

EVIDENCE-BASED REVIEW

respiratoryMEDICINE

Evidence for physical therapies (airway clearance and physical training) in cystic fibrosis: An overview of five Cochrane systematic reviews $\stackrel{\text{\tiny}}{\approx}$

Judy M. Bradley^{a,b,*}, Fidelma M. Moran^c, J. Stuart Elborn^{b,d}

^aHealth and Rehabilitation Sciences Research Institute, University of Ulster, BT37 OQB, UK ^bDepartment of Respiratory Medicine, Belfast City Hospital, Belfast, BT9 7AB, UK ^cSchool of Health Sciences, University of Ulster, BT37 OQB, UK ^dDepartment of Respiratory Medicine, Queen's University Belfast, Belfast, UK

Received 20 July 2005; accepted 11 November 2005

KEYWORDS Physical therapies; Airway clearance; Physical training; Cystic fibrosis (CF); Cochrane systematic reviews	Background: A range of physical therapies (including airway clearance and physical
	training) are used in cystic fibrosis (CF). The aim of this paper is to summarise the
	main findings from Cochrane systematic reviews that have considered the evidence
	to physical ulerapies in ci.
	summarised.
	Results: Review 1 provides some evidence from short-term trials of the benefit of
	airway clearance over no airway clearance in improved mucus transport but no
	definitive evidence from long-term trials to support the efficacy of airway clearance
	over no airway clearance; review 2 provides some evidence that conventional chest
	physiotherapy (CCPT) is at least as effective as other forms of airway clearance, but
	that patients may have a preference for self-administered treatments over CCPT;
	review 3 provides some evidence that positive expiratory pressure (PEP) is at least as
	effective as other forms of airway clearance; review 4 provides some evidence to
	support the use of non-invasive ventilation during airway clearance in patients with
	moderate to severe disease who have difficulty clearing sputum; review 5 provides
	some evidence of the benefits of different types of physical training.

 $^{^{\}diamond}$ Please see reference list for Cochrane reviews sited in this evidence-based review.

^{*}Corresponding author. Health and Rehabilitation Sciences Research Institute, University of Ulster, Northern Ireland, BT37 OQB, UK. Fax: +442890368419.

E-mail address: jm.bradley@ulster.ac.uk (J.M. Bradley).

^{0954-6111/\$ -} see front matter @ 2006 Published by Elsevier Ltd. doi:10.1016/j.rmed.2005.11.028

Conclusion: The Cochrane systematic reviews summarised in this paper provide some evidence to support the inclusion of physical therapies in the care-management plan of CF. They also provide information to steer the direction and focus of future research in this area.

© 2006 Published by Elsevier Ltd.

Background

Cystic fibrosis (CF) is a multisystem disease; however, the major clinical manifestations are related to respiratory disease. Patients with CF are infected early in life with Staphylococcus aureus and Haemophilus influenzae, and later with Pseudomonas aeruginosa. Numerous trials have shown how the host inflammatory response to these early infections contributes to the chronicity of infection and the progression of respiratory disease. The major clinical manifestations of CF respiratory disease are retention of sputum, reduced exercise capacity and breathlessness.¹ Physical therapy involves a range of interventions (including airway clearance and physical training), which have an overall aim of reducing progression of CF respiratory disease. Many different airway clearance techniques are available, but, in general, their goal is to reduce disease progression by augmenting the normal mucociliary clearance mechanism of the lungs and facilitating expectoration (Table 1).²⁻⁴ Outcome measures currently used to assess the efficacy of airway clearance frequently include the following: auscultation; spirometry; pulse oximetry and sputum weight or volume. Less frequently used outcome measures include radioaerosol clearance; arterial blood gases; cough frequency; health-related quality of life (QoL); breathlessness; sputum cultures; X-rays; antibiotic use and frequency of exacerbations. The primary aims of physical training are to improve exercise capacity, improve muscle strength, and reduce breathlessness, although it may also have an airway clearance effect. Outcome measures currently used to assess the efficacy of physical training include peak or endurance exercise tests; weight and body-mass index and breathlessness scales. Less frequently used outcome measures include specific muscle strength, endurance or flexibility tests; health-related QoL; activity diaries or monitors; antibiotic use and frequency of exacerbations.

It is essential that the benefit of these therapies are established in order to justify their inclusion in the demanding CF care package, and ensure that any future research will add to and not replicate existing evidence in this area.⁵

The aim of this paper is to summarise the main findings of Cochrane systematic reviews that have considered the evidence for physical therapies (airway clearance and physical training) in CF.

