Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)

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Abstract

Background
Chest physiotherapy is widely prescribed to assist the clearance of airway secretions in people with cystic fibrosis (CF). Positive expiratory pressure (PEP) devices provide constant back pressure to the airways during expiration. This may improve clearance by building up gas behind mucus via collateral ventilation. Given the widespread use of PEP devices, there is a need to determine the evidence for their effect.

Objectives
To determine the effectiveness and acceptability of PEP devices compared to other forms of physiotherapy as a means of improving mucus clearance and other outcomes in people with CF.

Search strategy
We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials Register comprising of references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings. The electronic database CINAHL was also searched from 1982 to 2001.


Selection criteria
Randomised controlled studies in which PEP was compared with any other form of physiotherapy in people with CF.

Data collection and analysis
Two authors independently applied the inclusion and exclusion criteria to publications and assessed the quality of the included studies.

Main results
Forty studies were identified and twenty-five studies involving 507 participants met the review inclusion criteria. Most included studies had low scores on a scale of study quality. Twenty of these studies involving 300 participants were cross-over in design. Data were not published in sufficient detail in most of these studies to perform meta-analysis.

Forced expiratory volume in one second (FEV₁) was the most frequently measured outcome. Single interventions or series of treatments continued for up to three months demonstrated no significant difference in effect between PEP and other methods of airway clearance on FEV₁. Long-term studies had equivocal or conflicting results regarding the effect on FEV₁. Participant preference was reported in nine studies. In all studies with an intervention period of at least one month, measures of participant preference were in favour of PEP. The results for the remaining outcome measures were not examined or reported in sufficient detail to provide any high level evidence.

Authors' conclusions
There was no clear evidence that PEP was a more or less effective intervention overall than other forms of physiotherapy. There was limited evidence that PEP was preferred by participants compared to other techniques, but this finding is from studies of low quality.
PLAIN LANGUAGE SUMMARY

Not enough strong evidence about the effects of positive expiratory pressure (PEP) devices for chest physiotherapy for people with cystic fibrosis

Cystic fibrosis (CF) causes frequent respiratory infection and blocks the airways with mucus secretions. Chest physiotherapy is frequently used to try to clear these secretions out of the lungs. Positive expiratory pressure (PEP) devices provide pressure behind the mucus to try to push it out of the lungs. The review of studies found only weak evidence about the effects of PEP. The evidence does not show that PEP is more effective than other methods of chest physiotherapy. There was some evidence that people with CF may prefer PEP to other chest physiotherapy methods, but more research is needed.

BACKGROUND

Cystic Fibrosis (CF) is a relatively common, inherited, life-limiting disorder. The genetic defect causes abnormal mucus secretion in the airways, potentially leading to airway obstruction and mucus plugging (Zach 1990). This predisposes the airways to infection and inflammation, which in turn promote further mucus secretion. Persistent infection and inflammation within the lungs are the major contributory factors to airway damage and the progressive loss of respiratory function (Cantin 1995; Konstan 1997). Treatment methods which improve mucus clearance are considered essential in optimising respiratory status and reducing the progression of lung disease. A variety of methods are used, some physical, e.g. chest physiotherapy, and some chemical, e.g. inhaled medications.

Ch Rent physiotherapy is widely prescribed to assist the clearance of airway mucus and is usually commenced as soon as the diagnosis of CF is made. Traditionally, chest physiotherapy relied on postural drainage (gravity assisted drainage positions) combined with percussion and vibration (performed by an assistant such as a physiotherapist or relative), and forced expirations (huffing and coughing). Some protocols included deep breathing exercises. This form of chest physiotherapy is time-consuming and sometimes uncomfortable. It also requires assistance, which may have an adverse effect on adherence. Recently, several self-administered alternatives that are able to be used in upright sitting positions have been developed. Among these are a range of positive expiratory pressure (PEP) devices, which provide a constant back pressure to the airways during expiration. A theory is that PEP devices are able to improve clearance by increasing gas pressure behind mucus via collateral ventilation, thus making expiratory manoeuvres more effective (Andersen 1979; Groth 1985). It has also been hypothesised that PEP may stabilise airways by splitting them open during expiration, which may facilitate airway clearance (Oberwaldner 1986). Oberwaldner has documented a modification of the standard PEP technique known as high pressure PEP (Hi-PEP). Hi-PEP incorporates forced expiratory manoeuvres through the PEP device, which generates higher pressures and may stimulate coughing (Oberwaldner 1986).

A Cochrane systematic review comparing any form of chest physiotherapy with no chest physiotherapy found evidence to demonstrate the benefit of chest physiotherapy for increasing mucus transport, but did not find evidence for any long-term outcomes (van der Schans 2004). Several narrative reviews have compared different types of chest physiotherapy, including PEP, with conflicting conclusions (McIlwaine 1996; Prasad 1993; Prasad 2000; Williams 1994; Zach 1987). This review will examine the effect and acceptability of PEP devices compared to other techniques used for secretion clearance.

The most effective technique for secretion clearance during an infective exacerbation of CF may differ from that which is most effective for maintenance therapy. PEP is also used in combination with various other interventions (e.g. pharmacological therapies, other physical therapy techniques, or the modification to the technique known as high pressure PEP). It is therefore important to establish the effect of PEP in each stage of CF lung disease and with and without co-interventions.

OBJECTIVES

The purpose of this review is to determine the effect of PEP on clearance of airway secretion compared to other forms of chest physiotherapy in people with CF.

The following hypotheses are tested:

(1) PEP improves outcomes for people with CF more than other forms of chest physiotherapy;
(2) PEP is more acceptable to people with CF than other forms of chest physiotherapy.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomised controlled studies.

Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)

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

Types of intervention
In the existing literature, variation occurs in the application of specific techniques. Separate analysis of variations within each technique would render this review unmanageable. For the purpose of this review, it is necessary to group these variations within broad definitions of the established treatment modalities.

One of the interventions used in the studies will be required to meet one of the following descriptions:

Positive expiratory pressure (PEP) mask, mouthpiece or bottle therapy as described by the authors is to be one of the interventions, with or without additional techniques. PEP was originally defined as breathing with a positive expiratory pressure of 10 - 20cm H₂O (Falk 1984), but for the purposes of this review, this will be expanded to include pressures from 5 - 25 cm H₂O.

High pressure PEP (Hi-PEP) mask therapy as described by the authors is to be one of the interventions, with or without additional techniques. Hi-PEP is a modification of the above technique which includes a full forced expiration against a fixed mechanical resistance which usually generates pressures ranging from 40 - 100cm H₂O (Oberwaldner 1986).

At least one comparator intervention used in the studies will be required to meet one of the following descriptions:

(1) Postural drainage with percussion and vibration (PDPV). In other reviews this has been described as conventional chest physiotherapy (CCPT).

(2) Active cycle of breathing techniques (ACBT). This comprises relaxation or breathing control, forced expiration technique (FET), thoracic expansion exercises and may include postural drainage or percussion.

(3) Autogenic drainage (AD). This breathing technique uses high expiratory flow rates at varying lung volumes to enhance mucous clearance while avoiding airway closure.

(4) Oral oscillatory devices include flutter, cornet, acapella and intrapulmonary percussive ventilation. The Flutter, cornet and acapella devices produce an oral oscillatory PEP effect within the airways. Intrapulmonary percussive ventilation provides continuous oscillation of the air pressure in the airways via the mouth.

(5) Thoracic oscillating devices such as Thairapy Vest and the Hiyak Oscillator provide external chest wall oscillation.

(6) Exercise prescribed for the purpose of airway clearance either independently or as an adjunct to other techniques.

Types of outcome measures
Primary Outcomes

(1) Forced expiratory volume at one second (FEV₁) Change in FEV₁ between baseline and post-intervention. Litre and percent (%) predicted values are both stated wherever possible.

(2) Number of respiratory exacerbations per year Respiratory exacerbations must have been defined either by symptoms or by changes in treatment after medical assessment.

(3) Number of days of intravenous antibiotics per year Intravenous antibiotics must have been prescribed in response to a respiratory exacerbation.

(4) Well-being Quality of life or well-being, or ability to participate in activities of daily living.

(5) Adverse effects Deaths or other adverse changes in condition from baseline (pre-treatment), such as pneumothorax, bronchospasm or haemoptysis.

(6) Survival

(7) Exercise tolerance Subjective exercise tolerance, or objective measures such as six-minute walk test.

(8) Participant preference Participant preference may be determined either as the nominated technique of choice by the participant at the conclusion of the study, or by a comparison of technique acceptability (e.g. visual analogue scale).

Secondary Outcomes

(1) Direct measures of mucus clearance Mucus transport rate or mucociliary clearance rate as assessed by radioactive tracer.

(2) Expectorated secretions, dry or wet weight, or volume An increase in the amount of expectorated secretions as a short-term (less than seven days) effect of the intervention is considered as beneficial. In long-term studies this outcome variable will not be included.

(3) Other pulmonary parameters Forced vital capacity (FVC), forced expiratory flow 25-75% (FEF₂₅₋₇₅), total lung capacity (TLC), residual volume (RV) and functional residual capacity (FRC) post-intervention change from baseline.

(4) Blood oxygen levels Measured by arterial blood gas, pulse oximetry or transcutaneous oximetry.

(5) Ventilation scanning Radiological or nuclear medicine imaging.

(6) Nutritional status Difference in growth (cm/year), weight (kg/year), or body composition (body mass index (BMI)).
(7) Cost of intervention (equipment and duration)

(8) Adherence to treatment

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Cystic Fibrosis and Genetic Disorders Group methods used in reviews.

Relevant studies were identified from the Group's Cystic Fibrosis Trials Register using the terms: physiotherapy AND PEP.

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), quarterly 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.

We performed an additional search of the electronic database CINAHL from 1982 to 2001. For the full search strategy, please see the appropriate additional table (Table 01).

The review authors contacted manufacturers of PEP devices regarding any additional studies. The authors contacted other centres where studies on PEP were being undertaken.

Date of the most recent search of the Cystic Fibrosis Trials Register: February 2006.

METHODS OF THE REVIEW

Two authors (ME, AJ) independently reviewed all citations and abstracts identified by the search to determine which papers assessed should be included. The authors resolved disagreements by consensus.

Each of the two authors independently assessed the methodological quality of selected studies. The authors evaluated study quality using the 11-item PEDro scale (Maher 2003), which is based on the Delphi List (Verhagen 1998). Quality items are: specification of source of participants and eligibility criteria; random allocation to groups; concealed allocation; groups similar at baseline; blinding of participants; blinding of therapists; blinding of assessors; outcome measurements obtained from more than 85% of participants; presence of an intention-to-treat analysis; reporting of results of between-group statistical comparisons; reporting of point measures and measures of variability. The review authors used both published data and additional data obtained from study authors in determining whether criteria were met. The review authors resolved any disagreements by consensus. There was a high level of agreement between them, with only three studies (12%) requiring consensus discussions (Darbee 2004; McIlwaine 2001; Pfeifer 1992).

Elbourne discusses methods for meta-analysing cross-over studies (Elbourne 2002). These methods rely on the data that are reported within the primary paper. The method that has been adopted within this review uses the data from the first period only, ignoring any data from the second period that was available. Each author extracted data for each of the outcome measures listed above. Where studies are published in insufficient detail, the review authors contacted the study authors with a request to provide the required data. The Cochrane Collaboration software - Review Manager 4.2 has been used to compile and analyse the data (Review Manager 2003).

For all studies included, the following details are given: criteria for diagnosis of CF, methods of participant selection, and baseline characteristics of the active and placebo groups including age, sex, genotype and lung function.

For continuous outcomes, the review authors recorded either the mean change from baseline for each group or mean post-treatment or intervention values and the standard deviation for each group. In the case of binary outcomes, the authors collected data on the number of participants with each outcome event by allocated treatment groups irrespective of compliance and whether or not the participant was later thought to be ineligible or otherwise excluded for treatment or follow up, in order to allow an intention-to-treat analysis.

For more information on the statistical methods used in this review, see Cystic Fibrosis and Genetic Disorders Group Editorial Information.

The authors analysed studies in which the intervention consists of a single treatment separately from those studies in which a course of treatments is used. Within the latter group, the authors analysed studies of up to seven days treatment separately from studies of longer duration. The authors grouped outcome data from longer-term studies (more than seven days) into those measured at one, three, six, twelve months, and annually thereafter. If outcome data are recorded at other time periods, then the authors consider examining these as well.

If the authors had been able to include adequate numbers of studies, they would have looked for heterogeneity between studies. To investigate this, they planned to perform subgroup analyses based on the following factors: level of PEP (<10 cm H$_2$O, 10 to 20 cm H$_2$O, >20 cm H$_2$O), use of Hi-PEP, disease state (exacerbation versus stable), use of co-interventions (positioning, other airway clearance techniques), age (pediatric, adolescent, adult), gender,
and disease severity (FEV1% pred >90%, 70% to 90%, 40% to 69%, <40%).

**DESCRIPTION OF STUDIES**

Sixty-six citations were retrieved by the search. These represented 40 studies. No extra studies were identified with the CINAHL search or through contacting manufacturers of PEP devices.

Twenty-five studies involving 507 participants met the inclusion criteria. Sixteen were published as full articles (Braggion 1995; Darbee 2004; Falk 1984; Hofmeyr 1986; Lannefors 1992; McIlwaine 1997; McIlwaine 2001; Mortensen 1991; Newbold 2005; Padman 1999; Pfleger 1992; Steen 1991; Tyrrell 1986; van Asperen 1987; van der Schans 1991; van Winden 1998). Nine were published in abstract form only (Balestri 2004; Battistini 2001; Costantini 2001; Darbee 1990; Falk 1993; Gaskin 1998; Kofer 1998; McIlwaine 1991; Placi2001).

Of the other 15 studies, nine studies were excluded after assessment. Two studies were excluded because no data were reported and the study authors confirmed that no data would become available (Castle 1994; Gotz 1995); one because the outcomes measured were not outcomes of interest for this review (Dosman 2003); one because it was not a randomised study (Orlik 2000); one because the intervention, to which PEP was compared, was not a physical airway clearance therapy (Laube 2000); one because neither of the interventions being compared were PEP (Oermann 2001); two because the use of PEP versus the other physical airway clearance therapy was not the factor which had been randomised (Fitzgerald 2001; Znotina 2000); and one because it was performed on participants with chronic bronchitis (van Hengstum 1987).

The remaining six studies are awaiting assessment. Of these six studies, two have not yet been obtained in their full published version with English translation (Sanchez Riera 1999; Tonnesen 1982). In the other four studies, all of which have been published in abstract form only, the study design or outcome data have been reported in insufficient detail to determine whether the inclusion criteria have been met (Falk 1984; Kofer 1994; Lagerkvist 1997; Wong 2000). These authors have been contacted where possible and we await further data which they may make available.

