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[Intervention Review]

Chest physiotherapy compared to no chest physiotherapy for cystic fibrosis

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ABSTRACT

Background

Chest physiotherapy is widely used in people with cystic fibrosis in order to clear mucus from the airways. This is an updated version of previously published reviews.

Objectives

To determine the effectiveness and acceptability of chest physiotherapy compared to no treatment or spontaneous cough alone to improve mucus clearance in cystic fibrosis.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials Register which comprises references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings.

Date of the most recent search of the Group's Cystic Fibrosis Trials Register: 02 June 2015.

Selection criteria

Randomised or quasi-randomised clinical studies in which a form of chest physiotherapy (airway clearance technique) were taken for consideration in people with cystic fibrosis compared with either no physiotherapy treatment or spontaneous cough alone.

Data collection and analysis

Both authors independently assessed study eligibility, extracted data and assessed the risk of bias in the included studies. There was heterogeneity in the published outcomes, with variable reporting which meant pooling of the data for meta-analysis was not possible.

Main results

The searches identified 157 studies, of which eight cross-over studies (data from 96 participants) met the inclusion criteria. There were differences between studies in the way that interventions were delivered, with several of the intervention groups combining more than one treatment modality. One included study looked at autogenic drainage, six considered conventional chest physiotherapy, three considered oscillating positive expiratory pressure, seven considered positive expiratory pressure and one considered high pressure positive expiratory pressure. Of the eight studies, six were single-treatment studies and in two, the treatment intervention was performed over two consecutive days (once daily in one, twice daily in the other). This enormous heterogeneity in the treatment interventions prevented any meta-analyses from being performed. Blinding of participants, caregivers or clinicians in airway clearance studies is

impossible; therefore this was not considered as a high risk of bias in the included studies. Lack of protocol data made assessment of risk of bias unclear for the majority of other criteria.

Four studies, involving 28 participants, reported a higher amount of expectorated secretions during chest physiotherapy as compared to a control. One study, involving 18 participants, reported no significant differences in sputum weight. In five studies radioactive tracer clearance was used as an outcome variable. In three of these (28 participants) it was reported that chest physiotherapy, including coughing, increased radioactive tracer clearance as compared to the control period. One study (12 participants) reported increased radioactive tracer clearance associated with all interventions compared to control, although this was only reported to have reached significance for postural drainage with percussion and vibrations; and the remaining study (eight participants) reported no significant difference in radioactive tracer clearance between chest physiotherapy, without coughing, compared to the control period. Three studies, involving 42 participants reported no significant effect on pulmonary function variables following intervention; but one further study did report significant improvement in pulmonary function following the intervention in some of the treatment groups.

Authors' conclusions

The results of this review show that airway clearance techniques have short-term effects in the terms of increasing mucus transport. No evidence was found on which to draw conclusions concerning the long-term effects.

PLAIN LANGUAGE SUMMARY

Chest physiotherapy compared to no chest physiotherapy for cystic fibrosis

Review question

We reviewed the evidence about the effect of using chest physiotherapy compared to no physiotherapy for clearing excess mucus from the lungs of people with cystic fibrosis.

Background

The lungs of people with cystic fibrosis produce excess mucus. This leads to repeated infection and tissue damage in the lungs. It is important to clear the mucus using drugs and chest physiotherapy. Physiotherapy clears mucus by different techniques or by using mechanical devices or both. Daily physiotherapy takes a lot of time and trouble so it is important to know if it works. We searched for studies where the people taking part had equal chances of being in the group using chest physiotherapy or the group with no chest physiotherapy. This is an update of previously published reviews.

Search date

The evidence is current to: 02 June 2015.

Study characteristics

We included eight studies in the review reporting results from a total of 96 people with cystic fibrosis. All the studies were very different and some looked at multiple treatments compared to no treatment. One study looked at autogenic drainage, six considered conventional chest physiotherapy, three considered oscillating positive expiratory pressure, seven considered positive expiratory pressure and one considered high pressure positive expiratory pressure. We could not combine the results to analyse them statistically.

Key results

Summarising the findings of these eight studies, we found that methods of clearing the airways have short-term benefits for moving mucus. Three studies measured sputum which had been coughed up and found those people using chest physiotherapy coughed up more sputum; four studies measured radioactive tracer clearance and found increased clearance with chest physiotherapy. Only one study reported an improvement in lung function in some of the treatment groups; but three other studies who reported this outcome did not find any significant effect from chest physiotherapy. At present there is no clear evidence of long-term effects in chest clearance, quality of life or survival with chest physiotherapy.

Quality of the evidence

Most of the included studies had some design problems which may affect confidence in the results. In just under half of the studies it was not clear as to whether all of the results were reported.

In physiotherapy studies the person and their physiotherapist will know which treatment they are receiving and this may affect some of the findings. Half the studies looked at amount of sputum coughed up and lung function testing, with a quarter asking the person's views on the treatment and these results may have been affected by being aware of the treatment. In all of the studies it was not clear if the person was experienced in carrying out the treatment. This may affect how well they were able to do the treatment which could affect confidence in the results.

BACKGROUND

Description of the condition

Cystic fibrosis (CF) is a common inherited life-limiting disorder. Persistent infection and inflammation within the lungs are the major contributory factors to severe airway damage and loss of respiratory function over the years (Cantin 1995; Konstan 1997). Excessive production of thick mucus may overwhelm the normal mucus transport mechanisms and thereby lead to airway obstruction and mucus plugging (Zach 1990). Removal of airway secretions is therefore an integral part of the management of CF. A variety of methods are used to help remove secretions from the lungs, some physical, i.e. chest physiotherapy, and some chemical, i.e. medications and inhalation therapies. Treatment methods which improve mucus clearance are considered essential in optimising respiratory status and reducing the progression of lung disease.

Description of the intervention

Chest physiotherapy has, for a long time, played an important role in assisting the clearance of airway secretions and is usually commenced as soon as the diagnosis of CF is made. However, the performance of chest physiotherapy may be unpleasant, uncomfortable, and time-consuming. Early chest physiotherapy relied on techniques for which the assistance of another person, such as a physiotherapist or relative, was needed and which included postural drainage, percussion, vibration, and shaking performed by an assistant and huffing or coughing. More recently, several self-administered alternatives to these conventional techniques have been developed. These include the active cycle of breathing techniques (ACBT), forced expiration technique (FET), autogenic drainage (AD), positive expiratory pressure (PEP), flutter, high frequency chest compression (HFCC) and exercise. We have defined all of these methods under the interventions below. These methods of treatment help to give the individual with CF more independence in their management.

Why it is important to do this review

Despite the expansion of treatment modalities, there remains little evidence supporting their efficacy (Prasad 1998; van der Schans 1996). A previous meta-analysis concluded that standard chest physiotherapy resulted in more mucus (phlegm or sputum) expectoration than no treatment in people with CF (Thomas 1995a). Similarly a review into airway clearance techniques used in the management of non-CF related bronchiectasis concluded that there may be improvements in sputum expectoration, selected measures of lung function and health-related quality of life (Lee 2013). Lee, however, also highlighted that data to establish long term efficacy of airway clearance techniques in this population were lacking (Lee 2013). In contrast to these findings a further review by Osadnik suggested the benefits achieved from airway clearance techniques for people with COPD may only confer small benefits in some of the measured clinical outcomes (Osadnik 2012). However, COPD is less frequently associated with the excessive sputum production as often manifested in CF or non-CF related bronchiectasis.

This review is an update of previously published reviews (van der Schans 2000; Warnock 2013). It compares the efficacy of any of the above interventions as compared to no treatment or spontaneous coughing alone. Subsequent reviews will aim to determine whether a specific type of treatment offers any advantage over others.