Methods

Five Cochrane systematic reviews were identified that assessed the efficacy of various physical therapies (chest physiotherapy,⁶ conventional physiotherapy,⁷ positive expiratory pressure (PEP),⁸ non-invasive ventilation (NIV)⁹ and physical training¹⁰) in CF. The trials in the Cochrane systematic reviews were all randomised trials, including patients with CF (diagnosed on the basis of clinical criteria, sweat testing or genotype analysis) of any age and any degree of disease severity. The search strategies and methods used for trial eligibility, trial guality and data extraction, followed the guidelines of the Cochrane Cystic Fibrosis and Genetic Disorders Group. Specific information on population, interventions, types of outcome measures and quality can be obtained from the "Table of Characteristics of Included Trials" in the individual Cochrane systematic reviews. Original trial data are also provided in the individual Cochrane systematic reviews. Only one of the reviews conducted a meta-analysis of results.⁷ For this paper, all outcomes reported in the Cochrane systematic reviews will be referred to.

Systematic review 1

Airway clearance compared with no airway clearance in CF

Six randomised, crossover trials were included in this review: all were short-term trials (five trials were single-treatment trials¹¹⁻¹⁵ and one trial lasted up to 7 days¹⁶), with a total of 66 participants. These trials involved a mixed population of adults and children.¹¹⁻¹⁶ No data on spirometry were available to facilitate classification of disease severity. Any form of

Table 1	Definition of	techniques	used in	this	review.

Airway clearance technique	Description			
Chest/conventional physiotherapy (CCPT) Postural drainage with percussion and vibration (PDPV) Active cycle of breathing techniques (ACBT)	This technique has traditionally included postural drainage, percussion and vibration. Postural drainage is a technique in which the patient is positioned to facilitate gravity drainage of secretions from the airways. Percussion is a technique of clapping the chest wall. Vibration applies fine shaking of the chest wall, usually during the expiratory phase. Percussion and vibration can be applied using either manual or mechanical techniques. This technique includes breathing control, thoracic expansion techniques, forced expiration technique (FET), and may include CPT.			
Forced expiration technique (FET)	Sometimes called huff coughing, this technique consists of one or two huffs from mid-to-low lung volumes with the glottis open, followed by relaxed diaphragmatic breathing.			
Positive expiratory pressure (PEP)	This technique uses a device, through which the patient exhales against a pressure of 10–20 cmH ₂ O. During high PEP, the patient exhales against a pressure ranging from 40 to 100 cmH_2O .			
Airway oscillating device (AOD): flutter	This technique uses a device that produces PEP with oscillations in the airway during the expiratory phase.			
Autogenic drainage (AD)	This is a three-level breathing sequence beginning at low lung volumes, followed by breathing at mid-lung volumes, followed by deep breathing, huff and coughing.			
Airway oscillating device (AOD): intrapulmonary percussive ventilation (IPV)	This technique uses a pneumatic, oscillating pressure device that generates oscillations in the range of $100-300$ /min at pressures of 535 cmH ₂ O.			
High-frequency chest compression (HFCC)	This technique uses an inflatable vest that attaches by hoses to an airpulse generator producing pressures to about $50 \text{ cmH}_2\text{O}$ at frequencies of 5–25 Hz.			
Mechanical percussion	Electrical hand-held device used to provide chest wall percussion.			
Pursed-lip breathing	Involves inhaling through nose slowly and exhaling through pursed lips.			
Non-invasive ventilation (NIV)	Device that consists of mouthpiece or facemask connected to generator that provides a set positive pressure on inspiration and expiration.			

airway clearance (conventional chest physiotherapy (CCPT),^{11,12,15,16} PEP,^{12–16} active cycle of breathing techniques (ACBT),¹⁶ autogenic drainage (AD),¹⁴ mechanical percussion,¹¹ high-frequency chest compression (HFCC)¹⁶) was compared with no airway clearance or spontaneous coughing alone.

Spirometry and plethysmography

Two trials found no significant difference between airway clearance and no airway clearance in post-

treatment total lung capacity (TLC) and functional residual capacity.^{13,16}

Secretion expectoration and mucus transport

Five trials found increased mucus transport^{11,12,15} or secretion expectoration^{11,14,17} during airway clearance than during no airway clearance. In the only trial that did not find a significant difference in mucus transport between airway clearance compared with no airway clearance,

coughing was not a component of the airway clearance regimen.¹³

Practice point

• The long-term effect of no airway clearance is unknown, and short-term trials provide some evidence of the benefit of airway clearance over no airway clearance in improved mucus transport

Systematic review 2

Conventional chest physiotherapy compared with other forms of airway clearance in CF

Fifteen trials of mixed designs were included in this review (seven trials in this review overlapped with those in systematic review 3,17-23 and one trial overlapped with those in systematic review 5^{24}), with a total of 475 participants. Four trials were undertaken during an acute exacerbation and were of 10-16 days duration; six trials were undertaken between 1 and 6 months and five trials were greater than 1 year. In this review, trials that were less than 7 days duration were excluded (21 trials), and the results for medium- and long-term trials were grouped together to facilitate meta-analysis. The trials involved adults only;^{17,26} children only^{18-21,23} and mixed populations of adults and children.^{22,24,27-30} The age of the participants was not recorded in two trials.^{23,31} Data on spirometry were available in 10 trials and, in these trials, patients had mild to moderate disease;^{20,22,30} two trials had moderate to severe disease;^{24,26} and five had a broad range of lung function.^{19,25,27–29} CCPT was compared with any other individual form of airway clearance: PEP;^{17–23} high-frequency chest compression, manual or acoustic percussion (HFCC/MP);^{26,27,31} forced expiration technique (FET);³⁰ airway oscillating devices (AOD);^{28,29} AD;^{23,25} or exercise.²⁴