Among the twenty-five included studies, 507 participants were involved, with sample sizes in individual studies ranging from 5 to 66 participants. Eight were single treatment studies (Darbee 2004; Falk 1984; Falk 1993; Kofer 1998; Lannefors 1992; Mortensen 1991; Pfleger 1992; van der Schans 1991). In five studies the duration of each treatment arm was less than seven days ( Balestri 2004; Battistini 2001; Braggion 1995; Hofmeyr 1986; Placi2001). In the remaining 12 studies, the duration of each treatment arm ranged from two weeks to two years (Costantini 2001; Darbee 1990; Gaskin 1998; McIlwaine 1997; McIlwaine 1991; McIlwaine 2001; Newbold 2005; Padman 1999; Steen 1991; Tyrrell 1986; van Asperen 1987; van Winden 1998).

Three studies were conducted in participants experiencing a respiratory exacerbation (Braggion 1995; Hofmeyr 1986; Placi 2001). All used a cross-over design with a duration of one or two days in each arm. Hence they provide limited evidence for the effect of PEP for treatment of an exacerbation.

In one of the included studies, the PEP intervention met the definition of Hi-PEP, because the intervention included a full forced expiration against a fixed mechanical resistance (Pfleger 1992).

One study was conducted exclusively with infants (Costantini 2001). Two studies were conducted exclusively with adolescents (McIlwaine 2001; Tyrrell 1986). Two studies were conducted exclusively with adults (Darbee 1990; Newbold 2005). Ten studies combined paediatric and older participants and ten studies combined adolescent and adult participants. Only one of these provided data for any age subgroup independently (Gaskin 1998).

Eighteen of the included studies involving 403 participants reported gender of the participants (Balestri 2004; Battistini 2001; Braggion 1995; Costantini 2001; Darbee 1990; Darbee 2004; Falk 1984; Gaskin 1998; Hofmeyr 1986; Kofer 1998; Lannefors 1992; McIlwaine 1997; McIlwaine 2001; Mortensen 1991; Newbold 2005; Pfleger 1992; Tyrrell 1986; van Winden 1998). One had an even gender ratio (Braggion 1995). Most had more male than female participants, resulting in an overall male: female ratio of 3:2.

Six studies did not report any measure of disease severity of the included participants. Fourteen studies reported the FEV1% predicted values of participants at baseline. In three of these studies, FEV1 values were only in the moderate to severe range (<70% predicted) (Darbee 2004; Falk 1984; Placi 2001). The remaining studies included participants with a wide range of lung function impairment, most commonly from severe to normal (<40% to >90% predicted). Those studies reporting Shwachman scores as a measure of disease severity also included participants with a wide range of scores, except one in which the range included only mild and moderate severity (70+ % predicted) (Padman 1999).

Twenty of the included studies involving 300 participants were cross-over studies. Data from the end of the first randomisation arm were obtained for three of these studies (Darbee 1990; Tyrrell 1986; van Asperen 1987), but could not be obtained for the remaining 17 studies (Balestri 2004; Battistini 2001; Braggion 1995; Darbee 2004; Falk 1984; Falk 1993; Hofmeyr 1986; Kofer 1998; Lannefors 1992; McIlwaine 1991; Mortensen 1991; Padman 1999; Pfleger 1992; Placi 2001; Steen 1991; van der Schans 1991; van Winden 1998).

Additional data were obtained from the authors of nine of the studies (Costantini 2001; Darbee 1990; Gaskin 1998; Kofer 1998; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Tyrrell 1986; van Asperen 1987).
METHODOLOGICAL QUALITY

The eleven criteria in the PEDro score of methodological quality and the studies which met each of them are detailed below (Maher 2003).

Criterion 1
The authors described both a list of criteria used to determine who was eligible to participate in the study and the source of participants. This criterion was met by 10 studies (Braggion 1995; Costantini 2001; Darbee 1990; Darbee 2004; Falk 1984; Falk 1993; Gaskin 1998; Hofmeyr 1986; Kofer 1998; Lanefors 1992; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Mortensen 1991; Newbold 2005; Pfieger 1992; van Asperen 1987).

Criterion 2
The participants were randomly allocated to groups (in a crossover study, to treatment order). This criterion was met by all studies (Balestri 2004; Battistini 2001; Braggion 1995; Costantini 2001; Darbee 1990; Darbee 2004; Falk 1984; Falk 1993; Gaskin 1998; Hofmeyr 1986; Kofer 1998; Lanefors 1992; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Mortensen 1991; Newbold 2005; Padman 1999; Pfieger 1992; Placidi 2001; Steen 1991; Tyrrell 1986; van Asperen 1987; van der Schans 1991; van Winden 1998).

Criterion 3
Allocation was concealed (ie, that the person who determined if a participant was eligible for inclusion in the study was unaware, when this decision was made, of which group the participant would be allocated to). This criterion was met by one study (Newbold 2005).

Criterion 4
The groups were similar at baseline regarding the most important prognostic indicators (i.e. based on at least one measure of the severity of CF and one outcome measure at baseline, the groups’ outcomes would not be expected to differ by a clinically significant amount). This criterion was met by 11 studies (Darbee 1990; Darbee 2004; Gaskin 1998; Hofmeyr 1986; McIlwaine 1997; McIlwaine 2001; Mortensen 1991; Newbold 2005; Pfieger 1992; van Asperen 1987; van Winden 1998).

Criterion 5
The participants did not know which group they had been allocated to. This criterion was not met by any of the studies.

Criterion 6
The person applying the therapy did not know which group the participants had been allocated to. This criterion was not met by any of the studies.

Criterion 7
The person assessing at least one outcome measure did not know which group the participants had been allocated to. This criterion was met by four of the studies (Falk 1984; McIlwaine 1997; McIlwaine 2001; Pfieger 1992). For self-reported outcomes (eg, visual analogue scale, pain diary), the assessor is considered to be blind if the participant was blind.

Criterion 8
The measures of at least one key outcome at one time point were obtained from more than 85% of the participants initially allocated to groups. This criterion was met by 14 studies (Balestri 2004; Battistini 2001; Darbee 1990; Falk 1984; Gaskin 1998; Hofmeyr 1986; Kofer 1998; Lanefors 1992; McIlwaine 1997; Mortensen 1991; Newbold 2005; Pfieger 1992; Steen 1991; van Winden 1998).

Criterion 9
All participants, for whom outcome measures were available, received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by “intention to treat”. This criterion was met by two studies (Falk 1984; Gaskin 1998). This criterion is satisfied, even if there is no mention of analysis by intention to treat, if the report explicitly states that all participants received treatment or control conditions as allocated.

Criterion 10
The results of between-group statistical comparisons are reported for at least one key outcome. This criterion was met by 19 studies (Balestri 2004; Braggion 1995; Falk 1984; Falk 1993; Gaskin 1998; Hofmeyr 1986; Kofer 1998; Lanefors 1992; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Mortensen 1991; Newbold 2005; Pfieger 1992; Steen 1991; Tyrrell 1986; van Asperen 1987; van der Schans 1991; van Winden 1998).

Criterion 11
Either (a) point measures and measures of variability for at least one continuous outcome or (b) the number of participants in each category for at least one categorical outcome are provided or both (a) and (b). This criterion was met by 22 studies (Balestri 2004; Braggion 1995; Costantini 2001; Darbee 1990; Falk 1984; Falk 1993; Gaskin 1998; Hofmeyr 1986; Kofer 1998; Lanefors 1992; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Mortensen 1991; Newbold 2005; Pfieger 1992; Placidi 2001; Steen 1991; Tyrrell 1986; van Asperen 1987; van der Schans 1991; van Winden 1998).

As a general indication of the relative methodological quality of the studies, the total number criteria met by each study are given in the additional tables (Table 02). Please note that because Criterion 1 relates to external validity (or “generalisability” or “applicability” of the results), it is not included in this summary score of internal validity (Maher 2003). Also note that the criteria could vary in their impact on potential bias in the results and thus the summary scores are not intended to be suitable for analysis as continuous data.
RESULTS

This review makes comparisons of PEP versus conventional physiotherapy (PDPV) for CF. These comparisons are also made by the Cochrane review 'Conventional chest physiotherapy compared to other airway clearance techniques for cystic fibrosis' (Main 2005). The statistical methods used in the two reviews differ. Main and colleagues used the generic inverse variance method. The current review has not used the generic inverse variance method, but it is intended that a statistician will be recruited to participate in the next update, thus allowing the generic inverse variance method to be used. Therefore, the data that could be included in the two reviews currently differ. This discrepancy will be resolved with the next version of this review.

Primary outcomes

(1) FEV₁


(a) Single treatment

Seven studies involving 95 participants measured FEV₁ after a single treatment (Darbee 2004; Falk 1993; Koffler 1998; Pfleger 1992; van Asperen 1987; van der Schans 1991; van Winden 1998). There was no significant difference in FEV₁ after PEP compared to the forced expiratory technique (FET) (Falk 1993), PDP (van Asperen 1987), non-invasive bilevel ventilatory support (nBVS) (Koffler 1998), Flutter (van Winden 1998), 5 cm H₂O PEP (van der Schans 1991), or >20 cm H₂O PEP (Darbee 2004). One study found that FEV₁ was significantly lower after a treatment of AD followed by Hi-PEP, compared to AD alone (Pfleger 1992). This is presented in an additional table (Table 03).

(b) Short-term (up to seven days)

Two studies involving 34 participants measured FEV₁ after four treatments (Braggion 1995; Hofmeyr 1986). Four treatments of PEP in sitting, PEP in postural drainage positions, or breathing exercises in postural drainage positions on a single day induced no significant differences in FEV₁ (Hofmeyr 1986). Four treatments of PEP, postural drainage with undefined chest physiotherapy techniques, or Flutter over two days induced no significant differences in FEV₁ (Braggion 1995).

(c) Long-term studies (more than seven days)

Ten studies involving 282 participants measured FEV₁ after a series of treatments over more than seven days (Darbee 1990; Gaskin 1998; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Newbold 2005; Padman 1999; Steen 1991; van Asperen 1987; van der Schans 1991; van Winden 1998). Please note that the data in Statistical Analysis for this section are incomplete, representing only six of the ten studies. The remaining four studies were cross-over studies from which data from the end of the first randomisation arm could not be obtained. No significant differences in FEV₁ were demonstrated after two weeks of treatment with either PEP or Flutter (van Winden 1998); after a month of PEP, AD, or Flutter (Padman 1999); after one month of PEP or PDP (for this study, weighted mean difference (WMD) 0.60% predicted (95% CI -6.33 to 7.53)) (van Asperen 1987); after one month of PEP, PEP followed by PDPV, PDPV, or PEP + FET (Steen 1991); after two months of PEP, AD, or PDP (McIlwaine 1991); or after three months of PEP or PDPV (WMD -0.50% predicted (95% CI -3.68 to 2.68) (Darbee 1990).

Four studies with 188 participants lasted at least one year. In a one-year study in children and adolescents, FEV₁ declined by a mean of 1.24% predicted in the PEP group, while in the Flutter group it deteriorated by 10.95%, WMD 9.71 (95% CI -2.12 to 21.54) (McIlwaine 2001). However, in a 13-month study, annual decline in FEV₁ was 4.2% predicted in the PEP group and 2% predicted in the Flutter group, WMD -2.20 (95% CI -7.07 to 2.67) (Newbold 2005). FEV₁ improved by a mean of 5.98% predicted for the PEP group, while in the PDPV group it deteriorated by 2.28% predicted in a one-year study, WMD 8.26 (95% CI 0.76 to 15.76) (McIlwaine 1997). In a two-year study, however, no significant difference in the rates of decline in FEV₁ were reported between the PEP group and the PDPV group, with mean annual declines of 2.94% predicted and 2.29% predicted, respectively, WMD -0.65 (95% CI -3.25 to 1.95) (Gaskin 1998).

(2) Number of respiratory exacerbations per year

Four cross-over studies involving 71 participants reported participants being withdrawn due to exacerbations, although these are not well-defined (Padman 1999; Pfleger 1992; Steen 1991; van Asperen 1987). It is also unclear which treatments the participants were randomised to at the time of departure from any of these studies.

Two parallel studies involving 82 participants reported the number of respiratory exacerbations severe enough to require hospitalisation (McIlwaine 2001; Newbold 2005). In a one-year study with 20 participants per group, respiratory exacerbations severe enough to require hospitalisation occurred five times in the PEP group and 18 times in the Flutter group. A Wilcoxon rank sum test indicated this difference was statistically significant (P = 0.03) but the number of hospitalisations per individual is not reported so this data does not appear in Statistical Analysis (McIlwaine 2001). Similarly, a 13-month study with 21 participants per group found respiratory exacerbations severe enough to require hospitalisation occurred six times in the PEP group and 14 times in the Flutter group (Newbold 2005). This represented a mean of 0.3 hospitalisations per participant in the PEP group and 0.7 hospitalisations per participant in the Flutter group, WMD -0.40 (95% CI -0.92 to 0.12). This is the only study entered in Statistical Analysis for this section.

(3) Number of days of intravenous antibiotics per year
One study with 26 participants and lasting one year measured intravenous antibiotic use, although it is unclear whether these were prescribed in response to a respiratory exacerbation (Costantini 2001). More days on intravenous antibiotics were reported with PEP (6.2 days per participant per year) than PDPV (1.8 days per participant per year), although no measures of variability could be obtained to determine whether this was statistically significant (Costantini 2001). This is presented in an additional table (Table 04).

(4) Well-being
One study reported well-being as an outcome measure (Gaskin 1998). In this two-year, parallel study of PEP versus PDPV, neither group demonstrated a significant change in quality of well-being (QWB) scores, which had been similar at baseline (Gaskin 1998).

(5) Adverse effects
Two studies with 66 participants reported adverse events as an outcome measure (Costantini 2001; McIlwaine 1997). In a year-long study of PEP versus conventional PDP in children and adolescents, no adverse events were reported by either group (McIlwaine 1997). In a one-year study of infants, side effects were described as rare. Although gastro-oesophageal reflux was reported more commonly in the PEP group than the PDPV group, RR 1.07 (95% CI 0.37 to 3.11), those in the PEP group described their reflux as mild. Reflux severe enough to cause withdrawal from the study was also examined, with all three cases occurring in the PDPV group, RR 0.12 (95% CI 0.01 to 2.18) (Costantini 2001). This is the only study entered in Statistical Analysis for this section.

(6) Survival
No studies reported survival rates per se. One study reported one death of a severely affected 18-year old girl, but it is not stated which treatment she was receiving (Steen 1991).

(7) Exercise tolerance
One study conducted exercise testing using cycle ergometry, but reported no data for this outcome measure (Gaskin 1998).

(8) Participant preference
Nine studies with 222 participants reported on technique acceptability or participant preference (Braggion 1995; Costantini 2001; Darbee 1990; Falk 1984; Kofler 1998; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Steen 1991).