OBJECTIVES

To determine the effectiveness of chest physiotherapy (airway clearance) compared to no treatment or cough alone in people with CF. This review does not address all possible comparisons between the multiple treatment techniques available for people with CF. This review is the first in a series of reviews which will compare the efficacy of different treatment modalities.

The following hypotheses will be tested: chest physiotherapy, whatever the type of intervention, is more:

1. effective than no chest physiotherapy;
2. effective than spontaneous coughing alone;
3. acceptable than no chest physiotherapy;
4. acceptable than spontaneous coughing alone.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised or quasi-randomised clinical studies.

Short-term studies (less than seven days duration, including single treatment studies) will be analysed separately from studies of longer duration.

Types of participants

People with CF, of any age, diagnosed on the basis of clinical criteria and sweat testing or genotype analysis.

Types of interventions

Chest physiotherapy of any type (see below) compared to no chest physiotherapy or spontaneous coughing alone.

In existing literature and in practical terms, variation occurs in the application of specific techniques. For the purposes of this series of reviews, it is necessary to group these variations under their broader headings. Separate analysis of each variation would render the reviews unmanageable. The following interventions aim to improve mucus transport or facilitate expectoration:

Conventional chest physiotherapy

This will include any combination of the following: postural drainage; percussion; chest shaking; huffing; and directed coughing. It should not include the use of exercise, PEP or other mechanical devices.

Positive expiratory pressure (PEP) mask therapy

As described by the authors to be the primary intervention, with or without additional techniques. PEP is defined as breathing with a positive expiratory pressure of 10 to 25 cmH_20.

High pressure PEP (hPEP) mask therapy

As described by the authors to be the primary intervention, with or without additional techniques. It is a modification of the above

PEP technique but includes a full forced expiration against a fixed mechanical resistance.

Active cycle of breathing techniques (ACBT)

This includes relaxation or breathing control, forced expiration technique (FET), thoracic expansion exercises and may include postural drainage or chest clapping.

Autogenic Drainage (AD)

As described originally by Chevalier or modified versions thereof. The authors should have identified AD to be the primary intervention, with or without additional techniques.

Exercise

With the sole purpose of improving mucus clearance as the primary intervention, with or without additional techniques.

Oscillating devices

Oscillating devices including flutter or cornet, thoracic oscillation, and oral oscillation. Flutter or cornet as described by the authors to be the primary intervention, with or without additional techniques. These devices produce an oscillatory PEP effect. Thoracic oscillation as defined by the authors to be the primary intervention, with or without additional techniques, to provide oscillation to the chest wall. Oral oscillation as defined by the authors to be the primary intervention, with or without additional techniques, to provide oscillation to the airways via the mouth.

Two authors independently categorised the physiotherapeutic interventions.

Types of outcome measures

Primary outcomes

1. Expectorated secretions (mucus, sputum, phlegm), dry or wet weight, or volume (an increase in the amount of expectorated secretions as a short-term effect of the intervention is considered as beneficial)
2. Mucus transport rate (assessed by radioactive tracer clearance)
3. Pulmonary function tests (post-intervention objective change from baseline compared to control)
   a. forced expiratory volume in one second (FEV_1)
   b. forced vital capacity (FVC)
   c. forced expiratory flow between 25% and 75% expired FVC (FEF_{25-75})

Secondary outcomes

1. Oxygen saturation measured by pulse or transcutaneous oximetry
2. Total lung capacity (TLC) and functional residual capacity (FRC) (objective change from baseline compared to control)
3. Radiological ventilation scanning
4. Subjective perception of well-being, ability to participate in activities of daily living
5. Therapy compliance
6. Objective change in exercise tolerance;
7. Nutritional status (assessed by growth, weight, body composition)
8. Number of respiratory exacerbations per year
9. Number of days in hospital per year
10. Number of days of intravenous antibiotics per year
11. Cost of intervention
    a. equipment
    b. duration
12. Deaths
13. Patient preference (*post hoc* change)

Search methods for identification of studies

Electronic searches

Relevant studies were identified from the Group's Cystic Fibrosis Trials Register using the terms: airway clearance techniques.

The Cystic Fibrosis Trials Register is compiled from electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL) (updated each new issue of *The Cochrane Library*), weekly searches of MEDLINE, a search of Embase to 1995 and the prospective handsearching of two journals - *Pediatric Pulmonology* and the *Journal of Cystic Fibrosis*. Unpublished work is identified by searching the abstract books of three major cystic fibrosis conferences: the International Cystic Fibrosis Conference; the European Cystic Fibrosis Conference and the North American Cystic Fibrosis Conference. For full details of all searching activities for the register, please see the relevant sections of the Cystic Fibrosis and Genetic Disorders Group Module.

Date of the most recent search of the Group's Trials Register: 02 June 2015.

Data collection and analysis

Selection of studies

For the original review two authors from different centres independently assessed which studies should be included. In the event of disagreement about inclusion of a study, they asked an independent author from a third centre to review the paper(s) in question. For updates since 2013, two new authors (AG, LW) from the same centre have independently assessed studies for inclusion in the review; if there was any disagreement they asked the third author (CvdS) to arbitrate.

Data extraction and management

Each author independently extracted data on the outcome measures listed above. Review authors planned to use the Cochrane Review Manager software to compile and analyse the data, but were only able to present a narrative summary (Review Manager 2011).

The authors planned to present short-term studies (defined as having a duration of seven days or less) separately to longer-term studies. The authors planned to group outcome data from longer-term studies (more than seven days) into those measured at one, three, six, 12 months and annually thereafter. If outcome data are recorded at other time periods, then the authors planned to consider examining these as well.

Assessment of risk of bias in included studies

In the original review, the authors independently assessed the methodological quality of the included studies using a system as

described by Jadad (Jadad 1996). In the event of disagreement about the quality score, they asked an independent author from a third centre to review the paper(s) in question. The authors considered aspects such as generation of randomisation sequence, the concealment of this sequence, degree of blinding and whether data were reported completely.

For the 2013 update of the review, the new author team assessed the risk of bias of the included studies according to the methods described in Chapter 8 of *The Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Specifically, the authors judged there to be either a high, low or unclear risk of bias from sequence generation, concealment of sequence allocation, blinding (from participants, clinicians and outcome assessors), missing data and reporting biases.

Measures of treatment effect

For continuous outcomes, the authors planned to record either the mean change from baseline for each group or mean post-treatment or intervention values and the standard deviation (SD) or standard error (SE) for each group. In the case of binary outcomes, the authors planned to calculate the odds ratios (OR) and their 95% confidence intervals (CIs).

Unit of analysis issues

If studies had a cross-over design, the authors planned to analyse the data from these as recommended by Elbourne; however this was not possible with the data currently available (Elbourne 2002).

Dealing with missing data

In order to allow an intention-to-treat analysis, the authors collected data on the number of participants with each outcome event by allocated treated group irrespective of compliance and whether or not the participant was later thought to be ineligible or otherwise excluded for treatment or follow up. Where there was evidence of missing data the authors contacted the primary investigator for clarification.

Assessment of heterogeneity

When the authors are able to include a sufficient number of studies in a meta-analysis, they plan to assess heterogeneity using the I^2 statistic (Higgins 2003). This measure describes the percentage of total variation across studies that are due to heterogeneity rather than by chance (Higgins 2003). The values of I^2 lie between 0% and 100%, and a simplified categorization of heterogeneity that we plan to use is of low (I^2 value of 25%), moderate (I^2 value of 50%), and high (I^2 value of 75%) (Higgins 2003).

Assessment of reporting biases

The authors assessed all included studies for potential reporting bias including missing outcome values and relationships with sponsors.

Where possible the authors sought the study protocols and compared these with the final publications to ensure all measured outcomes were reported. If a study protocol was not available, the review authors compared the 'Methods' and 'Results' sections of each final publication to identify any discrepancies in outcome reporting.