Spirometry and plethysmography

Meta-analysis showed no differences in forced expiratory volume in 1s (FEV₁), forced vital capacity (FVC) and forced expiratory flow₂₅₋₇₅, between CCPT and PEP,^{17,19-23} HFCC/MP,^{26,27,31} AOD,^{28,29} AD^{23,25} or exercise.²⁴

Preference and adherence to therapy

The reporting of preference and adherence to therapy outcomes were not always objective nor

in a format suitable for meta-analysis. In the trials that reported on preference, patients tended to prefer PEP,^{17–19,23} HFCC/MP,^{26,27} and $AD^{23,25}$ to CCPT. Only one trial reported on adherence, and showed little difference between adherence to CCPT and PEP.¹⁹ One other trial referred to an adherence device but no data were available.²²

Quality of life

Insufficient data on QoL were available for metaanalysis. One trial reported no difference in QoL between PEP and CCPT.²²

Number of days in hospital per year

Data on number of days in hospital per year were not in a format suitable for meta-analysis. Two trials reported on this outcome and found no difference in the number of hospital admissions in CCPT compared with AOD²⁸ or FET.³⁰

Number of admissions per year

Insufficient data on number of admissions per year were available for meta-analysis. Two trials reported on this outcome and found no difference in the number of hospital admissions in CCPT compared with PEP¹⁹ or FET.³⁰

Number of intravenous antibiotics per year

Insufficient data on the number of intravenous antibiotics per year were available for metaanalysis. Two trials reported on this outcome. One trial reported that days on antibiotic therapy was higher in the PEP group,¹⁸ and one trial showed no difference in the number of oral and intravenous antibiotics between the HFCC/MP and CCPT groups.²⁸

Other

Other outcomes were inconsistently reported in the trials, and, although few data were available on these outcomes, no clear differences between CCPT and other forms of airway clearance in exercise capacity were observed,^{22,24,30} in TLC and residual volume,^{17,24,26,29} mucus transport rate,¹⁷ Schwachmann scores,^{19,30} sputum production,^{20,21,26,31} bacteriology,^{19,30} cough,^{20,21} SpO₂,^{18,26} and nutritional status.^{26,28}

Adverse events

Adverse events were reported sporadically, and it was stated that they may have been spontaneous or unrelated to any of the interventions.

Practice points

- Medium- and long-term trials have shown that CCPT is at least as effective as other forms of airway clearance
- Patients tended to prefer techniques that promoted independence to CCPT

Systematic review 3

PEP compared with other forms of airway clearance in CF

Twenty trials of mixed designs were included in this review (seven trials in this review overlapped with those in systematic review 2,17-23 and one trial overlapped with systematic review 4.³² These trials involved adults only;¹⁷ children only^{18–21,23,33–35} and mixed populations of adults and children. $^{12-16,22,32,36-39}$ Data on spirometry were available in 10 trials to facilitate classification of disease severity. Spirometry ranged from normal to severe in these 10 trials. Seven trials were single-treatment trials,^{12–15,32,36,38} two trials were short-term trials (treatment interventions up to 7 days)^{15,37} and 11 were longer term trials (2 weeks up to 2 vears),^{17–23,33–35,39} with a total of 429 participants. PEP was compared with several different airway clearance regimens, and a number of trials had numerous comparison groups within each trial: postural drainage with a combination of vibrations breathing exercises, percussion, (PDPV);^{12,16–23,34,36–39} high-frequency chest compression;¹⁶ pursed-lipped breathing;³⁶ NIV;³² AD;^{14,23} flutter;^{33–35} and control/spontaneous coughing.^{12–16} PEP was also compared with exercise prescribed for the purpose of airway clearance.³⁸

Spirometry and plethysmography

Three single-treatment trials reported significant differences in post-treatment spirometry/plethysmography: one trial found FVC was significantly increased using PEP compared with conventional physiotherapy;³⁶ in one trial, functional residual capacity and TLC was significantly increased using PEP (15 cmH₂O) compared with PEP (5 cmH₂O);¹³ in one trial, FEV₁ and FVC was significantly lower using AD and PEP combined in one session compared with AD alone.¹⁴ The other single and shortterm trials found no differences in spirometry using PEP compared with any of the other airway clearance regimens.^{12,15,16,32,37,38} One long-term trial reported significant improvements in FEV₁ or FVC using PEP compared with PDPV.¹⁹ The other long-term trials found no difference in spirometry^{17,20–23,33–35,39} or plethysmography^{17,35} using PEP compared with other airway clearance regimens.

