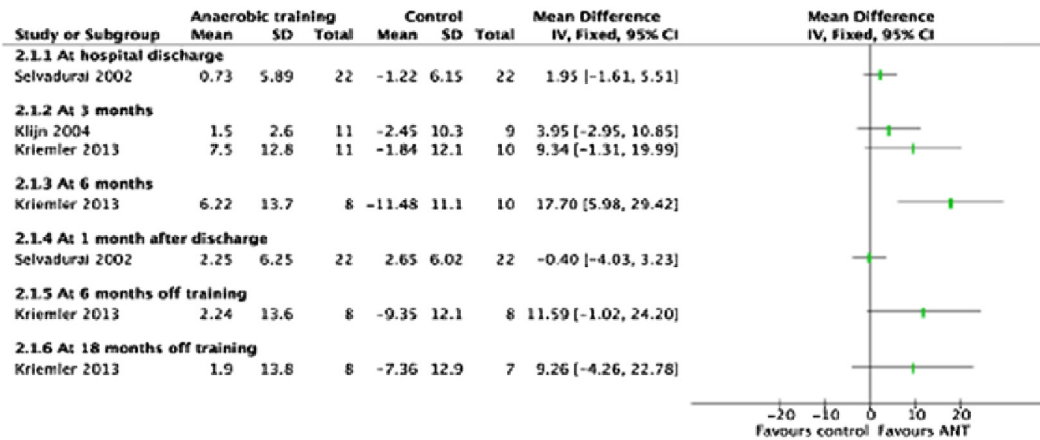
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## Change in VO<sub>2</sub>peak (mL/min per kg BW)

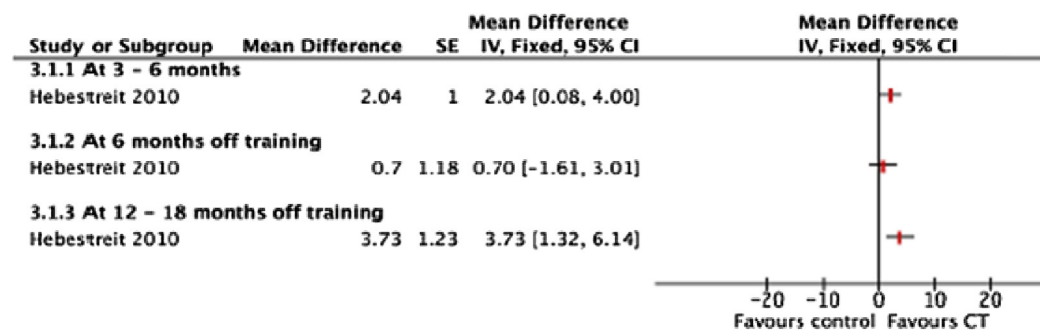
### Aerobic training (AT) versus control



### Anaerobic training (ANT) versus control



### Combined training (CT) versus control



**Figure 1.** Comparison of aerobic training (AT) versus no physical training; anaerobic training (ANT) versus no physical training and combined training (CT) versus no physical training on peak oxygen uptake (VO<sub>2peak</sub> in mL/min per kg BW).

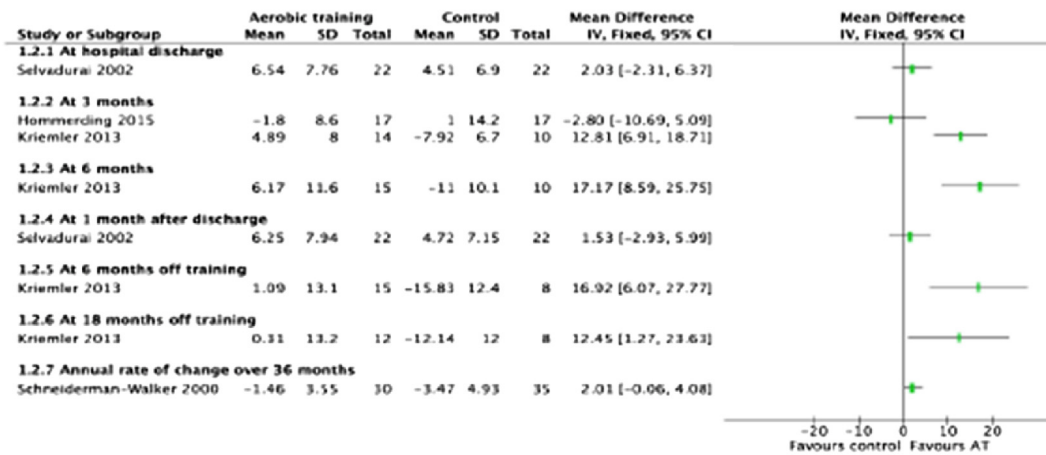
The training modalities and durations were heterogeneous, sometimes of insufficient duration and combined with additional treatments such as physiotherapy, nutritional therapy and intravenous antibiotic treatment in the short-term in-hospital studies [12,22-24].