Data synthesis

The authors were not able to present data in a meta-analysis for this version of the review. However, if in future they are able to perform a meta-analysis they will combine the data using a fixed-effect model if there is little or no heterogeneity (i.e. I^2 is less than 25%). If there is a moderate or high degree of heterogeneity (i.e. I^2 is equal to or greater than 50%), they plan to use a random-effects model.

Subgroup analysis and investigation of heterogeneity

If the authors identify a high degree of heterogeneity (i.e. I^2 is equal to or greater than 75%), they plan to investigate this using subgroup analyses including long-term versus short-term interventions. Subgroup analyses looking at the effects of specific interventions has been carried out in a series of separate physiotherapy reviews published by the Cochrane Cystic Fibrosis and Genetic Disorders Review Group (Elkins 2006; Main 2005; Morrison 2009; McKoy 2012).

Sensitivity analysis

The authors plan to test the robustness of their results by performing a sensitivity analysis of the data comparing results with and without quasi-randomised studies.

RESULTS

Description of studies

Results of the search

Of the 157 studies of airway clearance techniques identified by the literature searches, 149 were excluded and eight studies were included.

Included studies

Study design

The eight included studies were all cross-over in design and all included a control period (Braggion 1995; Elkins 2005; Falk 1993; Jarad 2010; Mortensen 1991; Pfleger 1992; Rossman 1982; van der Schans 1991).

Four studies compared two active therapies to control (Falk 1993; Jarad 2010; Mortensen 1991; van der Schans 1991). The study by Jarad, however, included one group which did not receive a recognised airway clearance technique (hydro acoustic therapy (HAT)) as one of the interventions and therefore this treatment arm of the study was excluded from the current review (Jarad 2010). One study compared three active therapies to control (Braggion 1995); and the remaining three studies compared four active therapies to control (Elkins 2005; Pfleger 1992; Rossman 1982).

Most studies undertook single treatments per day (Elkins 2005; Falk 1993; Mortensen 1991; Pfleger 1992; Rossman 1982; van der Schans 1991). One study administered therapy twice a day for two days (Braggion 1995), and one study repeated each intervention on two successive days (Jarad 2010).

Participants

The number of participants in the studies ranged from six (Rossman 1982) to 19 (Jarad 2010). The age of patients included in the studies ranged from 9.8 years (Pfleger 1992) to 34 years (Elkins 2005). One study included only males (Rossman 1982) and three studies did not report the gender of participants (Elkins 2005; Falk 1993; van

der Schans 1991). The remaining studies all included both male and female participants: eight male, eight female (Braggion 1995); 11 male, eight female (Jarad 2010); six male, four female (Mortensen 1991); five male, nine female (Pfleger 1992). The studies included participants with a wide range of disease severity. The mean (SD) FEV_1% predicted was reported in three studies: 61.7% (17%) (Braggion 1995); 53% (21%) (Pfleger 1992) and 70% (24%) (van der Schans 1991). Elkins included patients with a mean (range) FEV_1% predicted 53% (16% to 88%) (Elkins 2005). Mortenson included participants with a median (range) FEV_1% predicted 38.5% (26% to 101%); and Rossman included participants with FEV_1% predicted ranging from 12% to 77.7% (Rossman 1982). Jarad stated they included patients with FEV_1% predicted less than 80%, however only absolute values were reported in the 'Results' so the disease severity of those entered into this study is unclear (Jarad 2010). Falk did not report details on patients' severity of disease (Falk 1993).

Interventions

The active interventions studied varied greatly between the included studies. The most often used active intervention was PEP breathing combined with the FET (Braggion 1995; Falk 1993; Mortensen 1991); two studies combined postural drainage with FET (Falk 1993; Mortensen 1991) and another study combined HFCC with FET and also with postural drainage (Braggion 1995). Braggion also used postural drainage combined with vibrations, deep breathing, percussion and coughing after each of the active therapies as well as the control sessions (Braggion 1995). Elkins compared postural drainage with percussion and vibrations, PEP, oscillating PEP and matched cough (where participants coughed the maximum numbers of coughs during any of the preceding intervention groups,including control) (Elkins 2005). One study compared PEP breathing, AD, PEP breathing followed by AD or AD followed by PEP breathing with a control period (Pfleger 1992). Van der Schans also used PEP in comparison with control, but varied the water pressure between the two active treatment arms (5 cm water pressure and 15 cm water pressure respectively) and followed this with directed vigorous coughing (van der Schans 1991). Jarad investigated the effect of the flutter and HAT compared to control (although the HAT group has been excluded from this review as it is not a recognised form of airway clearance) (Jarad 2010). The remaining study compared directed vigorous cough, postural drainage, postural drainage with mechanical percussion and conventional physiotherapy with control (Rossman 1982).

The control intervention in three studies was directed coughing (Pfleger 1992; Rossman 1982; van der Schans 1991) and in four studies it was spontaneous coughing (Braggion 1995; Elkins 2005, Falk 1993; Mortensen 1991). The control intervention in the study by Jarad was a placebo form of HAT which involved sitting in a bath with sounds audible, but without delivery of the acoustic waves thought to provide external thoracic oscillation therapy (Jarad 2010).

Outcome measures

The most common outcomes measured by the studies were: sputum weight, assessed by five of the included studies (Braggion 1995; Jarad 2010; Mortensen 1991; Pfleger 1992; Rossman 1982), two of which specified both wet and dry sputum weight (Braggion 1995; Jarad 2010); and radioactive tracer clearance also assessed by five studies (Elkins 2005; Falk 1993; Mortensen 1991; Rossman 1982; van der Schans 1991). Additionally, four studies reported pulmonary function tests (Braggion 1995; Jarad 2010; Pfleger 1992; van der Schans 1991). Three of these reported FEV_1 and FVC (Braggion 1995; Jarad 2010; Pfleger 1992); and two studies additionally reported $FEF_{25-75\%}$ (Braggion 1995; Jarad 2010). Other pulmonary function tests reported were: forced expiratory flow at 75% (FEF_{75}) (Jarad 2010); residual volume as a fraction of total lung capacity (RV/TLC) and airway resistance (Raw) (Pfleger 1992); TLC and FRC (van der Schans 1991). Finally, two studies reported on patients' subjective assessment of the interventions (Braggion 1995; Jarad 2010).

Excluded studies

A total of 149 studies were excluded; 136 were excluded as they lacked a 'no treatment' or 'spontaneous coughing' control group. The remaining 13 studies were excluded for other reasons as follows: two studies were not clinical trials (Langenderfer 1998; Thomas 1995); four included diagnoses other than CF (Cochrane 1977; Parker 1984; Sutton 1985; van Hengstum 1988); four did not evaluate chest physiotherapy (Delk 1994; Fauroux 1999; Gayer 1988; Wordsworth 1996); one did not use any of the outcome measures defined for this review (Murphy 1988); one because the intervention was not thought to improve mucus clearance (Stites 2006); and one was in participants during an intra-operative period under anaesthesia (Tannenbaum 2001).

Risk of bias in included studies

The methodological quality scored using the Jadad score for the original review is as follows:

Study	Score
Braggion 1995	2
Falk 1993	1
Mortensen 1991	1
Pfleger 1992	2
Rossman 1982	1

The maximal score according to Jadad is five, however, two items are related to blinding of the investigator. Since blinding of the investigator is impossible in case of chest physiotherapy the maximal possible score for these studies is only three.

Details of the risk of bias assessment undertaken at the 2013 update follow.

Allocation

All eight studies were described as randomised; however, only one study gave any details on the method of randomisation (Latin square design) (Braggion 1995). We therefore judged the studies to have an unclear risk of bias for the generation of the randomisation sequence, except for the Braggion study which had a low risk of bias.

None of the eight studies discussed the concealment of the allocation and so all were deemed to have an unclear risk of bias.