Sputum expectoration or mucus clearance

Two single-treatment trials found significantly more secretions were expectorated during PEP compared with PDPV, pursed-lipped breathing³⁶ or AD.¹⁴ In one short-term trial, significantly more secretions were expectorated during PDPV compared with PEP.³⁷ Other single-treatment and short-term trials found no difference in sputum expectoration during PEP compared with other airway clearance regimens.^{12,16,20,21} Five single-treatment trials measured mucus clearance. One trial showed that clearance was significantly greater with PEP than FET alone.¹⁵ The other trials showed no difference in mucus clearance with PEP and the other techniques.^{12,13,17,38}

Preference and adherence to therapy

This outcome was measured in nine trials. In one single-treatment trial, patients preferred PEP to other techniques (PDPV or pursed-lip breathing)³⁶ and, in another trial, patients preferred NIV to PEP.³² One short-term trial showed no difference in preferences between PEP and other techniques (PDPV, HFCC or cough).¹⁶ In the six longer term trials, PEP was preferred to the other treatment techniques.^{17–19,23,33,39} Two long-term trials reported on adherence, and found no clear differences between PEP and PDPV¹⁹ and flutter.³³

Blood oxygen levels

In one single-treatment trial, the improvement in SpO_2 was significantly lower with PEP compared with NIV.³² In one short-term trial, no significant differences were found in SpO_2 in the middle or after treatment when PEP was compared with PDPV,³⁷ and, in the other short-term trial, SpO_2 was greater in PEP than in other techniques.³⁶

Number of respiratory exacerbations per year

In a long-term trial, the PEP group had a significantly reduced rate of hospital admissions compared with the flutter group. $^{\rm 33}$

Other

In two long-term trials, when PEP was compared with PDPV, no difference in well-being was observed.²² Increased bronchial markings were significantly less common in the PEP group compared with the PDPV group.¹⁸ In two other longer trials, no difference was reported in radiographic scores in PEP compared with PDPV¹⁹ and flutter.³³

Adverse events

Two long-term trials found no clear differences in the number of adverse events between PEP and PDPV.^{18,19}

Practice point

• Single, short and longer term trials show that PEP is at least as effective as other forms of airway clearance

Systematic review 4

Airway clearance with non-invasive ventilation compared with airway clearance with no non-invasive ventilation in CF

Three randomised, crossover trials, which compared a single-treatment session of airway clearance with NIV, with airway clearance without NIV were included, with a total of 62 participants (one trial overlapped with systematic review 3;³² one trial involved adults only;⁴⁰ one trial involved children only;⁴¹ and one trial involved a mixed population of adults and children.³² Data on spirometry indicated that one trial included patients with mild disease; one trial included patients in all disease categories and one trial included patients with severe disease. NIV for airway clearance was compared with PEP³² or ACBT/FET.^{40,41}

Spirometry and plethysmography

No difference was reported in post-treatment spirometry (FEV₁, FVC, FEF₂₅₋₇₅) using NIV compared with PEP or ACBT/FET. 32,40,41

Respiratory rate was significantly lower during NIV than during ACBT/FET.⁴¹ Post-treatment PI_{max} and PE_{max} were significantly greater after NIV compared with PEP or ACBT/FET.^{40,41}

Sputum expectoration and mucus clearance

No significant difference was observed in the amount of sputum expectorated during NIV compared with ACBT/FET.^{40,41}

Blood oxygen levels

SpO₂ improved significantly when NIV was used for airway clearance compared with PEP or ACBT/ FET.^{32,40,41}

Respiratory symptom scores

In one trial, most participants considered expectoration to be easier and felt less tired with NIV compared with FET.⁴¹ No difference was found in the Borg breathlessness score after treatment with NIV compared with ACBT.⁴⁰

Adherence to treatment and preference

Most patients stated that they preferred NIV to PEP or ACBT/FET.^{32,40,41} Most physiotherapists found it easier to perform airway clearance using NIV.⁴¹

Practice points

- Short-term trials show that NIV is more effective than other airway clearance regimens in patients with more severe disease who have difficulty clearing sputum
- The long-term effect of NIV used for airway clearance is unknown

Systematic review 5

Physical training compared with no physical training in CF

Seven trials using randomised parallel-group design were included (one trial in this review overlapped with those in systematic review 2^{24}); four short-term trials (inpatient up to 1 month) and three long-term trials (outpatient based up to 3 years), with a total of 231 participants. One trial included adults only,⁴² three trials included children only⁴³⁻⁴⁵ and three trials included a mixed

population of both adults and children.^{24,46,47} Disease severity based on spirometry ranged from mild to severe disease. Physical training was compared with airway clearance,²⁴ normal activity or no specific training.^{42–47} The results were reported under effects of aerobic training compared with no training and anaerobic training compared with no training.