Due to different study designs (type of exercise training, duration etc.), we did not combine results from different studies

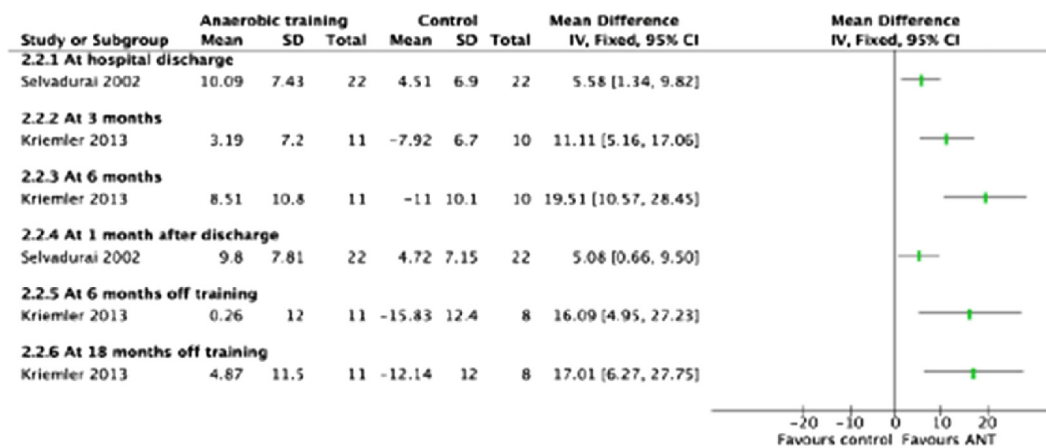
for meta-analysis. One short-term study [12] lasting less than 4 weeks reported improvements in VO<sub>2peak</sub> and HRQoL, but no effects on FEV<sub>1</sub>. The majority of longer-term studies showed improvements in VO<sub>2peak</sub>, with unclear effects on FEV<sub>1</sub> and HRQoL. Data for VO<sub>2peak</sub> and FEV<sub>1</sub> comparing physical exercise training versus no exercise training are shown in Figure 1 and Figure 2, respectively. There was limited

## Change in FEV<sub>1</sub> (% predicted)

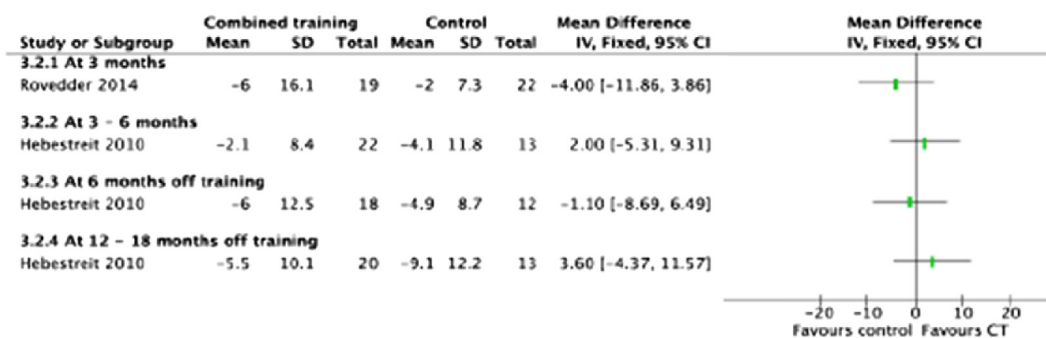
### Aerobic training (AT) versus control



### Anaerobic training (ANT) versus control



### Combined training (CT) versus control



**Figure 2.** Comparison of aerobic training (AT) versus no physical training; anaerobic training (ANT) versus no physical training and combined training (CT) versus no physical training on forced expiratory volume at 1s (FEV<sub>1</sub> in % predicted). Please note that the study by Moorcroft et al. [15] is not included in the graph displaying the change in FEV<sub>1</sub> (CT versus control), because FEV<sub>1</sub> was reported in mL in the original study. This study found no significant difference in FEV<sub>1</sub> between the training and the control group after 12 months.

evidence of beneficial training effects on secondary outcome measures.

#### WHAT ARE THE IMPLICATIONS OF THIS REVIEW FOR PRACTICE AND FOR RESEARCH?

This systematic review showed limited evidence from both short- and long-term studies that aerobic or anaerobic physical exercise training or a combination of both has a beneficial effect on exercise capacity, pulmonary function and HRQoL in individuals with CF lung disease. However, since physical exercise training appears to be safe in individuals with CF [25] and is already part of the regular care offered to most individuals with CF, there is no reason to discourage exercise training.

The majority of included studies showed methodological shortcomings. There is a clear need for high-quality randomised controlled studies with sufficient numbers of study participants and well-chosen, objectively measurable, reproducible and clinically relevant and participant-oriented outcome measures. Future studies should focus on the determination of the optimal training components (e.g. type, frequency, intensity, duration), as well as on effects of physical exercise training on understudied, but clinically most relevant outcomes such as bone health, diabetic control, HRQoL, exacerbations and hospitalisations.

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