Blinding

It is impossible to blind participants and caregivers or clinicians to physiotherapy interventions, but it is possible to blind the outcome assessors to the intervention. Only one study was described as single-blind, which we assume refers to the outcome assessors being blinded (Mortensen 1991). Since, except for the outcomes well-being and therapy compliance, all other outcome measurements are physiological data, we do not consider the fact that participants, caregivers or clinicians were not blinded as an important source of bias.

Incomplete outcome data

Six of the included studies did not mention any dropouts. One study reported that one participant withdrew from the study due to time constraints (Jarad 2010); and another study stated that one participant was excluded from the study due to respiratory infection (Pfleger 1992). Since all included studies were short term and the effect was measured immediately after the intervention we do not consider dropouts an important risk of bias.

Selective reporting

In order to assess for selective reporting, we planned to compare the study protocols with the final publication. However, it was only possible to obtain a study protocol for one study (Jarad 2010). The protocol in this instance stated secondary outcome data would be collected on oxygen saturation (SpO_2), respiratory rate (RR), heart rate (HR) and blood pressure (BP) during the interventions and this was confirmed in the 'Methods' section of the published paper; however, the published paper made no further reference to these variables in the 'Results' or 'Discussion' sections suggesting selective reporting and giving a high risk of bias.

Two of the included studies were only available in abstract form; therefore there was insufficient information available to assess for selective reporting. These studies were judged to be of unclear risk (Falk 1993; Elkins 2005).

For the remaining five studies which were published in full, there was no discrepancy identified between the methodology and results sections, thus raising no suspicion of selective reporting. Therefore these studies were judged to be at low risk (Braggion 1995; Mortensen 1991; Pfleger 1992; Rossman 1982; van der Schans 1991).

Other potential sources of bias

Mortenson was the only study in the current review to report a source of funding (Mortensen 1991). However, because the interventions being studied in the remaining studies either do not require equipment or use equipment widely available it was not considered by the authors that potential funding sources for the other studies in the review represented a significant risk of bias.

The study by Jarad included sputum wet and dry weight as an outcome, but did not report the unit of measurement in either the protocol or published study (Jarad 2010). If it is assumed that the measurement is in grams, then the participants appear to be non or low sputum producers (sputum wet weight ranging from 0.0 g to 5.3 g during the interventions analysed in this review). This would likely have impacted on treatment efficacy and the ability to detect a difference between control and active treatment groups.

The efficacy of any physiotherapy technique may be influenced by the proficiency and familiarity of the patient with that technique. Therefore, naivety of patients to some but not all interventions being studied could introduce a potential source of bias. No reference is made to how experienced patients were with each intervention in six of the studies reviewed (Braggion 1995; Elkins 2005; Falk 1993; Mortensen 1991; Rossman 1982; van der Schans 1991). In the study by Jarad, there was the potential for this practised effect as four of the eighteen participants' usual physiotherapy technique was the flutter with the remainder of participants naive to this treatment intervention (Jarad 2010). Only Pfleger stated that all participants were trained in the techniques being studied during the six month period preceding commencement of the study (Pfleger 1992).

Effects of interventions

Eight studies were included; all are cross-over studies and no meta-analysis was possible. All were short-term studies (less then seven days). Six studies were single treatment studies (Elkins 2005; Falk 1993; Mortensen 1991; Pfleger 1992; Rossman 1982; van der Schans 1991); in one study each intervention was performed twice on successive days (Jarad 2010); and in one study each physiotherapy treatment was given four times over two days (Braggion 1995).

Primary outcomes

1. Expectorated secretions

Expectorated secretions were reported in five studies (Braggion 1995; Jarad 2010; Mortensen 1991; Pfleger 1992; Rossman 1982), but sputum weight was not reported in the remaining three studies (Elkins 2005; Falk 1993; van der Schans 1991).

Four studies, involving 28 participants, found a higher amount of expectorated secretions during chest physiotherapy compared to the control period (Braggion 1995; Mortensen 1991; Pfleger 1992; Rossman 1982). Braggion found a mean wet weight of expectorated secretions during the control day of 6 g and during the chest physiotherapy sessions 23 g to 30 g (Braggion 1995). Mortenson reported medians and ranges, making comparisons between studies difficult but did report a significantly larger (P < 0.01) sputum weight in grams with FET + PEP median (range) 8.6 (3.5 to 19.9) and PD + FET 8.0 (2.3 to 13.9) compared to control 0.0 (0.0 to 2.1) during the treatment period; but this increase in sputum weight was not sustained in the post-intervention follow up (Mortensen 1991). In the paper by Pfleger, the mean (SD) weight of expectorated mucus was presented for each treatment arm as a figure, but no specific data is given in the text. Data extracted from the graphs show that during spontaneous coughing the mean weight of expectorated mucus was approximately 17 g, which was less than during the three forms of chest physiotherapy (range 34 g to 45 g) (Pfleger 1992). Pfleger also reported that PEP alone produced the highest amount of sputum, followed by a combination of PEP and AD (in either order); AD alone produced the lowest volume of sputum (Pfleger 1992). Rossman found a statistically significant higher volume of expectorated secretions during the different forms of chest physiotherapy compared to the control session (Rossman 1982). Jarad, however, found no significant differences in wet or dry weight of expectorated sputum between the placebo or flutter groups; the P values and absolute value of measurement for sputum weight were not stated in the results making it difficult to draw comparisons between the studies (Jarad 2010).

2. Mucus transport rate as assessed by radioactive tracer clearance

In five studies radioactive tracer clearance was used as an outcome variable (Elkins 2005; Falk 1993; Mortensen 1991; Rossman 1982; van der Schans 1991). In four of these (40 participants), it was found that chest physiotherapy, including coughing, increased radioactive tracer clearance as compared to the control period (Elkins 2005; Falk 1993; Mortensen 1991; Rossman 1982). Elkins found the mean percentage of radioactivity cleared from each region of interest (% C30) was 8.4% greater during postural drainage with percussion and vibrations compared to control (95% CI 2.4 to 14.5; P = 0.017). Elkins also reported greater % C30 with PEP, oscillating PEP and matched cough compared to control but these did not reach significance (Elkins 2005). Falk found approximately 6% clearance during the control measurement and 9% during chest physiotherapy (Falk 1993). In the study by Mortensen, median clearance after 30 minutes during control was 7% and during two different chest physiotherapy sessions was 33% and 34% (Mortensen 1991). Rossman found 32% radioactive tracer clearance during the control measurement and 40% to 46% during the different forms of chest physiotherapy (Rossman 1982). One study (eight participants) reported no significant difference between two different chest physiotherapy sessions of PEP breathing (clearance 10% and 6%), without coughing, compared to a control period (clearance 8%) (van der Schans 1991). Different outcomes between the study by van der Schans and the other studies can be explained by the fact that in the van der Schans study participants were requested not to cough, but coughing was encouraged in the other studies as a part of the treatment (van der Schans 1991).

3. Pulmonary function tests

Pulmonary function measures were used as an outcome in four of the available studies (Braggion 1995; Jarad 2010; Pfleger 1992; van der Schans 1991).

Braggion reported no significant difference between any of the three treatments or control in FEV_1, FEF_{25-75}, or FVC measured 30 minutes post intervention (Braggion 1995). Jarad reported a statistically significant reduction in values for FEV_1 (P = 0.028) and FEF_{25-75} (P = 0.03) following flutter but these were not observed in the placebo group (Jarad 2010). These changes were short-lived and values had returned to baseline on the second study day (each intervention was repeated on two successive days). No statistically significant changes in FVC were reported in either the flutter or control groups (Jarad 2010). Pfleger measured FEV_1 and FVC at five different time points during each intervention session and reported means and SDs at the end of the first and fifth intervention session where the intervention varied in a random order from session two to five, hence we are unable to enter the data in a meta-analysis (Pfleger 1992). The study found significant improvement in FEV_1 comparing the first and last time-point analysis in the PEP (P < 0.01), AD (P < 0.05) and AD-PEP (P < 0.01) groups but not in the control or AD-PEP groups. Significant improvement in FVC at the same time-points was also observed, but only in the PEP (P < 0.05) and PEP-AD (P < 0.02) groups (Pfleger 1992). In the study by van der Schans, no differences were reported in FEV_1 measures for the treatment or control, although data are not fully reported for this variable (van der Schans 1991).