Aerobic versus no physical training

Exercise capacity

One short-term trial showed a significant improvement in exercise tolerance⁴⁴ but a long-term trial did not.⁴⁷ Most short- and long-term trials reported no significant difference in physiological responses during exercise testing in physical training compared with airway clearance;²⁴ no training;⁴⁴ or normal activity.⁴⁷ However, in a long-term trial, training was significantly reduced compared with normal activity in the ratio of peak-minute ventilation/peak-load during arm ergometry; lactate was also significantly reduced during bicycle ergometry in training compared with normal activity.⁴²

Specific indices of strength, mass effort and general fatigue

In a short-term trial, aerobic training resulted in a significantly greater increase in lower limb strength than no specific physical training.⁴⁴

Spirometry/plethysmography

In two short-term trials, no significant differences were found in spirometry after aerobic training compared with bronchial hygiene²⁴ or no specific physical training.⁴⁴ Longer term trials showed that aerobic physical training had no significant effect on FEV₁ but a significant and positive effect on FVC compared with normal activity.^{42,47}

Symptom scores

In a short-term trial, no significant differences were found between physical training and bronchial hygiene in the number of coughs or in dry sputum weight or volume.²⁴

Weight

One short-term trial found no significant difference in weight change or fat-free mass when aerobic training was compared with no specific training.⁴⁴ The long-term trials also showed no significant change in body-mass index or annual rate of decline in per cent ideal weight for height in aerobic training compared with normal activity.^{42,47}

Adherance with physical training

In one long-term trial, adherence was rated between partial and full.⁴⁷

Other

Aerobic physical training did not significantly affect the number of acute exacerbations requiring hospitalisation or compliance with other treatments compared with normal activity.⁴⁷

Anaerobic training compared with no physical training

Exercise capacity

No improvement in exercise capacity was observed in short-term anaerobic physical training compared with no specific physical training;⁴⁴ however, a long-term trial showed a significantly greater improvement in VO₂ peak in anaerobic physical training compared with normal activity.⁴⁵ One longterm trial reported significantly lower lactate levels with anaerobic training compared with normal activity.⁴⁵

Specific indices of strength, mass effort and general fatigue

In both short- and long-term trials, parameters of strength in the physical training group was significantly increased compared with no specific physical training⁴⁴ or normal activity.⁴⁴

Spirometry/plethysmography

In a short-term trial, the anaerobic training group showed a significantly greater mean percentage increase in FEV₁ compared with no specific physical training.⁴⁴ No significant differences were observed in FVC in the anaerobic training group compared with no specific physical training⁴⁴ or normal activity.⁴⁵

QoL

In one long-term trial, physical function was no different between anaerobic training and normal activity.⁴⁵

Weight

In one short-term trial, there was significantly greater change in weight and change in fat-free mass in the anaerobic group than no specific training.⁴⁴ In one long-term trial, no significant difference was observed in change in body composition between anaerobic training and normal activity.⁴⁵

In one long-term trial, adherence was reported to be 98%. The reasons for absence were holidays or sickness. $^{\rm 45}$

Practice points

- Short- and longer term trials show some benefit of physical training compared with no physical training
- There is no evidence to support or refute the substitution of airway clearance sessions with physical training

Discussion and conclusions

This paper summarises the evidence from Cochrane systematic reviews regarding the efficacy of physical therapies (airway clearance and physical training) currently included in the CF care-management plan. No definitive evidence is available from the Cochrane systematic reviews regarding the longterm efficacy of airway clearance over no airway clearance. There is widespread consensus among patients and health professionals that airway clearance is an essential component of CF care and so, despite "lack of evidence", it is unlikely that any future trials will be carried out to establish the long-term efficacy of airway clearance compared with no airway clearance in CF. One exception to this is the role of airway clearance in asymptomatic patients with little consensus on whether airway clearance is necessary or if the proposed benefits are outweighed by proposed deleterious effects. Whether a trial to address this important question is ethical is currently a matter of much debate.

Irrespective of the exact mechanisms, airway clearance regimens promote mucociliary clearance by altering airflow and mucous viscosity. Evidence from the Cochrane systematic reviews support current expert opinion that no one airway clearance regimen is better than another. It is likely that specific airway clearance regimens may be more effective in some circumstances (e.g. one of the Cochrane systematic reviews supports the use of NIV compared with other airway clearance regimens in patients with more severe disease who have difficulty clearing sputum). Unfortunately, the reviews could not provide evidence-based guidance on what therapies are most effective in which circumstances, and this should be the focus of future research in this area (e.g. establishing efficacy of treatments in specific subgroups of patients⁵).