(a) Single treatment
Two studies involving 34 participants measured participant preference after a single treatment (Falk 1984; Kofler 1998). When compared to nBVS, 60% of participants preferred nBVS, 25% preferred PEP, and 15% had no preference (Kofler 1998). PEP in sitting was the preferred treatment for 11 of 14 participants, when compared to PEP in PD positions, PDPV, or pursed lip breathing. It was reported that "even though all participants had received postural drainage and percussion as an integral part of treatment, they did not hesitate to accept [PEP in sitting], which was easier, less time-consuming and could be used when needed” (Falk 1984).

(b) Short-term (up to seven days)
One study involving 16 participants measured participant preference after a short-term treatment course. A two-day course of four treatments with PEP was compared with the same regimen of PD with undefined chest physiotherapy techniques, or flutter. Three-point rating scales (criteria unspecified) of effectiveness and tolerance were recorded after each arm, with no significant differences between interventions (Braggion 1995).

(c) Long-term (more than seven days)
Six studies involving 172 participants measured participant preference after a treatment course of greater than seven days duration (Costantini 2001; Darbee 1990; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Steen 1991). Please note the data in Statistical Analysis for this section are incomplete, including only one of the six studies. Data from the remaining five studies could not be obtained in sufficient detail for inclusion in Statistical Analysis. The cross-over study comparing two months of PEP, conventional PDP, and AD recorded five subjective measures which may influence participant preference: treatment duration; treatment comfort; flexibility of treatment times; control in performing own treatment; and how disruptive treatment was to daily living. PEP had a significantly shorter reported treatment time than PDP or AD. PEP was rated significantly better than PDP and not significantly different to AD on each of the other four measures (McIlwaine 1991). Standard deviations were not available for these outcomes. Mean data are presented in an additional table (Table 05). PEP was the treatment of choice in the other two long-term, cross-over studies (Darbee 1990; Steen 1991). PEP in combination with FET was chosen by 23 of 24 participants as their long-term airway clearance physiotherapy, in preference to PEP alone, PDP & FET, or five minutes of PEP followed by PDP and FET (Steen 1991). When compared to PDPV, “patients... preferred PEP mask for convenience, independence and ease of use, as determined by a standardized written questionnaire” (not described) (Darbee 1990).

Participant preference also favoured PEP in the three one-year parallel studies (Costantini 2001; McIlwaine 1997; McIlwaine 2001). The study of PEP versus flutter reported “discontinuation due to lack of perceived effectiveness in clearing their secretions”. Of 40 participants, five discontinued for this reason, all from the flutter group, RR 0.09 (95% CI 0.01 to 1.54) (McIlwaine 2001). In the study of PEP versus PDPV, participant preference was only recorded in the PEP group, as all participants were PEP naive prior to starting the study. All 18 participants in the PEP group nominated the PEP intervention as their preferred airway clearance modality (McIlwaine 1997). Although it was not stated how participant preference was determined, the conclusion from the study of PEP versus PDPV in infants was that the parents and infants preferred PEP (Costantini 2001).
Secondary Outcomes

(1) Direct measures of mucus clearance

Five studies with 61 participants measured radiolabelled aerosol clearance after a single treatment of PEP (Darbee 1990; Falk 1984; Lannefors 1992; Mortensen 1991; van der Schans 1991). Please note, all were cross-over studies from which data from the end of the first randomisation arm could not be obtained so no data have been entered in Statistical Analysis. Radioisotope retention two hours after a 20-minute treatment of PEP and FET was significantly less than for FET alone (Falk 1993), this is presented in an additional table (Table 06). No significant difference in clearance was identified between PEP and PDPV (Darbee 1990) or voluntary cough (van der Schans 1991). No significant difference in clearance was identified between PEP plus FET and PD plus FET (Lannefors 1992; Mortensen 1991) or exercise plus FET (Lannefors 1992).

(2) Expectorated secretions, dry or wet weight, or volume

Twelve cross-over studies with 166 participants reported measures of expectorated sputum (Balestri 2004; Battistini 2001; Braggion 1995; Falk 1984; Hofmeyr 1986; McIlwaine 1991; Mortensen 1991; Pfleger 1992; Placidi 2001; Tyrrell 1986; van Asperen 1992). No significant difference in wet weight of sputum expectorated during and for 120 minutes after treatment demonstrated no significant difference between PEP and PD (Mortensen 1991). Dry weight of sputum was not significantly different after single treatments of PEP and >20 cm H2O PEP (Darbee 2004). One study demonstrated Hi-PEP produced significantly more sputum than either AD or AD then Hi-PEP (Pfleger 1992). This is presented in an additional table (Table 08).

(i) Single treatment

Four studies with 34 participants measured expectorated secretions after a single treatment (Darbee 2004; Falk 1984; Mortensen 1991; Pfleger 1992). One study found wet weight of sputum during and for 50 minutes after PEP (whether in sitting or PD positions) was greater than that induced by PDPV or pursed lip breathing (Falk 1984), this is presented in an additional table (Table 07). However, wet weight of sputum expectorated during and for 120 minutes after treatment demonstrated no significant difference between PEP and PD (Mortensen 1991). Dry weight of sputum was not significantly different after single treatments of PEP and >20 cm H2O PEP (Darbee 2004). One study demonstrated Hi-PEP produced significantly more sputum than either AD or AD then Hi-PEP (Pfleger 1992). This is presented in an additional table (Table 08).

(ii) Short-term (up to seven days)

No significant difference in expectorated secretions was identified between PEP and PDP, whether measured by sputum wet weight (Battistini 2001; Tyrrell 1986) or volume (van Asperen 1987). No significant difference in wet or dry weight of sputum was identified between PEP and PDPV or HFCC (Braggion 1995). No significant difference in wet or dry weight of sputum was identified between PEP and CPAP and nBVS and directed huffing or coughing (Placidi 2001). No significant difference in sputum weight was identified between PEP and cycling on an exercise bike (Balestri 2004). When wet weight of sputum was measured during and for 30 minutes after treatment, breathing exercises in postural drainage positions induced significantly greater sputum expectoration than PEP in postural drainage positions. The latter in turn produced significantly more expectorate than PEP in sitting (Hofmeyr 1986). This is presented in an additional table (Table 09).

(c) Long-term (more than seven days)

As outlined in the ‘Methods’ section, this review does not examine this outcome where it is measured after more than 7 days of treatment.

(3) Other pulmonary function tests

(a) FVC


(i) Single treatment

Seven studies involving 102 participants measured FVC after a single treatment (Darbee 2004; Kofler 1998; Pfleger 1992; Tyrrell 1986; van der Schans 1991; van Asperen 1987; van Winden 1998). Please note, the data in Statistical Analysis for this section are incomplete, representing only one of the six studies. The remaining five studies were cross-over studies from which data from the first randomisation arm could not be obtained. No significant difference in FVC was demonstrated with a single treatment of PEP versus 5 cm H2O PEP (van der Schans 1991). No significant difference in FVC was demonstrated with a single treatment of PEP versus >20 cm H2O PEP (Darbee 2004). After a single treatment with PEP or PDP, no significant difference in FVC was demonstrated, WMD 1.90 (95% CI -4.96 to 8.76) (Tyrrell 1986). A second study comparing a single treatment with PEP or PDP also showed no significant difference, WMD 2.20 (95% CI -11.04 to 15.44) (van Asperen 1987). No significant difference in FVC was demonstrated after one treatment with either PEP or flutter (van Winden 1998). No significant difference in FVC was noted after one treatment with PEP or nBVS (Kofler 1998). One study found that FVC was significantly lower after a treatment of AD followed by Hi-PEP, compared to AD alone (Pfleger 1992). This is presented in an additional table (Table 10).

(ii) Short-term (up to seven days)

After two days of twice-daily treatment, FVC significantly increased in a group performing PEP in sitting and significantly decreased in a group performing PDPV (Falk 1984). This is presented in an additional table (Table 11).

(iii) Long-term (more than seven days)

Ten studies involving 308 participants measured FVC after a series of treatments over more than seven days (Darbee 1990; Gaskin 1998; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Newbold 2005; Steen 1991; Tyrrell 1986; van Asperen 1987; van Winden 1998). Please note, the data in Statistical Analysis for this section are incomplete, representing only six of the nine studies. The remaining three studies were cross-over studies from which
data from the end of the first randomisation arm could not be obtained. After one month of twice-daily treatments with PEP or PDP, no significant difference in FVC was found in adolescents (Tyrrell 1986), or in children and adolescents (van Asperen 1987). Meta-analysis of these two studies indicated a significant difference in favour of PDP, WMD -4.18 (95% CI -12.92 to 4.56) (Tyrrell 1986; van Asperen 1987). Data from a third relevant study were not able to be included in the meta-analysis (Steen 1991). In this study, no significant differences in FVC were demonstrated after one month of PEP, PEP followed by PDPV, PDPV, and PEP + FET (Steen 1991). No significant difference in FVC was demonstrated after three months of PEP or PDPV, WMD 2.09 (95% CI -5.46 to 9.64) (Darbee 1990). No significant difference in FVC was 4.7% predicted in the PEP group and 3% predicted in the Flutter group, while in the Flutter group it deteriorated by 8.87% predicted, WMD 5.29 (95% CI -7.84 to 18.42) (McIlwaine 2001). However, in a 13-month study, annual decline in FEF_{25-75} was 3.1% predicted in the PEP group and 2% predicted in the Flutter group, WMD -1.10 (95% CI -6.50 to 4.30) (Newbold 2005).

(c) TLC

Three studies involving 50 participants measured total lung capacity (TLC) (Darbee 1990; van der Schans 1991; van Winden 1998). Please note, the data in Statistical Analysis for this section are incomplete, representing only four of the eight studies. The remaining four studies were cross-over studies from which data from the first randomisation arm could not be obtained. No significant differences in FEF_{25-75} were demonstrated after two weeks of treatment with either PEP or flutter (van Winden 1998). After a month of each of three therapies: PEP, PD, and flutter, no significant differences in FEF_{25-75} were identified (Padman 1999). Similarly, no significant differences in FEF_{25-75} were demonstrated after one month of PEP, PEP followed by PDPV, PDPV, and PEP + FET (Steen 1991); or after one month of PEP or PDP, WMD -6.20 (95% CI -14.41 to 2.01) (van Asperen 1987). A study comparing two months of PEP, PDP or AD also showed no significant differences in FEF_{25-75} (McIlwaine 1991). No significant difference in FEF_{25-75} was demonstrated after three months of PEP or PDPV, WMD -3.08 (95% CI -7.87 to 1.71) (Darbee 1990).

At the end of a one year study, mean FVC for the PEP group increased by 6.57% predicted, and mean FVC for the PDPV group decreased by approximately 2.17% predicted. This was a significant difference, WMD 8.74 (95% CI 1.44 to 16.04) (McIlwaine 1991). No significant difference in FVC was demonstrated after two weeks of treatment with PEP and Flutter (van Winden 1998). Over one year, a decrease in mean FVC was reported with Flutter of 8.62% predicted while in the PEP group mean FVC increased 0.06% predicted, WMD 8.68 (95% CI -0.54 to 17.90) (McIlwaine 2001). However, in a 13-month study, annual decline in FVC was 4.7% predicted in the PEP group and 3% predicted in the Flutter group, WMD -1.70 (95% CI -6.27 to 2.87) (Newbold 2005).

(b) FEF_{25-75}

Eleven studies with 263 participants reported FEF_{25-75} results (Darbee 1990; Darbee 2004; Koffer 1998; McIlwaine 1991; McIlwaine 1997; McIlwaine 2001; Newbold 2005; Padman 1999; Steen 1991; van Asperen 1987; van Winden 1998).

(i) Single treatment

No significant difference in FEF_{25-75} was noted after one treatment with PEP or nBVS (Koffer 1998); after one treatment with PEP or flutter (van Winden 1998); or after one treatment with PEP or >20 cm H_{2}O PEP (Darbee 2004).

(ii) Short-term (up to seven days)

No studies.

(iii) Long-term (more than seven days)

Eight studies involving 196 participants measured FEF_{25-75} after a series of treatments over more than seven days (Darbee 1990; McIlwaine 1997; McIlwaine 2001; Mortensen 1991; Padman 1999; Steen 1991; van Asperen 1987; van Winden 1998). Please note, the data in Statistical Analysis for this section are incomplete, representing only four of the eight studies. The remaining four studies were cross-over studies from which data from the first randomisation arm could not be obtained. No significant differences in FEF_{25-75} were demonstrated after two weeks of treatment with either PEP or flutter (van Winden 1998). After a month of each of three therapies: PEP, PD, and flutter, no significant differences in FEF_{25-75} were identified (Padman 1999). Similarly, no significant differences in FEF_{25-75} were demonstrated after one month of PEP, PEP followed by PDPV, PDPV, and PEP + FET (Steen 1991); or after one month of PEP or PDP, WMD -6.20 (95% CI -14.41 to 2.01) (van Asperen 1987). A study comparing two months of PEP, PDP or AD also showed no significant differences in FEF_{25-75} (McIlwaine 1991). No significant difference in FEF_{25-75} was demonstrated after three months of PEP or PDPV, WMD -3.08 (95% CI -7.87 to 1.71) (Darbee 1990).
(4) Blood oxygen levels

Eight studies with 119 participants measured blood oxygen levels (Balestri 2004; Battistini 2001; Costantini 2001; Darbee 2004; Falk 1984; Hofmeyr 1986; Kofler 1998; Padman 1999).

(a) Single treatment

The improvement in SpO\textsubscript{2} during a single nBVS treatment was statistically significantly greater than with one treatment with PEP (Kofler 1998), this is presented in an additional table (Table 13). The change in SpO\textsubscript{2} was not significantly different after a single treatment of PEP versus >20 cm H\textsubscript{2}O PEP (Darbee 2004).

(b) Short-term (up to seven days)

There were no significant mid- or post-treatment differences between four treatments of breathing exercises in postural drainage positions, PEP in postural drainage positions, and PEP in sitting in a single day (Hofmeyr 1986). No significant difference in the lowest oxygen saturation recorded during treatment was identified between PEP and cycling on an exercise bike (Balestri 2004) or between PEP and PDPV (Battistini 2001). In a study comparing four treatments once each over two days, the mean gain in SpO\textsubscript{2} at 35 minutes after treatment was significantly higher for PEP in sitting than for PEP in postural drainage (PD) positions, for pursed lip breathing, or for PDPV. Please note, the treatment durations were unequal in this study (Falk 1984). This is presented in an additional table (Table 14).

