Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis (Review)

Lee AL, Burge AT, Holland AE

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Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

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Abstract

Background

People with bronchiectasis experience chronic cough and sputum production and require the prescription of airway clearance techniques (ACTs). A common type of ACT prescribed is positive expiratory pressure (PEP) therapy. A previous review has suggested that ACTs including PEP therapy are beneficial compared to no treatment in people with bronchiectasis. However, the efficacy of PEP therapy in a stable clinical state or during an acute exacerbation compared to other ACTs in bronchiectasis is unknown.

Objectives

The primary aim of this review was to determine the effects of PEP therapy compared with other ACTs on health-related quality of life (HRQOL), rate of acute exacerbations, and incidence of hospitalisation in individuals with stable or an acute exacerbation of bronchiectasis.

Secondary aims included determining the effects of PEP therapy upon physiological outcomes and clinical signs and symptoms compared with other ACTs in individuals with stable or an acute exacerbation of bronchiectasis.

Search methods

We searched the Cochrane Airways Group Specialised Register of Trials, PEDro and clinical trials registries from inception to February 2017 and we handsearched relevant journals.

Selection criteria

Randomised controlled parallel and cross-over trials that compared PEP therapy versus other ACTs in participants with bronchiectasis.

Data collection and analysis

We used standard methodological procedures as outlined by Cochrane.
Main results

Nine studies involving 213 participants met the inclusion criteria, of which seven were cross-over in design. All studies included adults with bronchiectasis, with eight including participants in a stable clinical state and one including participants experiencing an acute exacerbation. Eight studies used oscillatory PEP therapy, using either a Flutter or Acapella device and one study used Minimal PEP therapy. The comparison intervention differed between studies. The methodological quality of studies was poor, with cross-over studies including suboptimal or no washout period, and a lack of blinding of participants, therapists or personnel for outcome measure assessment in most studies. Clinical heterogeneity between studies limited meta-analysis.

Daily use of oscillatory PEP therapy for four weeks was associated with improved general health according to the Short-Form 36 questionnaire compared to the active cycle of breathing technique (ACBT). When applied for three sessions over one week, minimal PEP therapy resulted in similar improvement in cough-related quality of life as autogenic drainage (AD) and L’expiration Lente Totale Glotte Ouverte en Decubitus Lateral (ELTGOL). Oscillatory PEP therapy twice daily for four weeks had similar effects on disease-specific HRQOL (MD -0.09, 95% CI -0.37 to 0.19; low-quality evidence). Data were not available to determine the incidence of hospitalisation or rate of exacerbation in clinically stable participants.

Two studies of a single session comparison of oscillatory PEP therapy and gravity-assisted drainage (GAD) with ACBT had contrasting findings. One study found a similar sputum weight produced with both techniques (SMD 0.54g (-0.38 to 1.46; 20 participants); the other found greater sputum expectoration with GAD and ACBT (SMD 5.6 g (95% CI 2.91 to 8.29; 36 participants). There was no difference in sputum weight yielded between oscillatory PEP therapy and ACBT with GAD when applied daily for four weeks or during an acute exacerbation. Although a single session of oscillatory PEP therapy was associated with less sputum compared to AD (median difference 3.1 g (95% CI 1.5 to 4.8 g; one study, 31 participants), no difference between oscillatory PEP therapy and seated ACBT was evident. PEP therapy had a similar effect on dynamic and static measures of lung volumes and gas exchange as all other ACTs. A single session of oscillatory PEP therapy (Flutter) generated a similar level of fatigue as ACBT with GAD, but greater fatigue was noted with oscillatory PEP therapy compared to ACBT alone. The degree of breathlessness experienced with PEP therapy did not differ from other techniques. Among studies exploring adverse events, only one study reported nausea with use of oscillatory PEP therapy.