Few of the trials in this review report on adherence; however, other trials have shown that adherence to airway clearance and exercise in CF is generally reported to be poor (40-55%).⁴⁸ Data are consistent that treatment factors (the duration and the complexity of the treatment) or trait factors (worry and confidence in medical practitioners) are important determinants of adherence; however, although they have some explanatory value, significant amounts of the variance in adherence behaviours is unaccounted for and warrants further trial. Research needs to focus on what the minimum criteria for adherence in relation to airway clearance and exercise is (i.e. how much is enough), and strategies to maximise adherence in different sub-groups of patients need to be developed and incorporated into care packages.

One of the reviews provided evidence that individuals may prefer airway clearance regimens that are self-administered and facilitate independence. The specific regimen chosen can be alternated within an airway clearance session and during different stages of disease (e.g. patients may prefer an independent airway regimen during a stable phase of disease and a more passive regimen during an acute exacerbation). Physical therapists involved in the care of patients with CF should ensure that they are competent in the use of currently available and any new physical therapy interventions, so that both the patients and physical therapist has maximum choice of treatment options.

Some patients (either on the advice of the cysticfibrosis team or independently) substitute airway clearance sessions with physical exercise. The reviews in this paper do not provide enough evidence to support or refute this practice. There is some evidence to support the inclusion of physical training in the care-management plan of CF. The benefits obtained from including physical training in a package of care may be influenced by the type of training programme, and the inclusion of both aerobic and anaerobic training are probably important. Physical training is already part of the care package offered to most patients with CF, and there is an absence of evidence to actively discourage this.

Potential adverse events from physical therapies include dyspnoea, gastro-oesophageal reflux, bronchospasm, hypoxaemia, pain, fatigue, dehydration and haemoptysis, and, to a lesser extent, rib fractures and pneumothorax. The incidence of adverse events reported in these reviews was low. Adverse events can be minimised by considering relative contra-indications to treatments. Where adverse events occur, most are reversible with termination or modification of the physical therapy. Therefore, the occurrence or potential for adverse events should be reported using a standard format in future trials so that they can be used to guide treatment choice.

A number of limitations apply to all the Cochrane systematic reviews included in this overview. Most of the trials in the individual reviews included relatively small numbers of patients. Not all trials reported on each key outcome, and outcomes are not reported in a consistent format. This resulted in only one review conducting a metaanalysis and, as such, summary estimates are not available on the overall effect of many of the interventions. Many of the trials in the systematic reviews were crossover trials, which compared the efficacy of one intervention with another intervention with no control, placebo group, or both. These Cochrane systematic reviews have only summarised the results of randomised trials and, in effect, ignored the huge amount of lower quality evidence (non-randomised trials) investigating efficacy of physical therapies in CF. It is important to highlight, however, that most lower-quality trials support the findings of these Cochrane systematic reviews.

The trials in these Cochrane systematic reviews are primarily short- to medium-term trials, and only limited evidence is available from long-term trials to support the inclusion of physical therapies in the care-management plan for CF. Short-term efficacy may not reflect long-term efficacy of an intervention, and is therefore of limited relevance in a chronic life-long condition such as CF. Shortterm trials should only be carried out to obtain preliminary data on new techniques in order to rationalise the need for a longer term trial.

A consensus urgently needs to be reached on which outcome measures are appropriate for physical therapy trials. Improved therapies have progressively slowed the decline in spirometry over the past few decades, and, consequently, the sensitivity of spirometry as a measure of short- to medium-term efficacy in physical therapy trials is probably questionable. Nevertheless, spirometry remains a strong predictor of mortality, and therefore should remain a primary outcome measure in longer term trials. As current evidence suggests that physical therapy interventions are equally beneficial, treatment duration, patient preference and patient adherence may be important primary outcomes. Other outcomes, such as frequency of exacerbations, guality of life or antibiotics may also be important. The association between sputum output and spirometry or disease progression is unclear, and consequently the relevance or validity of sputum output in physical therapies trials is often debated. Despite this, patients use sputum output to measure the relative effectiveness of different airwav clearance regimens and, therefore, in our opinion, this is an important outcome measure in airway clearance trials. To facilitate inclusion of future trials in systematic reviews, it is essential that consensus is reached on both the specific outcome measurement tools used and on the method of reporting outcomes.

Physical therapies are part of the care-management plan in CF. The Cochrane systematic reviews summarised in this review provide some evidence to support this practice and no evidence to discourage their inclusion. These Cochrane systematic reviews provide a clear summary of previous research findings as well as rationale for further research to expand the evidence base for physical therapies in CF.