(c) Long-term (more than seven days)

Two studies involving 41 participants measured SpO\textsubscript{2} after a series of treatments over more than seven days (Costantini 2001; Padman 1999). Please note, the data in Statistical Analysis for this section are incomplete, representing only one of the two studies. The remaining study did not present measures of variability for this outcome. In the one-year study of PEP versus PDPV, adherence was 96% in the PEP group and 92% in the PDPV group (McIlwaine 1997), this is presented in an additional table (Table 15). In the one-year study of PEP versus flutter, two participants were withdrawn from the PEP group due to non-compliance, RR 5.00 (95% CI 0.26 to 98.00). While none were withdrawn from the flutter group for non-compliance, five had dropped out due to perceived lack of treatment efficacy with the flutter, and a further two were withdrawn for clinical deterioration. Overall adherence was reported as 95.6% for the PEP group and 93.8% for the flutter group (McIlwaine 2001). This is presented in an additional table (Table 16).

Subgroup analyses

None of the intended subgroup analyses were possible due to small numbers of studies or insufficient detail allow the separate of subgroup data within any study. One study provided subgroup analysis based on age, which did not conform to the age groups for subgroup analysis defined in the protocol for this review. The data for the subgroup used are presented as an additional table (Table 17).

(5) Ventilation scanning/ Radiological Imaging

In a year-long study of infants, an increase in radiologic bronchic markings was less common in the PEP group than the PDPV group, RR 0.93 (95% CI 0.80 to 1.07) (Costantini 2001). In the same study, hyperinflation was assessed, but only data for the PDPV group are reported for this outcome. A one-year study of PEP versus PDP measured Brasfield chest radiograph score, and reported identical results for the two groups, WMD 0.00 (95% CI -1.20 to 1.20) (McIlwaine 1997). A two-year study of PEP versus PDP measured Brasfield chest radiograph score, but reported no data for this outcome measure (Gasik 1998).

In a one-year study of PEP versus flutter, a blinded radiologist evaluated changes in chest radiographs. The groups were not significantly different, although no data were published to support this (McIlwaine 2001).

(6) Nutritional status

No studies measured difference weight (kg per year) or body composition (BMI). One study with 26 participants reported having measured growth (Costantini 2001). Growth was described as “in the normal range for both groups”, but no data for this outcome were available.

(7) Cost of intervention (equipment and duration)

No studies measured cost.

(8) Adherence to treatment

Two studies with 80 participants monitored adherence with a series of treatments over one year (McIlwaine 1997; McIlwaine 2001). Please note, the data in Statistical Analysis for this section are incomplete, representing only one of the two studies. The remaining study did not present measures of variability for this outcome. In the one-year study of PEP versus PDPV, adherence was 96% in the PEP group and 92% in the PDPV group (McIlwaine 1997), this is presented in an additional table (Table 15). In the one-year study of PEP versus flutter, two participants were withdrawn from the PEP group due to non-compliance, RR 5.00 (95% CI 0.26 to 98.00). While none were withdrawn from the flutter group for non-compliance, five had dropped out due to perceived lack of treatment efficacy with the flutter, and a further two were withdrawn for clinical deterioration. Overall adherence was reported as 95.6% for the PEP group and 93.8% for the flutter group (McIlwaine 2001). This is presented in an additional table (Table 16).

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DISCUSSION

The searches found 40 studies that compared PEP with other physical interventions for airway clearance in people with CF. Nineteen of these 40 studies were only published in abstract form. The abstract format frequently limits the information on study design and results that can be obtained for use in the review without unpublished data from the author(s). Twenty-five studies met the inclusion criteria for this review.

It is unlikely that any studies of PEP have not been included. The search strategy was thorough, people with CF are often treated in
centres, and there are relatively few meetings for reporting research about CF. However, it is possible that some studies may have been published only as abstracts at physiotherapy conferences.

Amongst the studies, there was a wide range of therapies to which PEP was compared and variation in the duration of the intervention period. These factors, the frequent use of a cross-over design, the small number of studies, and the limited information provided by some authors limited the amount of meta-analysis that could be performed. Only four of the thirteen short-term studies enrolled participants with exacerbations. The other nine short-term studies are too short to determine the effect of therapy as maintenance when stable and do not help determine the relative effectiveness of the techniques during an infective exacerbation. PEP is also used in combination with various other interventions (e.g. pharmacological therapies, other physical therapy techniques, or the modification to the technique known as high pressure PEP). The evidence is therefore limited and it is difficult to make firm conclusions about the effects of PEP in comparison to other types of physiotherapy:

The measurement of lung function FEV$_1$ is important in CF because of its correlation with survival and quality of life (Liou 2001). No clear evidence was identified that PEP improves FEV$_1$ when compared to other methods. No difference in the effect of PEP versus other therapies on FEV$_1$ was identified in studies up to three months. Among the longer studies, results were either conflicting or also found no difference between the compared therapies.

A one-year study in children and adolescents reported a significantly reduced rate of hospital admission with PEP as opposed to Flutter (McIlwaine 2001). A similar study in adults showed the same trend (Newbold 2005). Unfortunately the data from the two studies were not in a form that allowed meta-analysis. Other studies reported some data regarding exacerbations and antibiotic use but these were not sufficiently well described to determine whether they met the definition of respiratory exacerbations and IV antibiotic use.

A small number of studies found significant differences in expectorated sputum measures when other types of chest physiotherapy were compared to PEP (Falk 1984; Hofmeyr 1986) or Hi-PEP (Pfleger 1992). However, such measures may be affected by swallowed secretions and expectorated saliva. In studies where these confounding factors were eliminated by measuring mucociliary clearance, these significant differences were not evident. All were cross-over studies (discussed further below).

Many other outcomes did not show a significant difference between PEP and the therapy to which it was compared. For example, when compared to PDPV, PEP achieved similar results for quality of well-being. In the year-long study in infants, blinded examination of chest radiographs showed no significant difference in the incidence of increased bronchial markings between the PEP and PDPV groups (Costantini 2001). When compared to flutter in children and adolescents, similar results occurred in FEF$_{25-75}$, and TLC (McIlwaine 2001).

No adverse events were recorded in the PEP group or in the PDPV group in the year-long study of 40 children (McIlwaine 1997). No adverse events were recorded in the PEP group or in the Flutter group in the year-long study of 40 children (McIlwaine 2001). There was no significant difference in the incidence of reflux between the PEP and PDPV groups in the year-long study of 26 infants. Gastro-oesophageal reflux severe enough to cause withdrawal from the study occurred in three participants in the PDPV group and in no participants in the PEP group, although this was not statistically significant (Costantini 2001).

In summary, there is not yet clear evidence to support the hypothesis that PEP is more effective in improving mucus clearance and other outcomes than other types of chest physiotherapy.

Limited evidence was identified in support of the hypothesis that PEP is more acceptable to people with CF than other types of chest physiotherapy. In all studies with an intervention period of less than one month, any measures of participant preference did not significantly favour PEP or the intervention to which it was compared. However, in all studies with an intervention period of at least one month, any measures of participant preference were in favour of PEP. The studies reporting participant preference were generally of low quality and the tools used to record participant preference were not well described or validated.

There were a large number of cross-over studies in the sample included in the review. The cross-over design has problems for studies of airway clearance therapies in CF. The magnitude and duration of carry-over effects are not known, although several included studies, which examined for these effects statistically, did not demonstrate them. The data from both arms of cross-over studies can only be incorporated in RevMan using the generic inverse variance method (Review Manager 2003). The current review has not used the generic inverse variance method, but it is intended that a statistician will be recruited to participate in the next update, thus allowing the generic inverse variance method to be used. Thus, data from cross-over studies will be able to be incorporated in the meta-analysis.

**AUTHORS’ CONCLUSIONS**

**Implications for practice**

There was no clear evidence to recommend PEP as a more or less effective intervention than other forms of physiotherapy for people with CF. The results for most of the key measures of treatment benefit were equivocal, or they differed between studies. There was some evidence to recommend PEP as a more acceptable intervention than other forms of physiotherapy for people with CF. How-
ever, the evidence that PEP was preferred over other techniques came from studies which were generally of low quality.

**Implications for research**

The abstract format frequently prevents evaluation of the scientific methodology of a study. Abstracts should be structured to contain essential information about methods and results. The large proportion of studies which were published only as abstracts highlights the need for full publication of studies in this area.

Cross-over studies are not a good design for clinical studies in CF due to the unstable nature of the disease (Southern 2003). They are potentially influenced by carry-over effects. More parallel, randomised clinical studies comparing PEP with other airway clearance modalities are needed. These studies should be adequately powered and a multi-centre approach may facilitate this. Such studies should, in particular, examine the influence of PEP and other therapies on FEV₁ and quality of life. Other important areas, which have not been assessed or reported, include survival, exercise tolerance, and cost.

Nine studies with 122 participants were conducted using short-term interventions on stable patients, which may be of little value given the nature of CF lung disease: a chronic course with acute exacerbations. Future studies should be planned to reflect clinical practice by focusing on short-term interventions during an exacerbation or long-term studies on initially stable patients.

The studies in this review frequently found no significant difference in efficacy between treatments. Future studies should include validated measures of participant preference, as this may help to determine a suitable treatment when measures of efficacy are equivocal. Similarly, cost and adverse effect outcome data would assist consumers in decision-making.

**Potential conflict of interest**

None known.

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**References**

References to studies included in this review

**Balestri 2004** *(published data only)*


**Battistini 2001** *(published data only)*


**Braggion 1995** *(published data only)*


**Costantini 2001**


**Darbee 1990** *(published and unpublished data)*


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**Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)**

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**Darbee 2004 [published data only]**


**Falk 1984 [published data only]**

**Falk 1993 [published data only]**


**Gaskin 1998 [published and unpublished data]**

**Hofmeyer 1986 [published data only]**


**Koehler 1998 [published data only]**

**Lannefors 1992 [published data only]**


**McIlwaine 1991 [published and unpublished data]**
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**Mortensen 1991 [published data only]**


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Padman 1999 [published data only]


Placidi 2001 [published data only]


Placidi 2001 [published and unpublished data]


Steen 1991 [published data only]


Tyrrell 1986 [published and unpublished data]


van Asperen 1987 [published and unpublished data]


van der Schans 1991 [published data only]


van Winden 1998 [published data only]


References to studies excluded from this review

Castle 1994


Dosman 2003


Fitzgerald 2001


Gottz 1995


Laube 2000


Oermann 2001

Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)

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Andersen 1979

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Main E, Prasad A, van der Schans C. Conventional chest physiotherapy compared to other airway clearance techniques for cystic fibrosis. In: The Cochrane Database of Systematic Reviews, Issue 1, 2005. Chichester, UK: John Wiley & Sons, Ltd.

McIlwaine 1996

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Prasad 1993

Prasad 2000
### Review Manager 2003

### Southern 2003

### van der Schans 2004

### Verhagen 1998

### Williams 1994
Williams MT. Chest physiotherapy and cystic fibrosis. Why is the most effective form of treatment still unclear? *Chest* 1994;106(6):1872–82.

### Zach 1987

### Zach 1990

*Indicates the major publication for the study

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## Tables

### Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Balestri 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>Randomised trial. Cross-over design. Treatments were given once during 1 week in random order, and once each in reverse order in the following week.</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>CF diagnosed by Centro Fibrosi Cistica (criteria not stated); stable (not defined); FEV1 54 - 95% predicted. 13 participants (10 males), age range 10 - 41 years.</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>2 interventions: (1) PEP treatment. Participants breathed through an underwater PEP device providing 10 cm H2O pressure. 15 expirations were followed by 3 bouts of coughing. This was performed in four positions: supine, right and left lateral decubitus, and sitting. (2) Exercise. Participants exercised on a cycle ergometer at 0.5 W/kg in 5 minute bouts, followed by 3 bouts of coughing. Each treatment was performed for 30 minutes.</td>
</tr>
</tbody>
</table>
### Characteristics of included studies (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Battistini 2001</th>
</tr>
</thead>
</table>
| Methods | Randomised trial.  
Cross-over design.  
Treatments were given once during 1 week in random order, and once each in reverse order in the following week. |
| Participants | CF diagnosed by Centro Fibrosi Cistica (criteria not stated); stable (not defined).  
8 participants (5 males); age range 9 - 43 years. |
| Interventions | 3 interventions:  
(1) PEP treatment. Participants breathed through an underwater PEP device providing 10 cm H2O pressure.  
15 expirations were followed by 5 forced, pursed-lip breaths, and vigorous coughing. This was performed in four positions: supine, right and left lateral decubitus, and sitting.  
(2) Postural drainage, percussion and vibration (PDPV). 1 minute of percussion was followed by 5 forced, pursed-lip breaths with vibration, then vigorous coughing. This was performed in six positions (unspecified).  
(3) Cough. Voluntary, vigorous coughing initiated every four minutes. |
| Outcomes | Sputum wet weight and transcutaneous pO2 during the intervention. |
| Notes | No statement regarding withdrawals or dropouts. |
| Allocation concealment | B – Unclear |

<table>
<thead>
<tr>
<th>Study</th>
<th>Braggion 1995</th>
</tr>
</thead>
</table>
| Methods | Randomised controlled trial.  
Cross-over design.  
Each treatment given twice daily for 2 days. |
| Participants | CF confirmed by sweat test.  
16 participants (8 male); mean age 20.3 years; mean FEV1 52.5, range 32 - 98% predicted; mean Schwachman score 65.1, range 45 - 87 points.  
Entry to study at time of hospital treatment of an acute pulmonary exacerbation. |
| Interventions | 4 interventions:  
(1) PEP treatment. Participants breathed through a Medipep, (Nuova Tecnomedica) mask with a steady PEP of 10 - 20 cm H2O;  
(2) Postural drainage with percussion and vibration (PDPV). 6 positions based on recent chest radiography for each participant;  
(3) High frequency chest compression (HFCC). Using ThAIRapy Bronchial Drainage System, chest compression in sitting at frequencies of 6, 8, 14, 15, 18 and 19 Hz were performed for 6 treatment sessions;  
Each treatment lasted 50 minutes: six 5-minute periods of the specific treatment, each followed by a 3-minute period of the forced expiratory technique (FET). |
| Outcomes | FEV1, FVC, and FEF25-75 were measured before and 30 minutes after each treatment. Expectorated sputum wet and dry weights during and for 30 minutes after each treatment were also measured. Technique acceptability was assessed using a three-point rating of effectiveness completed by the participant, and a three-point rating of tolerance, completed by the participant and also by the physiotherapist. |
| Notes | No statement on withdrawals or dropouts. |
| Participants were familiar with PD and PEP interventions. All were introduced to HFCC on the day before their first use. The participant’s usual airway clearance regimen was used for 2 days between the 2nd and 3rd treatment periods. |
Characteristics of included studies (Continued)

### Study: Costantini 2001

**Methods**
- Randomised trial.
- Parallel design.
- Treatment for 1 year.

**Participants**
- CF identified by newborn screening within the second month of life and confirmed on sweat test.
- 26 participants (14 male); aged under 4 months.

**Interventions**
- 2 interventions:
  2. Postural drainage, percussion and vibration (PDPV).

  Each treatment was performed for 30 minutes, twice daily.