Secondary outcomes

1. Oxygen saturation measured by pulse or transcutaneous oximetry

No data were available in any of the studies regarding this outcome.

2. Total lung capacity (TLC) and functional residual capacity (FRC)

Two studies, involving 24 participants, measured TLC or FRC (or both) after chest physiotherapy and found no significant effect on pulmonary function variables following the intervention (Braggion 1995; van der Schans 1991). Van der Schans did observe some significant improvements in FRC during PEP breathing only, but these quickly returned to baseline immediately after the intervention (van der Schans 1991).

3. Radiological ventilation scanning

No data were available in any of the studies regarding this outcome.

4. Subjective perception of well-being, ability to participate in activities of daily living

No data were available in any of the studies regarding this outcome.

5. Therapy compliance

No data were available in any of the studies regarding this outcome.

6. Objective change in exercise tolerance

No data were available in any of the studies regarding this outcome.

7. Nutritional status as assessed by growth, weight, body composition

No data were available in any of the studies regarding this outcome

8. Number of respiratory exacerbations per year

No data were available in any of the studies regarding this outcome.

9. Number of days in hospital per year

No data were available in any of the studies regarding this outcome.

10. Number of days of intravenous antibiotics per year

No data were available in any of the studies regarding this outcome.

11. Cost of intervention (equipment and duration)

No data were available in any of the studies regarding this outcome.

12. Deaths

No data were available in any of the studies regarding this outcome.

13. Patient preference

Only the Jarad study included a patient questionnaire to assess the acceptability and preference of the interventions (Jarad 2010). The questionnaire addressed breathlessness during treatment, ease of clearance, relaxation, how pleasant therapy was to perform and overall preference. The information from the completed questionnaires highlighted patient preference for placebo over flutter (results for the HAT group are not reported here following exclusion from the current review). The placebo treatment was rated as slightly or much better than the flutter regarding the ease at which phlegm is coughed up by 50.1% of participants; 35.3% of patients reported flutter therapy was slightly or very unpleasant, with none of the participants stating that they would prefer to use flutter for physiotherapy if available (Jarad 2010). These results should be considered in the context of the placebo treatment having involved the participant sitting in a bath of warm water receiving a sham form of HAT; as the effects of sitting in a warm bath on both secretion clearance and perceived ease of clearance is unknown. As it is unclear as to whether this represents a true control, these results should be interpreted with caution.

DISCUSSION

Chest physiotherapy has been a mainstay of the respiratory management of people with CF for so long that it may now be difficult for them, their parents, physiotherapists and medical staff to consider a study design that incorporates a 'no treatment' control group for any length of time. Despite there being a reasonable degree of equipoise with regard to whether physiotherapy is better than no treatment, many would argue that to recruit participants into a 'no treatment' group would be unethical. This explains in part why there are currently no long-term studies which use this design.

Summary of main results

The heterogeneity of treatments and outcome measures reported in the included studies make it impossible to pool their results. The short-term studies that were included in this review suggest that chest physiotherapy increases mucus transport in people with CF. Specifically, four out of the five studies included in the review which used sputum weight as an outcome found increased sputum weight produced with an intervention compared to control (with the remaining study reporting no significant differences). Also, four out of five of the included studies which assessed radioactive tracer clearance found positive effects associated with the active intervention groups compared to control; one study, which included only eight participants, observed no significant differences. Only one of the four studies which reported pulmonary function tests as an outcome observed any significant improvement following some of the interventions but not control. It is not reported, however, over how long a period these changes were sustained.

It is generally accepted that patient satisfaction or preference for airway clearance techniques is an important factor in treatment selection when considering likely adherence to treatment. Only one study included in the review addressed patient satisfaction; however in this study some of the participants were naive to the intervention. The authors consider that patient preference in a short-term, single-intervention study where a new intervention introduces a 'novelty' element could be misleading. Care should therefore be taken when extrapolating these findings for consideration of likely patient satisfaction or preference for a technique carried out in the long term as part of daily management.

Overall completeness and applicability of evidence

This review only included short-term studies where each of the interventions were only repeated over one or two days. Due to the nature of the disease the long-term clinical consequences of missing one or two treatments is unlikely to be significant. Therefore, the outcomes from these short-term studies may not represent the true effect of the interventions performed in the long term and should be interpreted with caution. Despite this limitation, the included cross-over studies may provide a potentially useful signal regarding the efficacy of physiotherapy treatments.

All of the studies included in the review recruited participants who were older children, adolescents or adults with the youngest participant 9.8 years of age. Extrapolation of these findings to the younger paediatric population should therefore be performed with caution; particularly when considering the efficacy of routine airway clearance technique for asymptomatic screened babies. In 2008 the Association of Chartered Physiotherapists in Cystic Fibrosis (ACPCF) produced a guidance paper on the management of screened infants. This document provides a review of the evidence for airway clearance applicable to this population and consensus clinical opinion on this issue (Prasad 2008).

Quality of the evidence

The included studies each recruited only a small number of participants. Furthermore, there was enormous heterogeneity of treatments and outcome measures reported so that it was impossible to pool results from different studies. There are inherent risks of bias in physiotherapy studies; firstly, due to a lack of control group since a sham or placebo treatment clearly cannot be substituted for a clearly physical intervention such as percussion, PEP or postural drainage. Similarly, participants and therapists cannot be 'blinded' from the treatment being received. This partly explains the low quality scores of the included studies as reported using the Jadad scoring system in the original review and the risk of

bias assessments in the current version, since these methods place significant emphasis on blinding.

Potential biases in the review process

The authors are not aware of potential bias in the review process. A comprehensive search of the literature was undertaken not limited by time or language and studies were then assessed independently for inclusion in the review. Authors worked independently to assess bias of the included studies and extract available data for inclusion in the final report to ensure accuracy of reporting.

Agreements and disagreements with other studies or reviews

The short-term studies that were included in this review suggest that chest physiotherapy increases mucus transport in people with CF. This finding supports the conclusion of an earlier review (Thomas 1995a). These studies also suggest that in the short term, airway clearance techniques have no sustained effects on pulmonary function. Other Cochrane reviews of physiotherapy interventions have assessed pulmonary function as an outcome in both short-term and long-term studies and, certainly in the short term, findings remain consistent (Elkins 2006; McKoy 2012; Morrison 2009).

AUTHORS' CONCLUSIONS

Implications for practice

Short-term cross-over studies suggest that airway clearance regimens have beneficial effects in people with CF with regard to improving mucus transport. However, based on this review, we have not been able to find any robust scientific evidence to support the hypothesis that chest physiotherapy for the purpose of clearing airway secretions has a long-term beneficial effect in people with CF, nor to support the claim by some authors that it is harmful.