References

- 1. Yankaskas JR, Marshall BC, Sufian B, Simon RH, Rodman D. Cystic fibrosis adult care. Concensus conference report. *Chest* 2004;125:1s–39s.
- 2. Pryor JAP, Prasad SA. *Physiotherapy for respiratory and cardiac problems: adults and paediatrics*, 3rd ed. Edinburgh: Churchill Livingstone; 2003.
- 3. ACPCF 2002. *Clinical guidelines for the physiotherapy management of cystic fibrosis.* Bromley, Kent: Cystic Fibrosis Trust; 2003.
- 4. Hess DR. The evidence for secretion clearance techniques. *Respir Care* 2001;46:1276–92.
- 5. Young C, Horton R. Putting clinical trials into clinical context. *Lancet* 2005;**366**:107–8.
- van der Schans C, Prasad A, Main E. Chest physiotherapy compared to no chest physiotherapy for cystic fibrosis. In: *The Cochrane Library, Issue 2*. Chichester: Wiley; 2000.
- 7. Main E, Prasad A, van der Schans C. Conventional chest physiotherapy compared to other airway clearance techniques for cystic fibrosis. In: *The Cochrane Library, Issue 1*. Chichester: Wiley; 2005.
- Elkins MR, Jones A, van der Schans C. Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis. In: *The Cochrane Library, Issue 1*. Chichester: Wiley; 2004.
- Moran F, Bradley J. Non-invasive ventilation for cystic fibrosis. In: *The Cochrane Library, Issue* 2. Chichester: Wiley; 2003.
- 10. Bradley J, Moran F. Physical training for cystic fibrosis. In: *The Cochrane Library, Issue* 2. Chichester: Wiley; 2002.
- 11. Rossman CM, Waldes R, Sampson D, Newhouse MT. Effect of chest physiotherapy on the removal of mucus in patients with cystic fibrosis. *Am Rev Respir Dis* 1982;126: 131–5.

- Mortensen J, Falk M, Groth S, Jensen C. The effects of postural drainage and positive expiratory pressure physiotherapy on tracheobronchial clearance in cystic fibrosis. *Chest* 1991;100:1350–7.
- 13. van der Schans CP, van der Mark TW, de Vries G, et al. Effect of positive expiratory pressure breathing in patients with cystic fibrosis. *Thorax* 1991;46:252–6.
- Pfleger A, Theißl B, Oberwaldner B, Zach MS. Selfadministered chest physiotherapy in cystic fibrosis: a comparative trial of high-pressure PEP and autogenic drainage. *Lung* 1992;170:323–30.
- Falk M, Mortensen J, Kelstrup M, Lanng S, Larsen L, Ulrik CS. Short-term effects of positive expiratory pressure and the forced expiration technique on mucus clearance and lung function in CF [abstract]. *Pediatr Pulmonol* 1993(Suppl 9):241.
- Braggion C, Cappelletti LM, Cornacchia M, Zanolla L, Mastella G. Short-term effects of three chest physiotherapy regimens in patients hospitalized for pulmonary exacerbations of cystic fibrosis: a cross-over randomized trial. *Pediatr Pulmonol* 1995;19:16–22.
- Darbee J, Dadparvar S, Bensel K, Jehan A, Watkins M, Holsclaw D. Radionuclide assessment of the comparative effects of chest physical therapy and positive expiratory pressure mask in cystic fibrosis [abstract]. *Pediatr Pulmonol* 1990(Suppl 5):251.
- Costantini D, Brivio A, Brusa D, et al. PEP mask versus postural drainage in CF infants a long-term comparative trial [abstract]. *Pediatr Pulmonol* 2001(Suppl 22):308.
- McIlwaine PM, Wong LT, Peacock D, Davidson AG. Long-term comparative trial of conventional postural drainage and percussion versus positive expiratory pressure physiotherapy in the treatment of cystic fibrosis. *J Pediatr* 1997;131: 570–4.
- 20. Tyrrell JC, Hiller EJ, Martin J. Face mask physiotherapy in cystic fibrosis. *Arch Dis Child* 1986;61:598–600.
- van Asperen PP, Jackson L, Hennessy P, Brown J. Comparison of a positive expiratory pressure (PEP) mask with postural drainage in patients with cystic fibrosis. *Aust Paediatr J* 1987;23:283–4.
- Gaskin L, Corey M, Shin J, Reisman JJ, Thomas J, Tullis DE. Long term trial of conventional postural drainage and percussion vs. positive expiratory pressure [abstract]. *Pediatr Pulmonol* 1998;17(Suppl):345.
- McIlwaine PM, Davidson AGF. Comparison of positive expiratory pressure and autogenic drainage with conventional percussion and drainage therapy in the treatment of CF [abstract]. In: Proceedings of the 17th European cystic fibrosis conference, June 18–21, 1991, Copenhagen, p. 58.4.
- 24. Cerny FJ. Relative effects of bronchial drainage and exercise for in-hospital care of patients with cystic fibrosis. *Phys Ther* 1989;69:633–9.
- Davidson AGF, Wong LTK, Pirie GE, McIlwaine PM. Long-term comparative trial of conventional percussion and drainage physiotherapy versus autogenic drainage in cystic fibrosis [abstract]. *Pediatr Pulmonol* 1992;235.
- Arens R, Gozal D, Omlin KJ, et al. Comparison of high frequency chest compression and conventional chest physiotherapy in hospitalized patients with cystic fibrosis. *Am J Respir Crit Care Med* 1994;150:1154–7.
- Bauer ML, McDougal J, Schoumacher RA. Comparison of manual and mechanical chest percussion in hospitalized patients with cystic fibrosis. J Pediatr 1994;124: 250–4.