  The airway clearance intervention was applied by the carer(s), who received a 2-week training period in either PEP or PDPV.

  Participants were followed as outpatients for 1 year.

**Outcomes**
- The number of courses of total and intravenous antibiotic treatment were recorded, although it is not stated whether these were prescribed in response to a respiratory exacerbation.
- Possible adverse effects were monitored.
- Oxygen saturation, chest radiographs, and growth were assessed. No method of radiograph assessment is mentioned. Measurements were conducted at 0, 6 and 12 months.

**Notes**
- 3 participants in the PDPV group withdrew from the study. These were among 4 participants in this group who developed gastro-oesophageal reflux. The three who withdrew did so “for the severity of their symptoms and were not evaluated”.

### Study: Darbee 1990

**Methods**
- Randomised trial.
- Cross-over design.
- Each treatment given 2 - 3 times daily for 3 months.

**Participants**
- CF confirmed by sweat test.
- 13 participants (7 male); mean age 25.7 years, range 18 - 34 years. Some outcome data on an additional 7 participants were received from the author.

**Interventions**
- 2 interventions:
  1. PEP treatment. Participants exhaled through a mask for 8 - 10 breaths, then exhaled to a low lung volume through the mask which usually stimulated a cough. This was repeated 5 - 6 times;
  2. Postural drainage, percussion and vibration (PDPV). Percussion was applied for 3 minutes over all segments. Participants breathed deeply several times at each minute. Three vibrations followed with exhalation through an open mouth, without force, until productive coughing occurred.

  Participants were instructed to treat until clear, 2 - 3 times per day.

**Outcomes**
- 2 measures of mucociliary clearance were repeated after each three-month treatment arm: the time taken for half the radiolabelled sputum in the whole lung to clear (T1/2-W) and the same in the peripheral region (T1/2-P). Convenience, independence and ease of use was determined with a standardised written questionnaire (not described).

**Notes**
- No statement on withdrawals or dropouts.
  
  Participants reported that they got clearer faster with PEP.

### Allocation concealment
- B – Unclear
**Characteristics of included studies (Continued)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Darbee 2004</th>
</tr>
</thead>
</table>
| Methods        | Randomised trial.  
                  Cross-over design.  
                  Each treatment given once. |
| Participants   | Cystic fibrosis confirmed by sweat test; stable (not defined) and not hospitalised during the previous month for management of an exacerbation.  
                  5 participants (3 female), mean age 18 years, range 13 years to 22 years; mean FEV1 52, range 35 - 68% predicted. |
| Interventions  | 2 interventions:  
                  (1) PEP treatment. Pressure 10 - 20 cm H2O. Participants breathed through a anaesthetic mask with an expiratory resistor for 8 - 10 breaths, followed by coughing. This was repeated 6 times.  
                  (2) PEP treatment as above, with pressure >20 cm H2O.  
                  Each intervention was applied on a different day (order randomised). A third intervention, control, was not randomised. |
| Outcomes       | FEV1, FEF25-75, RV, SVC, dry weight of sputum, and SpO2 were recorded before, after, and 45 minutes after each intervention session.  
                  Distribution of ventilation and gas mixing were also measured. |
| Notes          | One participant’s data was excluded when it was determined that there was a pulmonary exacerbation. |

<table>
<thead>
<tr>
<th>Study</th>
<th>Falk 1984</th>
</tr>
</thead>
</table>
| Methods        | Randomised trial.  
                  Cross-over design.  
                  Each treatment given once. |
| Participants   | CF diagnosis, chronic pseudomonas infection, and expectoration of greater than 1.5g/hr of sputum.  
                  14 participants (10 male); mean age 18 years, range 14 - 30 years; mean FEV1 34, range 15 - 55% predicted.  
                  Participants were excluded during or immediately after anti-pseudomonas treatment or a change in routine medication. |
| Interventions  | 4 interventions:  
                  (1) PEP treatment in sitting (PEPs). Pressure 17 cm H2O using an Astra Meditec PEP mask. Seated participants exhaled 6 - 12 times, followed by forced expirations with the glottis open and coughing as needed. This was repeated for 20 minutes;  
                  (2) PEP treatment in postural drainage positions (PEPpd). Participants performed the same breathing regimen for 4 - 5 minutes in each of 7 postural drainage positions. This intervention lasted 35 minutes;  
                  (3) Postural drainage, percussion and vibration (PDPV). During the same postural drainage regimen, participants received manual percussion, followed by 3 deep breaths with vibration, and FET. This intervention lasted 35 minutes;  
                  (4) Pursed lip breathing in sitting (PLBs). Seated participants inhaled slowly and exhaled through pursed lips 5 - 8 times, followed by FET. This intervention lasted 20 minutes.  
                  The 4 interventions were randomised over 2 days: one each morning and one each afternoon, with an interval of at least 5 hours. |
| Outcomes       | FEV1 and FVC were measured before and 50 minutes after each intervention session. Wet weight of expectorated sputum during and until 50 minutes after each intervention session. Transcutaneous pO2 was measured during the intervention and for 50 minutes after each intervention. Technique efficiency and acceptability were assessed using a questionnaire completed by the participant, although details of the questionnaire are not provided. |
| Notes          | No withdrawals nor dropouts. |
The authors state that 7 participants were studied during admission for their usual anti-pseudomonas treatment and the other 7 at least 1 month after treatment. This appears inconsistent with the exclusion criteria; see Participants.

<table>
<thead>
<tr>
<th>Allocation concealment</th>
<th>Falk 1993</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Methods Randomised controlled trial. Cross-over design. Each treatment given once.</td>
</tr>
<tr>
<td>Participants</td>
<td>CF diagnosis. 12 participants.</td>
</tr>
<tr>
<td>Interventions</td>
<td>3 interventions: (1) PEP treatment. Participants exhaled through a mask; (2) PEP with the forced expiratory technique (PEP+FET); (3) Control. Not defined. Each intervention was applied for 20 minutes on 1 of 3 consecutive days.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Retention of radiolabelled secretions in the lung was recorded at 0.5, 1, 2, and 24 hours after the start of the intervention. (The 24-hour value was used as a measure of the radioaerosol deposition.) Wet weight of sputum expectorated for the half hour during which the intervention was applied, and for the subsequent 1.5 hours was measured. The number of huffs and coughs during the half hour during which the intervention was applied, and for the subsequent 1.5 hours were counted.</td>
</tr>
<tr>
<td>Notes</td>
<td>No statement on withdrawals or dropouts.</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>B – Unclear</td>
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</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Gaskin 1998</th>
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</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Randomised trial. Parallel design. Treatment for 2 years.</td>
</tr>
<tr>
<td>Participants</td>
<td>CF diagnosed by Toronto CF Clinics (criteria not stated); FEV1 &gt; 40% predicted. 66 participants (34 males); mean age 21.6 years, range 11 - 45 years; mean FEV1 70.2% predicted (PEP group) and 65.3% predicted (PD&amp;P group).</td>
</tr>
<tr>
<td>Interventions</td>
<td>2 interventions: (1) PEP treatment. Participants exhaled through the Astra Meditec PEP mask; (2) Postural drainage and percussion (PD&amp;P). Not described beyond “conventional postural drainage and percussion”. The daily regimen for use of the devices is not described.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>FEV1, FVC, Quality of Well Being (QWB) score, a cycle ergometer exercise test, and the Brasfield chest radiograph score. All were recorded at three-monthly intervals. The participants also kept adherence and exercise diaries.</td>
</tr>
<tr>
<td>Notes</td>
<td>5 participants withdrew from the study, but none were lost to follow up. 4 from the PD&amp;P group withdrew soon after randomisation and one from the PEP group moved away, but returned to the clinic. No reason is provided for the withdrawals.</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>B – Unclear</td>
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<thead>
<tr>
<th>Study</th>
<th>Hofmeyr 1986</th>
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</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Randomised trial.</td>
</tr>
</tbody>
</table>

Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)
### Characteristics of included studies (Continued)

Cross-over design.  
Each treatment given 4 times daily for 1 day.

| Participants | CF confirmed by positive sweat test, malabsorption, and chronic lung infection.  
18 participants (12 male); mean age 22.5 years, range 13 - 37 years; mean FEV1 1.3, range 0.45 - 3.25 litres; and FVC was 2.5, range 1.1 - 5.1 litres.  
All participants were studied close to the end of an admission to hospital with an exacerbation of their lung infection. |
|---|---|
| Interventions | 3 interventions:  
(1) PEP treatment in sitting (PEPs). Pressure 12 - 17 cm H2O using an Astra Meditec PEP mouthpiece. Seated participants exhaled 6 times through the mouthpiece, followed by relaxed breathing, 1 - 2 forced expirations (huffs) from mid to low lung volume, relaxed breathing, and a huff or cough from high lung volume if secretions reached the upper airways;  
(2) PEP in postural drainage (PEPpd). The same breathing regimen was performed in (usually) two postural drainage positions chosen before the start of the study as the most appropriate from (undescribed) clinical assessment.  
(3) Breathing exercises in postural drainage positions (BEpd). Participants performed the same breathing and positioning regimen, but did not exhale through the PEP mask when deep breathing.  
In each intervention, the respiratory manoeuvres described above were continued in cycles until the participant and physiotherapist felt that forced expiration and coughing no longer resulted in expectoration.  
Four treatment sessions were performed per day. |
| Outcomes | FEV1 and FVC were measured before and 30 minutes after each intervention session. Wet weight of sputum expectorated during and for 30 minutes after the intervention session was measured. SpO2 was recorded before, during, and for 30 minutes after each intervention session. |
| Notes | There were no withdrawals or dropouts. |
| Allocation concealment | B – Unclear |

### Kofer 1998

Methods  
Randomised trial.  
Cross-over design.  
Each treatment given once.

| Participants | CF diagnosed by CF Clinic at Children's Hospital, Rome.  
20 participants (11 males); mean age 15.25, range 6 - 23 years; mean Schwachman score 80.8, SD 15.3 points. |
|---|---|
| Interventions | 2 interventions:  
(1) PEP treatment. While sitting, participants exhaled through a Vitapep Markos mask with 10 - 20 cm H2O pressure, followed by a pause, 2 - 3 huffs and coughing.  
(2) Non-invasive bi-level ventilatory support (nBVS). While sitting, participants breathed against 11cm H2O inspiratory positive pressure and 9 cm H2O expiratory positive pressure applied via a mask attached to a Puritan Bennett 335, followed by a pause, 2 - 3 huffs and coughing.  
Single treatments of 15 minutes were applied on consecutive days. All participants were using PEP as their regular therapy before the study. |
| Outcomes | FEV1, FVC and FEF25-75 were measured at the beginning, at the end, 15 min after and 30 min after each session. Oxygen saturation and heart rate were continuously monitored throughout this time via pulse-oximetry. Following the two sessions, participant preference was recorded. |
| Notes | No statement on withdrawals or dropouts.  
All participants were performing PEP prior to the study. PEP and nBVS were applied “according to the Danish protocol” (not defined). |
| Allocation concealment | B – Unclear |
### Characteristics of included studies (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Participants</th>
<th>Interventions</th>
<th>Outcomes</th>
<th>Notes</th>
<th>Allocation concealment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lannefors 1992</td>
<td>Randomised trial.</td>
<td>CF with daily sputum production.</td>
<td>3 interventions:</td>
<td>Mucus clearance was measured by delivering a radioaerosol (99mTc-labelled colloidal albumin) to the airways and measuring the distribution of radiolabelled secretions in the lung fields. Anterior and posterior planar gamma camera images of the thorax were collected for 2 minutes at baseline, after 15 minutes rest in sitting, after the 20-minute intervention, and after another 15 minutes rest in sitting. Clearance was calculated as a reduction in count rate between successive images. Whole lung clearance was calculated. In addition, the planar images were divided into a central 'hilar' region and peripheral region, and clearance from these regions was calculated.</td>
<td>No withdrawals or dropouts.</td>
<td>B – Unclear</td>
</tr>
</tbody>
</table>

### Study

| Method          | CF diagnosis.                  | 18 participants.                                                            | 3 interventions:                                                                                                                                | FEV1, FVC, and FEF25-75 were measured at the start and end of each two-month treatment period. Other measures included reported treatment duration, treatment comfort, requirement for assistance with treatment, flexibility of treatment times, control in performing own treatment, and how interruptive treatment was to daily living. | No statement on withdrawals or dropouts.                                                       | B – Unclear                                                      |

### Study

| Method          | Randomised trial.             | Parallel design.                                                           | Treatment for 1 year.                                                                             |                                                                                                   |                                                                                                 |                        |

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Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)

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Characteristics of included studies (Continued)

Participants  
CF confirmed by sweat test.  
40 participants (22 male); age range 6 - 17 years; mean age 10.40 years (PEP group) and 9.75 years (PD&P group); mean FEV1 80.47, range 37 - 115% predicted.  
Participants were excluded if their condition was not stable as judged by clinical evaluation, chest radiograph and pulmonary function. Also, no participant entered the study within 1 month of discharge from hospital or use of IV antibiotics or other intensive therapy for an exacerbation.

Interventions  
2 interventions:  
(1) PEP treatment. Pressure 10 - 20 cm H2O using an Astra Meditec PEP mask. Seated participants breathed 15 times through the mask, followed by 2 - 3 forced expirations, cough and relaxed breathing. This was repeated 6 times, over a 20-minute session;  
(2) PDP. In 5 - 6 positions, 3 - 5 minutes of percussion, 2 - 4 minutes of expiratory vibrations, forced expirations and vigorous coughing were performed. These sessions lasted 30 minutes.

Both interventions were performed twice daily.

Outcomes  
FEV1, FVC, and FEF25-75 were measured quarterly for one year. Compliance was measured via daily record keeping, with those compliant with less than 85% of the twice-daily sessions over a one month period being withdrawn from the study. Adverse events and participant preference were assessed via questionnaire.

Notes  
2 dropouts from each arm, due to non-compliance (<85% of twice-daily sessions performed) or non-attendance at clinic.

Allocation concealment  
B – Unclear

Study  
McIlwaine 2001

Methods  
Randomised trial.  
Parallel design.  
Treatment for 1 year.

Participants  
CF confirmed by sweat test.  
40 participants (24 male); age range 7 - 17 years; FEV1 range 47 - 107% predicted; Schwachman score range 54 - 98 points. Participants were excluded if they had been hospitalised within the past month for a pulmonary exacerbation, or if they were not stable on clinical evaluation, chest radiograph or pulmonary function.