Implications for research

The gold standard for establishing efficacy of therapy is the randomised controlled study with a 'no treatment' group. The application of this study design to the question in this review would be very effective. However, several ethical considerations could be raised in the discussion with regard to the withdrawal of an established and trusted treatment like chest physiotherapy in people with CF, even in the absence of firm evidence. On the other hand, it could be argued that in view of scant evidence to support the use of chest physiotherapy for people with CF and the fact that this intervention can be unpleasant, uncomfortable, and time-consuming, we believe that a study with a 'no treatment' control group is justified in some circumstances. Therefore, we propose that in future research, control groups or control periods should be included with sufficient numbers of included participants. This would be best studied as a parallel study over a time period of months rather than days or weeks.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Braggion 1995

Methods	Cross-over study, interventions given in random order.
Participants	16 patients with CF (8 males; 8 females). Mean (SD) age 20.3 (4) years. Mean (SD) FEV_1% predicted 61.7% (17%).
Interventions	High-frequency chest compression. Postural drainage, breathing exercises, vibrations, manual percussion. PEP breathing. Control.
Outcomes	Wet and dry weight expectorated mucus; pulmonary function tests (FVC, FEV_1, $FEF_{25-75\%}$); subjective assessment.
Notes	Measurement 30 minutes after intervention.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random order of the interventions performed according to Latin square design described by Williams (Williams 1949). In order to balance distribution between sexes, two 4 x 4 Latin squares were used for male participants and two for female participants.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Interventions did not allow participants or clinicians to be blinded, not discussed whether outcome assessors were blinded.

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* Indicates the major publication for the study

Braggion 1995 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of any dropouts.
Selective reporting (reporting bias)	Low risk	Protocol not available for comparison, but data on expected outcomes reported. Immediate measurement after intervention.
Other bias	Unclear risk	Funding source not reported, however potential sources not thought to introduce a significant risk of introducing bias. Unknown whether patients naive to all interventions prior to study.

Elkins 2005

Methods	Randomised cross-over study.
Participants	12 adults with CF, gender split not stated. Mean (range) age 25 (17 - 34) years. Mean (range) FEV_1 % predicted 53 (16 - 88).
Interventions	Participants inhaled ^{99m}Technetium-labelled sulphur colloid aerosol matching a target breathing pattern followed by 20 min of one of 4 interventions (randomised): • postural drainage with percussion; • PEP; • oscillating PEP; • matched cough (voluntary coughing to a maximum number of times coughed during previous interventions). Then on 5th study period participants voluntarily coughed the maximum number of times they had coughed during any of the previous interventions.
Outcomes	Mean % radioactive tracer clearance (10 minute baseline dynamic SPECT scan after inhalation and scan at 90 min).
Notes	Study supported by NHMRC.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Abstract states random order of the interventions, but no details of randomisation method given.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not possible to blind participants or clinicians, not discussed if outcome assessors blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of any dropouts.

Elkins 2005 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Protocol not available for comparison and insufficient information to assess whether all outcomes reported.
Other bias	Unclear risk	Washout period unclear, not stated if interventions took place on same day or different days. Unknown whether patients naive to all interventions prior to study.

Falk 1993

Methods	Cross-over study, interventions given in random order.
Participants	12 patients with CF, gender split not stated. Age and disease severity also not reported.
Interventions	FET, postural drainage. FET, PEP breathing. Control.
Outcomes	Radioactive tracer clearance.
Notes	Measurements 30 minutes, 1 hour, 2 hours and 24 hours after intervention.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Paper states random order of the interventions, but no details of randomisation method given.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Interventions did not allow participants or clinicians to be blinded, not discussed whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of any dropouts.
Selective reporting (reporting bias)	Unclear risk	Protocol not available for comparison and insufficient information to assess whether all outcomes reported.
Other bias	Unclear risk	Funding source not reported, however potential sources not thought to introduce a significant risk of introducing bias. Unknown whether patients naive to all interventions prior to study.

Jarad 2010

Methods	Cross-over study, interventions given in random order.

Jarad 2010 *(Continued)*

Participants	19 adults with CF (11 males; 8 females). Mean (SD) age 24 (4.8) years.
Interventions	HAT (this group excluded from the current review as not a recognised ACT). Flutter. Control (sitting in a bath with sham form of HAT).
Outcomes	Expectorated sputum wet and dry weight. FEV_1, FVC, $FEF_{25-75\%}$, FEF_{75}. Patient questionnaire.
Notes	Measurements at 60 min post treatment.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	States treatment order was randomised but no details of randomisation method reported.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Interventions did not allow participants or clinicians to be blinded, not discussed whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There was one dropout reported following enrolment; this was due to time constraints. Complete data was presented for the remaining 18 participants.
Selective reporting (reporting bias)	High risk	Study protocol and methods section state SpO_2, RR, HR and BP would be measured throughout the interventions, but there is no reference to this data in the results or discussion.
Other bias	Unclear risk	Funding source not reported, however paper states the authors had no conflict of interest. HAT group excluded from this analysis therefore potential bias from equipment provision not relevant. Unit of measurement for sputum weight not reported. 4/18 participants used flutter as usual main physiotherapy method prior to study.

Mortensen 1991

Methods	Cross-over study, interventions given in random order on 3 occasions each separated by 48 hours.
Participants	10 patients with CF (6 male; 4 female). Mean (SD) age 20 (3.4) years.

Mortensen 1991 *(Continued)*

	Median (range) FEV_1% predicted 38.5% (26% - 101%).
Interventions	20 min session of intervention immediately after ultrasonic nebulisation of ^{99m}TC-human albumin colloid: - postural drainage, FET, thoracic expansion exercises, relaxation; - PEP breathing, FET; - control, spontaneous coughing.
Outcomes	Radioactive tracer clearance (measured every 30 min for 3 hours on each occasion). Sputum weight. Penetration index (median and range). Retention at 24 hours (median and range). Number of huffs performed during treatment sessions (median and range). Number of cough maneuvers (median and range). (only radioactive tracer clearance, sputum weight and FEV_1 reported outcomes in this review).
Notes	Measurements 30 minutes, 1 hour and 24 hours after intervention. Study approved by local ethical committee of Copenhagen.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Paper states random order of the interventions, but no details of randomisation method given
Allocation concealment (selection bias)	Unclear risk	Not discussed
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Described as single-blind, since participants and care-givers could not be blinded due to type of intervention, assume that outcome assessors were blinded but no detail of how this was achieved.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No mention of any dropouts, however data for all 10 patients present.
Selective reporting (reporting bias)	Low risk	Protocol not available for comparison, but data on expected outcomes reported.Immediate measurement after intervention.
Other bias	Unclear risk	Funding source reported. Unknown whether patients naive to all interventions prior to study.

Pfleger 1992

Methods	Cross-over study, interventions given in random order.
Participants	14 patients with CF (5 males; 9 females). Mean (range) age 14 (9.8 - 22.4) years.

Pfleger 1992 *(Continued)*

	Mean (SD) FEV_1% predicted 53% (21%).
Interventions	PEP breathing. AD. PEP followed by AD. AD followed by PEP. Control, spontaneous coughing.
Outcomes	Pulmonary function tests (FVC, FEV1, RV/TLC, Raw); weight of expectorated mucus.
Notes	Measurements during and immediately after intervention. Patients trained in interventions 6 months before commencement of the study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Paper states random order of the interventions, but no details of randomisation method given.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Interventions did not allow participants or clinicians to be blinded. Assessor for sputum weight blinded, but not discussed whether assessment of other outcomes blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Abstract and paper state that 15 participants were randomly selected from local clinic, but data from 14 only as 1 developed symptoms of acute respiratory viral infection during study and was excluded.
Selective reporting (reporting bias)	Low risk	Protocol not available for comparison, but data on expected outcomes reported. Immediate measurement after intervention.
Other bias	Low risk	Funding source not reported, however potential sources not thought to introduce a significant risk of introducing bias.

Rossman 1982

Methods	Cross-over study, interventions given in random order.
Participants	6 patients with CF (all male). Mean (SD) age: 22.8 (5.6) years. Range FEV_1% predicted 12 to 77.7%.
Interventions	Postural drainage. Postural drainage, mechanical percussion. Regimented coughing. Chest physiotherapy, breathing exercises, vibrations, manual percussion, postural drainage. Control, spontaneous coughing.
Outcomes	Radioactive tracer clearance; sputum weight.