- Homnick DN, White F, de Castro C. Comparison of effects of an intrapulmonary percussive ventilator to standard aerosol and chest physiotherapy in treatment of cystic fibrosis. *Pediatr Pulmonol* 1995;20:50–5.
- 29. Homnick DN, Anderson K, Marks JH. Comparison of the flutter device to standard chest physiotherapy in hospitalized patients with cystic fibrosis: a pilot trial. *Chest* 1998; 114:993–7.
- Reisman JJ, Rivington-Law B, Corey M, et al. Role of conventional physiotherapy in cystic fibrosis [see comments]. J Pediatr 1988;113:632–6.
- Kraig R, Kirkpatrick KR, Howard D, Ter-Pogossian M, Kollef MH. A direct comparison of manual chest percussion with acoustic percussion, an experimental treatment for cystic fibrosis [abstract]. Am J Respir Crit Care Med Suppl 1995;151:A738.
- Kofler AM, Carlesi A, Cutrera R, et al. BiPAP versus PEP as chest physiotherapy in patients with cystic fibrosis [abstract]. *Pediatr Pulmonol* 1998(Suppl 17):344.
- McIlwaine PM, Wong LT, Peacock D, Davidson AGF. Long-term comparative trial of positive expiratory pressure versus oscillating positive expiratory pressure (flutter) physiotherapy in the treatment of cystic fibrosis. J Pediatr 2001;138: 845–50.
- Padman R, Geouque DM, Engelhardt MT. Effects of the flutter device on pulmonary function trials among pediatric cystic fibrosis patients. *Del Med J* 1999;71: 13–8.
- van Winden CM, Visser A, Hop W, Sterk PJ, Beckers S, de Jongste JC. Effects of flutter and PEP mask physiotherapy on symptoms and lung function in children with cystic fibrosis. *Eur Respir J* 1998;12:143–7.
- Falk M, Kelstrup M, Andersen JB, et al. Improving the ketchup bottle method with positive expiratory pressure, PEP, in cystic fibrosis. *Eur J Respir Dis* 1984;65: 423–32.
- Hofmeyr JL, Webber BA, Hodson ME. Evaluation of positive expiratory pressure as an adjunct to chest physiotherapy in the treatment of cystic fibrosis. *Thorax* 1986;41:951–4.
- Lannefors L, Wollmer P. Mucus clearance with three chest physiotherapy regimes in cystic fibrosis: a comparison between postural drainage, PEP and physical exercise. *Eur Respir J* 1992;5:748–53.
- Steen HJ, Redmond AO, O'Neill D, Beattie F. Evaluation of the PEP mask in cystic fibrosis. *Acta Paediatr Scand* 1991; 80:51–6.
- Holland AE, Denehy L, Ntoumenopoulos G, Naughton MT, Wilson JW. Non-invasive ventilation assists chest physiotherapy in adults with acute exacerbations of cystic fibrosis. *Thorax* 2003;**58**:880–4.
- 41. Fauroux B, Boule M, Lofaso F, et al. Chest physiotherapy in cystic fibrosis: improved tolerance with nasal pressure support ventilation. *Pediatrics* 1999;103:1–9.
- Moorcroft AJ, Dodd ME, Morris J, Webb AK. Individualised unsupervised exercise training in adults with cystic fibrosis: a 1 year randomised controlled trial. *Thorax* 2004;59: 1074–80.
- 43. Turchetta A, Bella S, Calzolari A, et al. Effect of controlled physical activity on lung function test of cystic fibrosis children [abstract]. In: *Proceedings of the 17th European cystic fibrosis conference*, June 18–21, 1991, Copenhagen, p. 134.
- 44. Selvadurai HC, Blimkie CJ, Meyers N, Mellis CM, Cooper PJ, Van Asperen PP. Randomized controlled trial of in-hospital exercise training programs in children with cystic fibrosis. *Pediatr Pulmonol* 2002;33:194–200.

- 45. Klijn PHC, Oudshoorn A, ban der Ent CK, van der Net J, Kimpen JL, Helders PJM. Effects of anaerobic training in children with cystic fibrosis: a randomised controlled trial. *Chest* 2004;**123**:1299–305.
- Michel SH, Darbee JC, Pequignot E. Exercise, body composition and strength in cystic fibrosis [abstract]. *Pediatr Pulmonol* 1989(Suppl 4):116.
- 47. Schneiderman-Walker J, Pollock SL, Corey M, et al. A randomised controlled trial of a 3-year home exercise program in cystic fibrosis. J Pediatr 2000;136: 304–10.
- Kettler LJ, sawyer SM, Winefield HR, Greville HW. Determinants of adherence in adults with cystic fibrosis. *Thorax* 2002;57:459–64.