Interventions  
2 interventions:  
(1) PEP treatment. Participants inhaled and exhaled through the Astra Meditec PEP mask in sitting. The resistor which produced 10 to 20 cm H2O pressure during mid-expiration was used. Over approximately 2 minutes, 15 tidal breaths with slightly active expiration were performed. Participants then removed the mask, performed 2 or 3 forced expirations, and coughed, followed by 1-2 minutes of relaxed breathing. This sequence was repeated 6 times. This 20 minutes session was repeated twice daily;  
(2) Oscillating PEP. Participants exhaled through the Flutter device (Flutter). The device was angled to maximise the sensation of vibration in the chest. In sitting, subjects inhaled deeply through the nose, followed by a breath hold for 2 - 3 seconds, and exhalation through the device slightly in to the expiratory reserve volume. After 10 - 15 breaths, participants huffed through the device, increasing the tidal volume and speed of exhalation to precipitate coughing and expectoration. This sequence was repeated “until clear” and not for less than 15 minutes per session, twice daily.

The daily regimen for use of the devices is not described.

Outcomes  
FEV1, FVC, and FEF25-75 were measured at the beginning and at three-monthly intervals throughout the study. Compliance with the interventions was recorded daily by the participants. A monthly questionnaire recorded physical activity, general well-being, cough, sputum production, subjective impression of the therapy, and adverse events. Clinical status was assessed by physicians blinded to the allocation group, using Schwachman and Huang clinical scores. Chest radiographs were evaluated by a blinded radiologist at the beginning and end of the study. Hospitalisations were also recorded.
Characteristics of included studies (Continued)

Notes 2 participants were withdrawn due to non-compliance (<85% of twice-daily sessions performed over 1 month) in the PEP group. 5 participants dropped out from the Flutter group stating that subjectively the Flutter did not appear to clear their secretions. A further two participants withdrew from the Flutter arm due to clinically significant deterioration in pulmonary function.

Allocation concealment B – Unclear

Study Mortensen 1991

Methods Randomised controlled trial.
Cross-over design.
Each treatment given once.

Participants CF diagnosis and chronic pseudomonas infection.
10 participants (6 male); mean age was 20 years, range 15 - 26 years; mean FEV1 38.5, range 26 - 101% predicted.
Participants entered the study in the last 2 weeks of regular hospital admission for intravenous anti-pseudomonas treatment.

Interventions 3 interventions:
(1) PEP treatment. Pressure 15 - 20 cm H2O using a mask. Seated participants breathed deeply for one minute, followed by 1 - 2 forced expirations from mid to low lung volume, relaxed breathing and cough. This breathing regimen was repeated for 20 minutes;
(2) Breathing exercises in postural drainage positions (BEpd). Participants breathed deeply 4 times followed by relaxed breathing for 10 minutes in each of right and left side lying with 20 degrees head down tilt. relaxed breathing were performed. This was again followed by 1 - 2 forced expirations from mid to low lung volume, relaxed breathing and cough. The same number of huffs and coughs performed with the first treatment were matched with the subsequent active intervention.
(3) Control (CONT). Twenty minutes of resting in sitting with spontaneous coughing allowed.

Outcomes Mucus clearance was measured directly by delivering a radioaerosol (99mTc-labelled albumin colloid) to the airways and then measuring the distribution of radiolabelled secretions within the lung fields. Posterior planar gamma camera images of the thorax were collected as single 5-minute exposures every 30 minutes for 3 hours. Clearance was calculated as a reduction in count rate between successive images. Whole lung clearance was calculated. In addition, the planar images were divided into central, mid and peripheral regions, and upper, mid and basal regions. Clearance from these regions was calculated. Wet weight of sputum expectorated during the initial 30-minute (intervention) period and for the remainder of the 3-hour clearance measurement period was measured.

Notes No statement on withdrawals or dropouts.
Allocation concealment B – Unclear

Study Newbold 2005

Methods Randomised trial.
Parallel design.
Treatment for 13 months.

Participants CF diagnosed by St Michael’s Hospital CF Clinic, Toronto.
42 participants (24 male).
PEP Group: 21 participants (15 male); mean age 28, SD 8.1 years; mean FEV1 2.5, SD 1.2 litres; mean FEV1 66, SD 19.9% predicted.
Flutter Group: 21 participants (9 male); mean age 31, SD 8.7 years; mean FEV1 2.2, SD 0.7 litres; mean FEV1 69, SD 18.5% predicted.
Participants were excluded if they had been hospitalised within the past month for a pulmonary exacerbation, had changed their medication within the past month, or did not have a daily cough or daily sputum.

Interventions 2 interventions:
Characteristics of included studies (Continued)

(1) PEP treatment. Pressure 10 - 20 cm H2O using an Astra Meditec PEP mask. Seated participants breathed 10 - 15 times through the mask, followed by huffing, coughing and relaxed breathing. This was repeated 5 - 6 times, over a 20-minute session, twice daily.

(2) Oscillating PEP. Participants exhaled through the Flutter device (Axcan Scandipharm). The device was angled to maximise the sensation of vibration in the chest. In sitting, subjects inhaled deeply through the nose, followed by a breath hold for 2 - 3 seconds, and exhalation through the device. After 5 - 10 breaths, participants increased the tidal volume and speed of exhalation through the device, to precipitate coughing and expectoration. This sequence was repeated "until clear" or for approximately 20 minutes, twice daily.

Outcomes
Slope of change in FEV1, FVC, and FEF25-75 (absolute and % predicted). Number of hospitalisations. Adherence.

Notes
1 participant was withdrawn when he stopped attending the CF clinic.

Allocation concealment
A – Adequate

Study Padman 1999

Methods
Randomised trial.
Cross-over design.
Each treatment given for 1 month.

Participants
CF defined by mild-mod Schwachman score and a productive cough.
15 participants (gender unspecified); age range 5 - 17 years.
Participants were excluded if they had a hospital admission during the month prior to the start of the study or were clinically unstable (based on respiratory rate, heart rate, oxygen saturation, breath sounds, sputum production and medication use).

Interventions
3 interventions:
(1) PEP treatment. Participants breathed through a Vital Signs 9000 mask;
(2) Postural drainage and chest physiotherapy (CPT). Not defined;
(3) Oscillating PEP (Flutter). Participants breathed through a Scandipharm Flutter device. Not further defined.

Each therapy was performed for 15 minutes, 3 times a day, for 1 month. Chest physiotherapy and postural drainage was used between the therapies to return each of the participants to his or her baseline status. (The period required for this to occur is not stated. It appears unstandardised.)

Outcomes
FEV1, FEF25-75, and oxygen saturation were measured at the beginning and end of each intervention period.

Notes
5 withdrawals because of hospital admission due to pulmonary exacerbation and 4 dropouts.

Allocation concealment
B – Unclear

Study Pfleger 1992

Methods
Randomised controlled trial.
Cross-over design.
Each treatment given once.

Participants
CF confirmed by repeat sweat tests, and sputum production of >20 ml per day.
15 participants (9 female, 1 unspecified); mean age 16 years, range 9.8 - 22.4 years; mean Schwachman score 62.2, range 26 - 90 points.
Participants were excluded if unstable at the time of investigation (criteria unspecified). 6 months before the study, each participant was trained in the 2 self-administered techniques (PEP and AD).

Interventions
5 interventions:
(1) Hi-PEP intervention. Expiratory resistance chosen to increase the FVC to the greatest extent when performed through the PEP mask. Participants exhaled 8 - 10 times followed by a forced expiratory manoeuvre, all through the mask;
Characteristics of included studies (Continued)

(2) AD. Participants breathed at low lung volumes with progressive increases in the lung volume at which breathing was performed in response to evidence of secretion transport. Coughing and forced expiratory manoeuvres were avoided;
(3) Hi-PEP for the first half of the session, followed by AD;
(4) AD for the first half of the session, followed by Hi-PEP;
(5) Control (CONT). Spontaneous coughing only.

Each intervention session was equal to the time taken for the individual participant to clear their lungs using AD, as judged from pre-study experience.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>FEV1, FVC, RV, and TLC were measured at all PFT measurement points. Wet weight of expectorated sputum during the complete (both halves) intervention period was also measured.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notes</td>
<td>1 withdrawal due to development of an acute respiratory viral infection during the study.</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>B – Unclear</td>
</tr>
</tbody>
</table>
**Characteristics of included studies (Continued)**

(2) PEP & FET intervention. The following was added to the above technique: 1 or 2 forced expirations with an open glottis from mid-lung volume to low-lung volume followed by a period of relaxed diaphragmatic breathing (FET);

(3) PDP & FET intervention. Participants received percussion in postural drainage positions, with FET;

(4) SPEP-PDP & FET intervention. Participants performed PEP (position not defined) for five minutes, followed by PDP & FET.

Frequency and duration of treatment sessions was not specified. There was no washout period between months.

**Outcomes**

FEV1 and FVC were measured at the start and finish of each month. At the end of each month, the wet weight of expectorated sputum over a 2-hour period which included a treatment with that month's intervention was measured. At the end of the study period, participants nominated which intervention they would use as ongoing airway clearance physiotherapy.

**Notes**

2 withdrawals (1 death, 1 non-compliance) and 2 dropouts (1 pneumothorax, 1 subjective lack of effect). A fifth intervention, FET alone, was undertaken by a subset of 5 participants. This treatment was performed after the 4 randomly-assigned interventions and therefore does not form part of the randomised trial.

**Allocation concealment**

B - Unclear

---

**Study**

**Tyrell 1986**

**Methods**

Randomised trial.

Cross-over design.

Each treatment given for 1 month.

**Participants**

CF diagnosed by the Nottingham City Hospital Cystic Fibrosis Clinic.

19 participants (after withdrawals, 9 females and 7 males); mean age 13 years, range 10 - 18 years; mean Schwachman score 62, range 47 - 85 points.

**Interventions**

2 interventions:

1. PEP treatment. Pressure 10 - 15 cm H2O. Seated participants exhaled 10 times through an Astra mask, followed by "forced expiratory coughing";

2. Postural drainage and percussion (PDP). Participants received percussion and performed coughing in postural drainage positions.

Treatment was performed for 20 minutes, twice daily.

**Outcomes**

Forced expiratory volume in 0.75 sec (FEV 0.75), FVC, PEFR were recorded before, 20 minutes after, and 90 minutes after a single supervised treatment at the beginning of the randomisation month. Wet weight of sputum expectorated during the therapy was also measured. The same measures were repeated over a single treatment at the end of the randomisation month.

In addition, during each treatment month, diary card records were kept regarding the following symptoms: sleep, cough, wheeze, activity, sputum production. (Details of the scoring system for these symptoms are not provided.) Although not listed as a formal outcome measures, antibiotic use and participant preference are also discussed in the results section.

**Notes**

3 withdrawals due to non-adherence.

Those children who showed airway reversibility with salbutamol were asked to use it before treatment throughout the whole study.

**Allocation concealment**

B - Unclear

---

**Study**

**van Asperen 1987**

**Methods**

Randomised trial.

Cross-over design.

Each treatment given for 4 weeks.

**Participants**

CF diagnosed by Camperdown or Westmead Hospitals, and daily sputum production.
### Characteristics of included studies (Continued)

<table>
<thead>
<tr>
<th>Characteristics of included studies</th>
<th>van Winden 1998</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interventions</strong></td>
<td>2 interventions:</td>
</tr>
<tr>
<td></td>
<td>(1) PEP treatment. Pressure 10 - 15 cm H2O. Participants exhaled 10 - 15 times through an Astra mask (position unspecified), followed by forced expiration and coughing;</td>
</tr>
<tr>
<td></td>
<td>(2) Postural drainage and percussion (PD&amp;P). Participants received manual percussion to all areas in postural drainage positions, followed by forced expiration and coughing.</td>
</tr>
<tr>
<td></td>
<td>The PEP intervention was continued for 20 minutes. PD&amp;P lasted “at least 20 minutes”. Each intervention treatment was administered twice daily for 4 weeks. There was no washout period.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>FEV1 and FVC were measured before and 1 hour after the first treatment of each randomisation period. Volume of expectorated sputum was measured over one hour which commenced with the first treatment of the randomisation period.</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>2 withdrawals due to infective exacerbations and one dropout.</td>
</tr>
<tr>
<td><strong>Allocation concealment</strong></td>
<td>B – Unclear</td>
</tr>
<tr>
<td><strong>Study</strong></td>
<td>van der Schans 1991</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>Randomised trial.</td>
</tr>
<tr>
<td></td>
<td>Cross-over design.</td>
</tr>
<tr>
<td></td>
<td>Each treatment given for 2 weeks.</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>CF confirmed by sweat tests or DNA mutation analysis.</td>
</tr>
<tr>
<td></td>
<td>22 participants (12 male); median age 12 years, range 7 - 17 years; median FEV1 82, range 55 - 129% predicted.</td>
</tr>
<tr>
<td></td>
<td>Participants were excluded if they had been clinically unstable during the 2 weeks prior to entering the study, according to PEFR and symptoms scores (criteria not specified).</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>2 interventions:</td>
</tr>
<tr>
<td></td>
<td>(1) PEP treatment. Pressure 8 - 12 cm H2O. Seated participants breathed through an Astra Meditec PEP mask 15 times, followed by 3 huffs and coughing. This sequence was repeated 5 times;</td>
</tr>
<tr>
<td></td>
<td>(2) Oscillating PEP (Flutter). Participants inhaled deeply, held their breath for 2 - 3 seconds, then exhaled through the VarioRaw Flutter device 15 times, following which the participant again huffed 3 times and coughed. This sequence was also repeated 5 times. The flutter was tilted upwards or downwards a few degrees from horizontal until the maximum vibration sensation was obtained.</td>
</tr>
<tr>
<td></td>
<td>Each intervention was performed twice per day for 2 weeks, preceded by a one-week washout period. During the washout weeks, all participants performed “routine physiotherapy” with huff and cough manoeuvres.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>FEV1, FVC, and TLC were measured before the initial, 1-week washout period. These measures were repeated on the first day of each of the 2 treatment periods, before and 30 minutes after the first session of therapy. At the end of the 2-week treatment periods, these measures were again taken 30 minutes after physiotherapy. Oxygen saturation via pulse oximetry was measured before during and after the first and last treatments of each 2-week period.</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>No withdrawals or dropouts.</td>
</tr>
<tr>
<td><strong>Allocation concealment</strong></td>
<td>B – Unclear</td>
</tr>
</tbody>
</table>

---

**Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)**

Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd
8 participants (gender unspecified); mean age 16 years, range 13 - 21 years; mean FEV1 70 % predicted. Participants were excluded if they were not in a clinically stable phase of their disease, as assessed by lung function tests and a short questionnaire (criteria unspecified).

**Interventions**

3 interventions:
1. PEP treatment. Pressure 15 cm H2O. Participants breathed through a Vital Signs PEP mask for 2 minutes, followed by undisturbed breathing for 2 minutes. This was repeated 5 times. The participant then coughed as productively as possible every 30 seconds for a further 5 minutes;
2. PEP treatment as above, with pressure 5 cm H2O;
3. Control (CONT). Participants rested in supine in place of the PEP breathing in the above regimen, followed by coughing as above.