Rossman 1982 *(Continued)*

Notes	Measurements during and up to 2 hours after intervention.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Paper states random order of the interventions, but no details of randomisation method given.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Interventions did not allow participants or clinicians to be blinded, not discussed whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of any dropouts but data appears complete.
Selective reporting (reporting bias)	Low risk	Protocol not available for comparison, but data on expected outcomes reported. Immediate measurement after intervention.
Other bias	Unclear risk	Funding source not reported, however potential sources not thought to introduce a significant risk of introducing bias. Unknown whether patients naive to all interventions prior to study.

van der Schans 1991

Methods	Cross-over study, interventions given in random order.
Participants	8 patients with CF, gender split not reported. Mean (SD) age: 16 (3) years. Mean (SD) FEV_1% predicted 70% (24%).
Interventions	PEP breathing with a resistance of 5 cmH_2O followed by 5 minutes of coughing. PEP breathing with a resistance of 15 cmH_2O followed by 5 minutes of coughing. Control followed by 5 minutes of coughing.
Outcomes	Radioactive tracer clearance; TLC, FRC.
Notes	Measurements during intervention.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Paper states random order of the interventions, but no details of randomisation method given.
Allocation concealment (selection bias)	Unclear risk	Not discussed.

van der Schans 1991 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Interventions did not allow participants or clinicians to be blinded, not discussed whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No dropouts mentioned.
Selective reporting (reporting bias)	Low risk	Protocol not available for comparison, but data on expected outcomes reported. Immediate measurement after intervention.
Other bias	Unclear risk	Funding source not reported. however potential sources not thought to introduce a significant risk of introducing bias. Unknown whether patients naive to all interventions prior to study.

AD: autogenic drainage;
BP: blood pressure
CF: cystic fibrosis
FEF25-75%: forced expiratory flow 25-75%
FET: forced expiration technique
FEV1: forced expiratory volume at one second
FRC: functional residual capacity
FVC: forced vital capacity
HAT: hydroacoustic therapy
HR: heart rate
PEP: positive expiratory pressure breathing
RR: respiratory rate
RV: residual volume
SD: standard deviation
SpO_2: blood oxygen saturation
TLC: total lung capacity

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
App 1998	No control group without chest physiotherapy.
Aquino 2012	No control group without chest physiotherapy.
Arens 1994	No control group without chest physiotherapy.
Bain 1988	No control group without chest physiotherapy.
Baldwin 1994	No control group without chest physiotherapy.
Balestri 2004	No control group without chest physiotherapy.
Baran 1977	No control group without chest physiotherapy
Battistini 2001	No control group without chest physiotherapy.
Bauer 1994	No control group without chest physiotherapy.
Bilton 1992	No control group without chest physiotherapy.

Study	Reason for exclusion
Blomquist 1986	No control group without chest physiotherapy.
Borka 2012	No control group without chest physiotherapy.
Braggion 1996	No control group without chest physiotherapy.
Button 1997	No control group without chest physiotherapy.
Castile 1998	No control group without chest physiotherapy.
Castle 1994	No control group without chest physiotherapy.
Cegla 1993	No control group without chest physiotherapy.
Cerny 1989	No control group without chest physiotherapy.
Chatham 1998	No physiotherapy to improve mucus clearance.
Chatham 2004	No control group without chest physiotherapy.
Cochrane 1977	Mixed group of participants (cystic fibrosis, chronic bronchitis, and bronchiectasis).
Costantini 1998	No control group without chest physiotherapy.
Darbee 1990	No control group without chest physiotherapy.
Darbee 2005	No control group without chest physiotherapy.
Davidson 1988	No control group without chest physiotherapy.
Davidson 1992	No control group without chest physiotherapy.
Davidson 1998	No control group without chest physiotherapy.
Davies 2012	No control group without chest physiotherapy.
de Boeck 1984	No control group without chest physiotherapy.
Delk 1994	No physiotherapy to improve mucus clearance.
Desmond 1983	No control group without chest physiotherapy.
Dosman 2003	No control group without chest physiotherapy.
Dunn 2013	No control group without chest physiotherapy.
Elkins 2000	No control group without chest physiotherapy.
Fainardi 2011	No control group without chest physiotherapy.
Falk 1984	No control group without chest physiotherapy.
Falk 1988	No control group without chest physiotherapy.
Fauroux 1999	No chest physiotherapy (airway clearance technique) studied.

Study	Reason for exclusion
Gaskin 1998	No control group without chest physiotherapy.
Gayer 1988	No chest physiotherapy (airway clearance technique) studied.
Giles 1995	No control group without chest physiotherapy.
Giles 1996	No control group without chest physiotherapy.
Gondor 1999	No control group without chest physiotherapy.
Gotz 1995	No control group without chest physiotherapy.
Grasso 2000	No control group without chest physiotherapy.
Grzincich 2008	No control group without chest physiotherapy.
Gursli 2013	No control group without chest physiotherapy.
Hare 2002	No control group without chest physiotherapy.
Hartsell 1978	No control group without chest physiotherapy.
Hofmeyr 1986	No control group without chest physiotherapy.
Holland 2003	No control group without chest physiotherapy.
Homnick 1995	No control group without chest physiotherapy.
Homnick 1998	No control group without chest physiotherapy.
Jacobs 1981	No control group without chest physiotherapy.
Keller 2001	No control group without chest physiotherapy.
Kerrebijn 1982	No control group without chest physiotherapy.
Klig 1989	No control group without chest physiotherapy.
Kluft 1996	No control group without chest physiotherapy.
Kofler 1994	No control group without chest physiotherapy.
Kofler 1998	No control group without chest physiotherapy.
Konstan 1994	No control group without chest physiotherapy.
Kraig 1995	No control group without chest physiotherapy.
Lagerkvist 2006	No control group without chest physiotherapy.
Langenderfer 1998	Not a clinical trial.
Lannefors 1992	No control group without chest physiotherapy.
Lindemann 1992	No control group without chest physiotherapy.

Study	Reason for exclusion
Lorin 1971	No control group without chest physiotherapy.
Lyons 1992	No control group without chest physiotherapy.
Maayan 1989	No control group without chest physiotherapy.
Majaesic 1996	No control group without chest physiotherapy.
Marks 1999	No control group without chest physiotherapy.
Maxwell 1979	No control group without chest physiotherapy.
McCarren 2006	No control group without chest physiotherapy.
McDonnell 1986	No control group without chest physiotherapy.
McIlwaine 1997	No control group without chest physiotherapy.
McIlwaine 2010	No control group without chest physiotherapy.
McIlwaine 2012	no control group without chest physiotherapy.
Miller 1995	No control group without chest physiotherapy.
Milne 2004	No control group without chest physiotherapy.
Morris 1982	No control group without chest physiotherapy.
Mulholland 1994	No control group without chest physiotherapy.
Murphy 1983	No control group without chest physiotherapy.
Murphy 1988	No outcome measures that were the primary purpose of this review were used.
Natale 1994	No control group without chest physiotherapy.
Newhouse 1998	No control group without chest physiotherapy.
Oberwaldner 1986	No control group without chest physiotherapy.
Oberwaldner 1991	No control group without chest physiotherapy.
Orlik 2000	No control group without chest physiotherapy.
Orlik 2000a	No control group without chest physiotherapy.
Orlik 2001	No control group without chest physiotherapy.
Osman 2010	No control group without chest physiotherapy.
Padman 1999	No control group without chest physiotherapy.
Parker 1984	Mixed group of participants: 4 with cystic fibrosis, 5 with bronchiectasis, 1 with asthma.
Parreira 2008	No control group without chest physiotherapy.