Each intervention was applied on a different day (order randomised) at the same time of day.

**Outcomes**

On the measurement days, the intervention protocol was carried out twice: first with measurement of mucus clearance and the second time with lung function measurements. FEV1, TLC, FRC, and RV were assessed before and after PEP breathing, or before and after the coughing period on the control day. Mucus clearance was measured directly by delivering a radioaerosol (99mTc-labelled tin colloid) to the airways and then measuring the distribution of radiolabelled secretions within the lung fields. Posterior planar gamma camera images of the thorax were collected continuously for 10 minutes before the intervention, during the 25-minute intervention, and for a further 10 minutes. Decreases in radioactivity in the peripheral region and in the whole lung were calculated for the 30-minute (incl. PEP or relaxed breathing periods) and 45 minutes (incl. PEP or relaxed breathing and voluntary cough periods). Clearance was calculated as a reduction in count rate.

**Notes**

No statement on withdrawals or dropouts.

**Allocation concealment**

B – Unclear

AD: autogenic drainage
CE: cycle ergometry
CF: cystic fibrosis
FEF25-75: forced expiratory flow 25-75%
FEV1: forced expiratory volume at one second
FRC: functional residual capacity
FVC: forced vital capacity
HFCC: high frequency chest compression
Hi-PEP: High-pressure PEP
IV: intravenous
PD: postural drainage
PDP: postural drainage with percussion
PDPV: postural drainage, percussion and vibration
PEP: positive expiratory pressure
PEFR: peak expiratory flow rate
PFT: pulmonary function test
pO2: blood test measuring oxygen in the blood
RV: residual volume
SD: standard deviation
SpO2: saturation of haemoglobin with oxygen using pulse oximetry
TLC: total lung capacity
nBVS: non-invasive bilevel ventilatory support
SVC: slow vital capacity
W/kg: watt per kilogram

**Characteristics of excluded studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Castle 1994</td>
<td>No outcome data were reported.</td>
</tr>
</tbody>
</table>
Characteristics of excluded studies (Continued)

<table>
<thead>
<tr>
<th>Study Author</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosman 2003</td>
<td>No data were reported for the outcomes of interest.</td>
</tr>
<tr>
<td>Fitzgerald 2001</td>
<td>Factor randomised is not PEP versus other airway clearance.</td>
</tr>
<tr>
<td>Gotz 1995</td>
<td>No data were reported for the outcomes of interest.</td>
</tr>
<tr>
<td>Laube 2000</td>
<td>The intervention to which PEP was compared was not a physical airway clearance therapy.</td>
</tr>
<tr>
<td>Oermann 2001</td>
<td>Neither of the interventions being compared was PEP.</td>
</tr>
<tr>
<td>Orlik 2000</td>
<td>The use of PEP versus the other physical airway clearance therapies was not the factor which was random in this study.</td>
</tr>
<tr>
<td>Znotina 2000</td>
<td>The use of PEP versus the other physical airway clearance therapy (oscillating PEP) was not the factor which was randomised in this study.</td>
</tr>
<tr>
<td>van Hengstum 1987</td>
<td>The study was performed in participants with chronic bronchitis.</td>
</tr>
</tbody>
</table>

PEP: Positive expiratory pressure

ADDITIONAL TABLES

Table 01. Search Strategy CINAHL

1982 to 2001

#1. Positive expiratory pressure OR PEP OR High pressure PEP
#2. Cystic fibrosis OR CF OR Mucoviscidosis
#3. #1 AND #2

Table 02. Quality criteria met by included studies (Maher 2003)

<table>
<thead>
<tr>
<th>Study Name</th>
<th>No. of criteria met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balestri 2004</td>
<td>4</td>
</tr>
<tr>
<td>Battistini 2001</td>
<td>2</td>
</tr>
<tr>
<td>Braggion 1995</td>
<td>3</td>
</tr>
<tr>
<td>Costantini 2001</td>
<td>2</td>
</tr>
<tr>
<td>Darbee 1990</td>
<td>4</td>
</tr>
<tr>
<td>Darbee 2000</td>
<td>2</td>
</tr>
<tr>
<td>Falk 1984</td>
<td>6</td>
</tr>
<tr>
<td>Falk 1993</td>
<td>3</td>
</tr>
<tr>
<td>Gaskin 1998</td>
<td>6</td>
</tr>
<tr>
<td>Hofmeyr 1986</td>
<td>5</td>
</tr>
<tr>
<td>Kofler 1998</td>
<td>4</td>
</tr>
<tr>
<td>Lannefors 1992</td>
<td>4</td>
</tr>
<tr>
<td>McIlwaine 1991</td>
<td>3</td>
</tr>
<tr>
<td>McIlwaine 1997</td>
<td>6</td>
</tr>
<tr>
<td>McIlwaine 2001</td>
<td>5</td>
</tr>
</tbody>
</table>
Table 02. Quality criteria met by included studies (Maher 2003)  (Continued)

<table>
<thead>
<tr>
<th>Study Name</th>
<th>No. of criteria met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortensen 1991</td>
<td>5</td>
</tr>
<tr>
<td>Newbold 2000</td>
<td>6</td>
</tr>
<tr>
<td>Padman 1999</td>
<td>1</td>
</tr>
<tr>
<td>Pfleger 1992</td>
<td>6</td>
</tr>
<tr>
<td>Placidi 2001</td>
<td>2</td>
</tr>
<tr>
<td>Steen 1991</td>
<td>4</td>
</tr>
<tr>
<td>Tyrrell 1986</td>
<td>3</td>
</tr>
<tr>
<td>van Asperen 1987</td>
<td>4</td>
</tr>
<tr>
<td>van der Schans 1991</td>
<td>3</td>
</tr>
<tr>
<td>van Winden 1998</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 03. FEV1 after single treatment Pfleger 1992

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SD) FEV1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hi-PEP</td>
<td>54 (20) % predicted</td>
</tr>
<tr>
<td>AD</td>
<td>56 (19) % predicted</td>
</tr>
<tr>
<td>Hi-PEP then AD</td>
<td>55 (18) % predicted</td>
</tr>
<tr>
<td>AD then Hi-PEP</td>
<td>54 (19) % predicted</td>
</tr>
</tbody>
</table>

Table 04. Days of intravenous antibiotic use per participant per year (Costantini 2001)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP</td>
<td>6.2 days per participant per year</td>
</tr>
<tr>
<td>PDPV</td>
<td>1.8 days per participant per year</td>
</tr>
</tbody>
</table>

Table 05. Measures of technique acceptability (McIlwaine 1991)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Duration of Rx</th>
<th>Comfort Score</th>
<th>Flexibility Score</th>
<th>In Control of Own Rx</th>
<th>Disruption Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP</td>
<td>21</td>
<td>75</td>
<td>73</td>
<td>89</td>
<td>33</td>
</tr>
<tr>
<td>AD</td>
<td>25</td>
<td>84</td>
<td>73</td>
<td>87</td>
<td>35</td>
</tr>
<tr>
<td>PDPV</td>
<td>27</td>
<td>49</td>
<td>42</td>
<td>62</td>
<td>63</td>
</tr>
</tbody>
</table>

0 = very uncomfortable 100 = very comfortable
0 = very rigid 100 = very flexible
0 = no control 100 = full control
0 = Rx not interruptive 100 = Rx very interruptive
### Table 05. Measures of technique acceptability (McIlwaine 1991) (Continued)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Duration of Rx</th>
<th>Comfort Score</th>
<th>Flexibility Score</th>
<th>In Control of Own Rx</th>
<th>Disruption Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 06. Percentage of radioaerosol retention (Falk 1993)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SD) at 0.5 hr</th>
<th>Mean (SD) at 1.0 hr</th>
<th>Mean (SD) at 2.0 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP + FET</td>
<td>92.4 (5.0) %</td>
<td>90.1 (4.8) %</td>
<td>86.9 (5.1) %</td>
</tr>
<tr>
<td>FET</td>
<td>92.7 (5.3) %</td>
<td>90.8 (5.4) %</td>
<td>89.9 (6.4) %</td>
</tr>
</tbody>
</table>

### Table 07. Wet weight of sputum during and 50 minutes after Rx (Falk 1984)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (range) weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP in sitting</td>
<td>21.6 (12.5 - 53.5) g</td>
</tr>
<tr>
<td>PEP in PD positions</td>
<td>17.4 (5.8 - 50.7) g</td>
</tr>
<tr>
<td>Pursed Lip Breathing</td>
<td>15.0 (5.4 - 44.9) g</td>
</tr>
<tr>
<td>PDPV</td>
<td>10.0 (1.9 - 51.1) g</td>
</tr>
</tbody>
</table>

### Table 08. Wet weight of sputum during Rx (Pfleger 1992)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SD) weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hi-PEP</td>
<td>50 (29) g</td>
</tr>
<tr>
<td>AD</td>
<td>35 (25) g</td>
</tr>
<tr>
<td>Hi-PEP then AD</td>
<td>44 (29) g</td>
</tr>
<tr>
<td>AD then Hi-PEP</td>
<td>39 (23) g</td>
</tr>
</tbody>
</table>

NB Data measured from graph

### Table 09. Wet weight of sputum during and for 30 minutes after Rx (Hofmeyer 1986)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (range) weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE in PD positions</td>
<td>79.8 (30.7 - 219.8) g</td>
</tr>
<tr>
<td>PEP in PD positions</td>
<td>70.6 (24.7 - 256.8) g</td>
</tr>
<tr>
<td>PEP in sitting</td>
<td>66.1 (15.3 - 189.4) g</td>
</tr>
</tbody>
</table>
Table 10. FVC after single treatment (Pfleger 1992)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SD) FVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hi-PEP</td>
<td>73 (20) % predicted</td>
</tr>
<tr>
<td>AD</td>
<td>74 (19) % predicted</td>
</tr>
<tr>
<td>Hi-PEP then AD</td>
<td>73 (20) % predicted</td>
</tr>
<tr>
<td>AD then Hi-PEP</td>
<td>71 (21) % predicted</td>
</tr>
</tbody>
</table>

Table 11. FVC change after four treatments (Falk 1984)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (range) change</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP in sitting</td>
<td>+6.6 (0 - 11) %</td>
</tr>
<tr>
<td>PDPV</td>
<td>- 4.7 (0 - 7.9) %</td>
</tr>
<tr>
<td>PEP in PD positions</td>
<td>not stated</td>
</tr>
<tr>
<td>Pursed Lip Breathing</td>
<td>not stated</td>
</tr>
</tbody>
</table>

NB It is unclear whether these percentages refer to absolute percentage change or change in % predicted.

Table 12. TLC and FRC during treatment (van der Schans 1991)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SD) TLC</th>
<th>Mean (SD) FRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP 15 cm H2O</td>
<td>6.9 (1.1) litres</td>
<td>4.4 (1.4) litres</td>
</tr>
<tr>
<td>PEP 5 cm H2O</td>
<td>5.9 (0.8) litres</td>
<td>3.6 (0.8) litres</td>
</tr>
</tbody>
</table>

Table 13. Oxygenation change during Rx (Kofler 1998)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SD) Chg SpO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP</td>
<td>0.04 (1.28) %</td>
</tr>
<tr>
<td>nBVS</td>
<td>1.2 (2.12) %</td>
</tr>
</tbody>
</table>

Table 14. Oxygenation change by 35 min after Rx (Falk 1984)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (1-3 quartile)</th>
<th>Mean Rx duration *</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP in sitting</td>
<td>14.4 (4.6 - 27.4) %</td>
<td>20 min</td>
</tr>
<tr>
<td>PEP in pd</td>
<td>3.2 (0 - 15.4) %</td>
<td>39 min</td>
</tr>
<tr>
<td>PLB</td>
<td>2.4 (-8.0 - 11.3) %</td>
<td>21 min</td>
</tr>
<tr>
<td>PDPV</td>
<td>4.3 (-9.4 - 12.1) %</td>
<td>37 min</td>
</tr>
</tbody>
</table>

NB Treatment durations unequal
Table 15. Adherence at one year (McIlwaine 1997)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP</td>
<td>92% (SD not stated)</td>
</tr>
<tr>
<td>PDPV</td>
<td>96% (SD not stated)</td>
</tr>
</tbody>
</table>

Table 16. Adherence at one year (McIlwaine 2001)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP</td>
<td>95.6% (SD not stated)</td>
</tr>
<tr>
<td>Flutter</td>
<td>93.8% (SD not stated)</td>
</tr>
</tbody>
</table>

Table 17. FEV1 change over two years in participants under 19 years of age (Gaskin 1998)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>FEV1 change</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP</td>
<td>-1.58% predicted per year (SD not stated)</td>
</tr>
<tr>
<td>PDPV</td>
<td>-1.65% predicted per year (SD not stated)</td>
</tr>
</tbody>
</table>

A N A L Y S E S

Comparison 01. PEP compared with Postural Drainage, Percussion & Vibration

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Forced expiratory volume in 1 second (FEV1)</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>02 Adverse effects: gastro-oesophageal reflux</td>
<td></td>
<td></td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>03 Adverse effects: gastro-oesophageal reflux sufficient to cause withdrawal</td>
<td></td>
<td></td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>04 Forced vital capacity (FVC)</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>05 Forced expiratory flow 25 - 75 % (FEF 25-75)</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>06 Total lung capacity (TLC)</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>07 Radiological imaging: increased bronchial markings</td>
<td></td>
<td></td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>08 Radiological imaging: change in Brasfield score</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>
Comparison 02. PEP compared with oscillating PEP (Flutter)

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Forced expiratory volume in 1 second (FEV1)</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>02 Hospitalisations for respiratory exacerbation (number per participant)</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>03 Participant preference: self-withdrawal due to lack of perceived effectiveness</td>
<td></td>
<td></td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>04 Forced vital capacity (FVC)</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>05 Forced expiratory flow 25 - 75 % (FEF 25-75)</td>
<td></td>
<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>06 Adherence: at least 85% of prescribed treatments performed</td>
<td></td>
<td></td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>

INDEX TERMS

Medical Subject Headings (MeSH)

Cystic Fibrosis [complications; *therapy]; Forced Expiratory Volume; Mucociliary Clearance; Mucus [*secretion]; Positive-Pressure Respiration [*methods]; Randomized Controlled Trials; Vital Capacity

MeSH check words

Humans

COVER SHEET

Title
Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

Authors
Elkins MR, Jones A, van der Schans C

Contribution of author(s)
Mark Elkins, Alice Jones and Cees van der Schans drafted and wrote the protocol. Mark Elkins and Alice Jones independently assessed studies for inclusion in the full review, contributed to data extraction, and collaborated on consensus decisions. Mark Elkins wrote the text of the review, with contributions from Alice Jones. Mark Elkins updated the review with contributions from Alice Jones. Mark Elkins acts as guarantor of the review.