Study	Reason for exclusion
Parsons 1995	No control group without chest physiotherapy.
Patel 2013	No control group without chest physiotherapy.
Phillips 1998	No control group without chest physiotherapy.
Phillips 2004	No control group without chest physiotherapy.
Pike 1999	No control group without chest physiotherapy.
Placidi 2006	No control group without chest physiotherapy.
Pollard 2000	No control group without chest physiotherapy.
Prasad 2005	no control group without chest physiotherapy
Pryor 1979a	No control group without chest physiotherapy.
Pryor 1979b	No control group without chest physiotherapy.
Pryor 1981	No control group without chest physiotherapy.
Pryor 1990	No control group without chest physiotherapy.
Pryor 1994	No control group without chest physiotherapy.
Pryor 2010	No control group without chest physiotherapy.
Reisman 1988	No control group without chest physiotherapy.
Reix 2009	No control group without chest physiotherapy.
Rodriguez 2013	No control group without chest physiotherapy.
Roos 1987	No control group without chest physiotherapy.
Salh 1989	No control group without chest physiotherapy.
Samuelson 1994	No control group without chest physiotherapy.
Sanchez 1999	No control group without chest physiotherapy.
Scherer 1998	No control group without chest physiotherapy.
Sokol 2012	No control group without chest physiotherapy, primary intervention outside scope of this review.
Sontag 2010	No control group without chest physiotherapy.
Steen 1991	No control group without chest physiotherapy.
Steven 1992	No control group without chest physiotherapy.
Stites 2006	Intervention not thought to improve mucus clearance.

Study	Reason for exclusion
Sutton 1985	Mixed group of participants: 5 with bronchiectasis, 2 with chronic bronchitis and only 1 with cystic fibrosis.
Tannenbaum 2001	Study in participants during intra-operative period under anaesthesia and mechanical ventilation.
Tecklin 1976	No control group without chest physiotherapy.
Thomas 1995	Not a clinical trial, a review.
Tonnesen 1982	No control group without chest physiotherapy.
Toral 1997	No control group without chest physiotherapy.
Tugay 2000	No control group without chest physiotherapy.
Tyrrell 1986	No control group without chest physiotherapy.
van Asperen 1987	No control group without chest physiotherapy.
Van Ginderdeuren 2000	No control group without chest physiotherapy.
Van Ginderdeuren 2008	no control group without chest physiotherapy.
van Hengstum 1987	No cystic fibrosis participants.
van Hengstum 1988	No control group without chest physiotherapy.
van Winden 1998	No control group without chest physiotherapy.
Vanlaethem 2008	No control group without physiotherapy.
Verboon 1986	No control group without chest physiotherapy.
Warwick 1990	No control group without chest physiotherapy.
Warwick 1991	No control group without chest physiotherapy.
Warwick 2004	No control group without chest physiotherapy.
Webber 1985	No control group without chest physiotherapy.
West 2010	No control group without chest physiotherapy.
Wheatley 2013	No control group without chest physiotherapy.
White 1997	No control group without chest physiotherapy.
Wilson 1995	No control group without chest physiotherapy.
Wong 1999	No control group without chest physiotherapy.
Wordsworth 1996	No chest physiotherapy.
Zapletal 1983	No control group without chest physiotherapy.

Study	Reason for exclusion
Znotina 2000	No control group without chest physiotherapy.

WHAT'S NEW

Date	Event	Description
25 November 2015	New search has been performed	A search of the Cystic Fibrosis and Genetic Disorders Review Group's Cystic Fibrosis Trials Register identified 29 potentially eligible new references. Eight references were additional references to four already excluded studies (Castile 1998; McIlwaine 2012; Parsons 1995; Reix 2009). The remaining 21 references were excluded as none of these studies included a no physiotherapy or spontaneous cough alone control group.
25 November 2015	New citation required but conclusions have not changed	One author, Cees van der Schans, has now stepped down from the review team. None of the newly identified references were eligible for inclusion in the review and hence our conclusions remain the same.

HISTORY

Protocol first published: Issue 1, 1999
Review first published: Issue 2, 2000

Date	Event	Description
5 August 2013	New search has been performed	A search of the Group's CF Trials Register identified 23 new references which were potentially eligible for inclusion in the review; two of these studies were assessed as suitable for inclusion (Elkins 2005; Jarad 2010) and the remaining 21 were excluded.
5 August 2013	New citation required but conclusions have not changed	A new review team have taken on this review at this update. Despite the inclusion of two new studies in this updated review, the conclusions remain the same.
18 February 2009	Amended	The Methods section has been updated in light of new guidance and functionality of RevMan 5.
18 February 2009	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register identified one additional reference to an already included study (Braggion 1995) and one to an already excluded study (Tannenbaum 2001).
12 November 2008	Amended	Converted to new review format.
20 February 2008	Amended	The Plain Language Summary has been updated in line with guidance from The Cochrane Collaboration. Also, in a post hoc change and in line with Group guidelines, the outcome measures have been split into 'Primary outcomes' and 'Secondary outcomes'.

Date	Event	Description
20 February 2008	New search has been performed	The search of the Group's Cystic Fibrosis Trials Register identified one new reference which was the main paper to a previously excluded abstract (Lagerkvist 2006).
14 November 2006	New search has been performed	The search of the Group's Cystic Fibrosis Trials Register identified two new references. Both studies were excluded (Stites 2006; Warwick 2004).
14 November 2005	New search has been performed	The search of the Group's Cystic Fibrosis Trials Register identified four new references. One study identified was not eligible for inclusion in the review and has been added to the 'Excluded studies' section (Chatham 2004). The remaining three references were to three already excluded studies (Darbee 1990; Marks 1999; McIlwaine 1997).
18 May 2004	New search has been performed	Additional references (providing no additional information) have been added to the following already 'Included studies': Mortensen 1991; Falk 1993. Additional references have been added to the following already 'Excluded studies': Button 1997a; Costantini 1998; Orlik 2001. Three new studies have been added to 'Excluded studies': Hare 2002; Orlik 2000; Tannenbaum 2001.
14 August 2002	New search has been performed	Six crossover trials, previously cited in "Excluded Studies" have now been moved to the "Included Studies" section (Braggion 1995; Falk 1993; Mortensen 1991; Pfleger 1992; Rossman 1982; van der Schans 1991). Relevant changes to the text of the review have been made. Four new "Excluded Studies" have been incorporated into the review (Battistini 2001; Keller 2001; Pollard 2000; Orlick 2001). Additional references to studies already listed in "Excluded Studies" have been incorporated into the review within the following study ID's: Button 1997a; Gondor 1999; Grasso 2000; Marks 1999; Newhouse 1998).
9 February 2000	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Original review

Ammani Prasad and Eleanor Main independently assessed studies for inclusion in this review and assisted in writing of text. Cees van der Schans acted as guarantor of the review.

Updates from 2013

Alison Gates and Louise Warnock independently assessed studies for inclusion in this review, re-assessed the risk of bias of the included studies and updated the text to include two additional studies (Elkins 2005; Jarad 2010).

Cees van der Schans commented on a draft of the updated review.

Updates from 2015

Cees van der Schans has stepped down from the author team.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- National Institute for Health Research, UK.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The Methods section has been updated in light of new guidance and functionality of RevMan 5.1 (Review Manager 2011).

The secondary outcome of patient preference was added during the 2013 review update as it is generally accepted that patient satisfaction or preference for airway clearance techniques is an important factor in treatment selection when considering likely adherence to treatment.

INDEX TERMS

Medical Subject Headings (MeSH)

*Physical Therapy Modalities; Cough; Cross-Over Studies; Cystic Fibrosis [*therapy]; Drainage, Postural; Mucus [metabolism]; Percussion; Randomized Controlled Trials as Topic; Respiratory Function Tests; Respiratory Therapy [methods]

MeSH check words

Humans