Issue protocol first published
2001/3

Review first published
2004/1

Date of most recent amendment
22 February 2006

Date of most recent SUBSTANTIVE amendment
15 December 2005

What’s New
Cees van der Schans has stepped down as co-author on this review as from February 2006. Five studies have been added to the list of included studies in this update (Balestri 2004; Battistini 2001; Darbee 2004; Newbold 2005; Placidi 2001).
Five studies have been added to the list of excluded studies (Castle 1994; Dosman 2003; Fitzgerald 2001; Oermann 2001; Orlik 2000).

Date new studies sought but none found
Information not supplied by author

Date new studies found but not yet included/excluded
Information not supplied by author

Date new studies found and included/excluded
02 February 2006

Date authors’ conclusions section amended
Information not supplied by author

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Editorial group
Cochrane Cystic Fibrosis and Genetic Disorders Group

Editorial group code
HM-CF

GRAPHS AND OTHER TABLES
Analysis 01.01.  Comparison 01 PEP compared with Postural Drainage, Percussion & Vibration, Outcome 01
Forced expiratory volume in 1 second (FEV1)

Review:  Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis
Comparison: 01 PEP compared with Postural Drainage, Percussion % Vibration
Outcome: 01 Forced expiratory volume in 1 second (FEV1)

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP</th>
<th>PDPV</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weight (%)</th>
<th>Weighted Mean Difference (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Asperen 1987</td>
<td>5</td>
<td>5</td>
<td>0.60 [-6.33, 7.53]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>01 8 days to 1 month</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>5</td>
<td>5</td>
<td>0.60 [-6.33, 7.53]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect z=0.17 p=0.9</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Darbee 1990</td>
<td>12</td>
<td>8</td>
<td>-0.50 [-3.68, 2.68]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>02 2 to 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>12</td>
<td>8</td>
<td>-0.50 [-3.68, 2.68]</td>
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<tr>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McIlwaine 1997</td>
<td>18</td>
<td>18</td>
<td>8.26 [0.76, 15.76]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>03 7 to 12 months</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>18</td>
<td>18</td>
<td>8.26 [0.76, 15.76]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect z=2.16 p=0.03</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Gaskin 1998</td>
<td>33</td>
<td>33</td>
<td>-0.65 [-3.25, 1.95]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>04 2 years</td>
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<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
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<td>33</td>
<td>-0.65 [-3.25, 1.95]</td>
<td>100.0</td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect z=0.49 p=0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Analysis 01.02.  Comparison 01 PEP compared with Postural Drainage, Percussion & Vibration, Outcome 02
Adverse effects: gastro-oesophageal reflux

Review:  Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis
Comparison: 01 PEP compared with Postural Drainage, Percussion % Vibration
Outcome: 02 Adverse effects: gastro-oesophageal reflux

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP</th>
<th>PDPV</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
</tr>
<tr>
<td>Costantini 2001</td>
<td>5/15</td>
<td>4/11</td>
<td>0.92 [0.32, 2.65]</td>
</tr>
</tbody>
</table>

01 07 to 12 months |      |      | 0.92 [0.32, 2.65]     |

Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)
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**Analysis 01.03. Comparison 01 PEP compared with Postural Drainage, Percussion & Vibration, Outcome 03**

**Adverse effects: gastro-oesophageal reflux sufficient to cause withdrawal**

Review: Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

Comparison: 01 PEP compared with Postural Drainage, Percussion % Vibration

Outcome: 03 Adverse effects: gastro-oesophageal reflux sufficient to cause withdrawal

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP n/N</th>
<th>PDPV n/N</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costantini 2001</td>
<td>0/15</td>
<td>3/11</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Costantini 2001: 0.11 [0.01, 1.88]

**Analysis 01.04. Comparison 01 PEP compared with Postural Drainage, Percussion & Vibration, Outcome 04**

**Forced vital capacity (FVC)**

Review: Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

Comparison: 01 PEP compared with Postural Drainage, Percussion % Vibration

Outcome: 04 Forced vital capacity (FVC)

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP N</th>
<th>Mean(SD)</th>
<th>PDPV N</th>
<th>Mean(SD)</th>
<th>Weighted Mean Difference (Fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Weighted Mean Difference (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single treatment</td>
<td>7</td>
<td>4.57 (8.26)</td>
<td>9</td>
<td>2.67 (4.74)</td>
<td>100.0 1.90 [-4.96, 8.76]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>7</td>
<td></td>
<td>9</td>
<td></td>
<td>100.0 1.90 [-4.96, 8.76]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td>p=0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 days to 1 month</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tyrrell 1986</td>
<td>7</td>
<td>-11.43 (13.44)</td>
<td>9</td>
<td>-2.33 (9.21)</td>
<td>56.4 -9.10 [-20.73, 2.53]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>van Asperen 1987</td>
<td>5</td>
<td>2.78 (14.94)</td>
<td>5</td>
<td>0.58 (2.24)</td>
<td>43.6 2.20 [-11.04, 15.44]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>12</td>
<td></td>
<td>14</td>
<td></td>
<td>100.0 -4.18 [-12.92, 4.56]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: chi-square=1.58 df=1 p=0.21 I² =36.7%</td>
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<td></td>
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<tr>
<td>Test for overall effect z=0.94 p=0.3</td>
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<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>&gt;1 to 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darbee 1990</td>
<td>12</td>
<td>1.09 (9.95)</td>
<td>8</td>
<td>-1.00 (7.25)</td>
<td>100.0 2.09 [-5.46, 9.64]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>12</td>
<td></td>
<td>8</td>
<td></td>
<td>100.0 2.09 [-5.46, 9.64]</td>
<td></td>
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</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect z=0.54 p=0.6</td>
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<td></td>
</tr>
<tr>
<td>&gt;6 to 12 months</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McIlwaine 1997</td>
<td>18</td>
<td>6.57 (8.06)</td>
<td>18</td>
<td>-2.17 (13.58)</td>
<td>100.0 8.74 [1.44, 16.04]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Continued...)

---

Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)  
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### Analysis 01.05. Comparison 01 PEP compared with Postural Drainage, Percussion & Vibration, Outcome 05 Forced expiratory flow 25 - 75 % (FEF 25-75)

Review: Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

Comparison: 01 PEP compared with Postural Drainage, Percussion & Vibration

Outcome: 05 Forced expiratory flow 25 - 75 % (FEF 25-75)

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP</th>
<th>N</th>
<th>Mean(SD)</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weight (%)</th>
<th>PDPV</th>
<th>N</th>
<th>Mean(SD)</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
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<td></td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>18</td>
<td>18</td>
<td>1.00 (1.41)</td>
<td>-6.20 [-14.41, 2.01]</td>
<td>100.0</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect z=1.48</td>
<td>p=0.1</td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>18</td>
<td>18</td>
<td>-0.24 (13.58)</td>
<td>3.56 [-6.18, 13.30]</td>
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<td>Test for overall effect z=0.72</td>
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</tbody>
</table>
### Analysis 01.06. Comparison 01 PEP compared with Postural Drainage, Percussion & Vibration, Outcome 06 Total lung capacity (TLC)

Review: Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

Comparison: 01 PEP compared with Postural Drainage, Percussion % Vibration

Outcome: 06 Total lung capacity (TLC)

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP</th>
<th>PDPV</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weighted Mean Difference (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>95% CI</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 &gt;1 to 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darbee 1990</td>
<td>12 2.00 (9.87)</td>
<td>8 5.38 (12.47)</td>
<td>-3.38 [-13.67, 6.91]</td>
<td></td>
</tr>
</tbody>
</table>

### Analysis 01.07. Comparison 01 PEP compared with Postural Drainage, Percussion & Vibration, Outcome 07 Radiological imaging: increased bronchial markings

Review: Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

Comparison: 01 PEP compared with Postural Drainage, Percussion % Vibration

Outcome: 07 Radiological imaging: increased bronchial markings

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP</th>
<th>PDPV</th>
<th>Relative Risk (Fixed)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 &gt;6 to 12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costantini 2001</td>
<td>13/15</td>
<td>11/11</td>
<td>0.87 [0.71, 1.06]</td>
<td></td>
</tr>
</tbody>
</table>

### Analysis 01.08. Comparison 01 PEP compared with Postural Drainage, Percussion & Vibration, Outcome 08 Radiological imaging: change in Brasfield score

Review: Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

Comparison: 01 PEP compared with Postural Drainage, Percussion % Vibration

Outcome: 08 Radiological imaging: change in Brasfield score

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP</th>
<th>PDPV</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weighted Mean Difference (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>95% CI</td>
<td>95% CI</td>
</tr>
<tr>
<td>01 &gt;6 to 12 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McIlwaine 1997</td>
<td>18 0.37 (1.86)</td>
<td>18 0.37 (1.80)</td>
<td>0.00 [-1.20, 1.20]</td>
<td></td>
</tr>
</tbody>
</table>
Analysis 02.01. Comparison 02 PEP compared with oscillating PEP (Flutter), Outcome 01 Forced expiratory volume in 1 second (FEV1)

Review: Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis
Comparison: 02 PEP compared with oscillating PEP (Flutter)
Outcome: 01 Forced expiratory volume in 1 second (FEV1)

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP N</th>
<th>Mean(SD)</th>
<th>Flutter N</th>
<th>Mean(SD)</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weight (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 &gt;6 to 12 months</td>
<td>17</td>
<td>-1.24 (9.90)</td>
<td>13</td>
<td>-10.95 (19.96)</td>
<td>9.71 [-2.12, 21.54]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>McIlwaine 2001</td>
<td>17</td>
<td>-1.24 (9.90)</td>
<td>13</td>
<td>-10.95 (19.96)</td>
<td>9.71 [-2.12, 21.54]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>17</td>
<td>13</td>
<td>9.71 [-2.12, 21.54]</td>
<td>100.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect z=1.61 p=0.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 &gt;1 to 2 years</td>
<td>21</td>
<td>-4.20 (8.00)</td>
<td>21</td>
<td>-2.00 (8.10)</td>
<td>-2.20 [-7.07, 2.67]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Newbold 2005</td>
<td>21</td>
<td>-4.20 (8.00)</td>
<td>21</td>
<td>-2.00 (8.10)</td>
<td>-2.20 [-7.07, 2.67]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>21</td>
<td>21</td>
<td>-2.20 [-7.07, 2.67]</td>
<td>100.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect z=0.89 p=0.4</td>
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</tbody>
</table>

Analysis 02.02. Comparison 02 PEP compared with oscillating PEP (Flutter), Outcome 02 Hospitalisations for respiratory exacerbation (number per participant)

Review: Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis
Comparison: 02 PEP compared with oscillating PEP (Flutter)
Outcome: 02 Hospitalisations for respiratory exacerbation (number per participant)

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP N</th>
<th>Mean(SD)</th>
<th>Flutter N</th>
<th>Mean(SD)</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>Weighted Mean Difference (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 &gt;1 to 2 years</td>
<td>21</td>
<td>0.30 (0.70)</td>
<td>21</td>
<td>0.70 (1.00)</td>
<td>-0.40 [-0.92, 0.12]</td>
<td>-0.40 [-0.92, 0.12]</td>
</tr>
<tr>
<td>Newbold 2005</td>
<td>21</td>
<td>0.30 (0.70)</td>
<td>21</td>
<td>0.70 (1.00)</td>
<td>-0.40 [-0.92, 0.12]</td>
<td>-0.40 [-0.92, 0.12]</td>
</tr>
</tbody>
</table>
### Analysis 02.03. Comparison 02 PEP compared with oscillating PEP (Flutter), Outcome 03 Participant preference: self-withdrawal due to lack of perceived effectiveness

**Review:** Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

**Comparison:** 02 PEP compared with oscillating PEP (Flutter)

**Outcome:** 03 Participant preference: self-withdrawal due to lack of perceived effectiveness

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP</th>
<th>Flutter</th>
<th>Relative Risk (Fixed)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>McIlwaine 2001</td>
<td>0/20</td>
<td>5/20</td>
<td>0.09 [ 0.01, 1.54 ]</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>01 &gt;6 to 12 months</th>
<th>0.01</th>
<th>0.1</th>
<th>1</th>
<th>10</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favours PEP</td>
<td>ovi Flutter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Analysis 02.04. Comparison 02 PEP compared with oscillating PEP (Flutter), Outcome 04 Forced vital capacity (FVC)

**Review:** Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

**Comparison:** 02 PEP compared with oscillating PEP (Flutter)

**Outcome:** 04 Forced vital capacity (FVC)

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP</th>
<th>Flutter</th>
<th>Weighted Mean Difference (Fixed)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>McIlwaine 2001</td>
<td>17 0.06 (7.90)</td>
<td>13 -8.62 (15.50)</td>
<td>8.68 [-0.54, 17.90 ]</td>
<td></td>
</tr>
<tr>
<td>Newbold 2005</td>
<td>21 -4.70 (8.00)</td>
<td>21 -3.00 (7.10)</td>
<td>-1.70 [-6.27, 2.87 ]</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>01 &gt;6 to 12 months</th>
<th>0.01</th>
<th>0.1</th>
<th>1</th>
<th>10</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favours Flutter</td>
<td>ovi PEP</td>
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</tr>
</tbody>
</table>

Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)  
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### Analysis 02.05. Comparison 02 PEP compared with oscillating PEP (Flutter), Outcome 05 Forced expiratory flow 25 - 75 % (FEF 25-75)

**Review:** Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

**Comparison:** 02 PEP compared with oscillating PEP (Flutter)

**Outcome:** 05 Forced expiratory flow 25 - 75 % (FEF 25-75)

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP N</th>
<th>Mean(SD)</th>
<th>Flutter N</th>
<th>Mean(SD)</th>
<th>Weighted Mean Difference (Fixed) 95% CI</th>
<th>Weighted Mean Difference (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>McIlwaine 2001</td>
<td>17</td>
<td>-3.58 (15.49)</td>
<td>13</td>
<td>-8.87 (20.00)</td>
<td>5.29 [-7.84, 18.42]</td>
<td></td>
</tr>
<tr>
<td>Newbold 2005</td>
<td>21</td>
<td>-3.10 (6.20)</td>
<td>21</td>
<td>-2.00 (11.00)</td>
<td>-1.10 [-6.50, 4.30]</td>
<td></td>
</tr>
</tbody>
</table>

### Analysis 02.06. Comparison 02 PEP compared with oscillating PEP (Flutter), Outcome 06 Adherence: at least 85% of prescribed treatments performed

**Review:** Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis

**Comparison:** 02 PEP compared with oscillating PEP (Flutter)

**Outcome:** 06 Adherence: at least 85% of prescribed treatments performed

<table>
<thead>
<tr>
<th>Study</th>
<th>PEP n/N</th>
<th>Flutter n/N</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>McIlwaine 2001</td>
<td>2/20</td>
<td>0/20</td>
<td>5.00 [0.26, 98.00]</td>
<td></td>
</tr>
</tbody>
</table>

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*Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis (Review)*

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