Authors’ conclusions

PEP therapy appears to have similar effects on HRQOL, symptoms of breathlessness, sputum expectoration, and lung volumes compared to other ACTs when prescribed within a stable clinical state or during an acute exacerbation. The number of studies and the overall quality of the evidence were both low. In view of the chronic nature of bronchiectasis, additional information is needed to establish the long-term clinical effects of PEP therapy over other ACTs for outcomes that are important to people with bronchiectasis and on clinical parameters which impact on disease progression and patient morbidity in individuals with stable bronchiectasis. In addition, the role of PEP therapy during an acute exacerbation requires further exploration. This information is necessary to provide further guidance for prescription of PEP therapy for people with bronchiectasis.

Plain Language Summary

PEP therapy in bronchiectasis

Review question: We reviewed the evidence to identify the effects of positive expiratory pressure (PEP) therapy compared to other airway clearance techniques (ACTs) in people with bronchiectasis.

Background: People with bronchiectasis have a chronic cough and frequently produce mucus. ACTs assist in the removal of mucus in people with bronchiectasis, with PEP therapy a technique which is commonly prescribed. A previous review suggested that ACTs may be beneficial compared to no treatment, although the strength of this evidence was low. We wanted to discover what the effects were of PEP therapy compared to other ACTs when used by people with bronchiectasis, and whether it provided advantages over other ACTs.

Study characteristics: Nine studies were included, with a total of 213 people. The average age of participants ranged from 45 to 74 years. Treatment duration ranged from a single session to up to four weeks of treatment. Eight studies examined people who were stable and one study examined people who were experiencing an exacerbation (flare-up) of bronchiectasis. PEP therapy was compared to a range of ACTs.

Key results: Two small studies indicated that PEP therapy is as effective as other ACTs at improving quality of life. The duration of hospitalisation when using PEP therapy or other ACTs during a flare-up was similar. Both PEP therapy and other techniques appear to
have a similar effect on the clearance of mucus from the lungs and on lung function. Similar levels of breathlessness were experienced with PEP therapy and other ACTs. Other outcomes of interest were the rate of hospitalisation but these have not yet been reported. On the basis of this information, the prescription of PEP therapy for people with bronchiectasis is as suitable as any other type of ACT, with no greater advantage of PEP therapy.

**Quality of the evidence:** Because of inadequate reporting of methods and small number of participants, the quality of evidence was low.

This Cochrane plain language summary is current to May 2017.
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of Participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Patient or population: people with bronchiectasis</td>
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<td>Settings: hospital inpatient and outpatient department, home-based therapy</td>
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<td>Intervention: positive expiratory pressure (PEP) therapy</td>
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<td>Comparison: other airway clearance techniques (ACTs)</td>
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<td>Cough-related quality of life (QOL) assessed with: Leicester cough questionnaire total score. Higher score indicates better QOL. 19 questions on 7-point Likert scale. Scale from: 3 to 21 follow-up: mean 1 week</td>
<td>The median change in cough-related quality of life (QOL) was 0.5 points (95% CI 0.1 to 0.5)</td>
<td>The median change in cough-related quality of life (QOL) in the intervention group was 0.1 points lower</td>
<td>31 participants (one study)</td>
<td>⊕⊕</td>
<td>Randomised cross-over trial of minimal PEP therapy vs Autogenic drainage. Duration of intervention of 1 week per ACT</td>
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<tr>
<td>Cough-related quality of life (QOL) assessed with: Leicester cough questionnaire total score. Higher score indicates better QOL. 19 questions on 7-point Likert scale. Scale from: 3 to 21 follow-up: mean 1 week</td>
<td>The median change in cough-related quality of life (QOL) was 0.9 points (95% CI 0.5 to 2.1)</td>
<td>The median change in cough-related quality of life (QOL) in the intervention group was 0.4 points lower</td>
<td>31 participants (one study)</td>
<td>⊕⊕</td>
<td>Randomised cross-over trial of minimal PEP therapy vs ELTGOL. Duration of intervention of 1 week per ACT</td>
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<tr>
<td>Health-related quality of life (HRQOL) disease-specific HRQOL assessed with: Chronic respiratory disease questionnaire total score</td>
<td>not provided</td>
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<td>The mean difference 17 participants (one low(^1)) (95% CI between study) groups was -0.09 points per item (-0.37 to 0.19) in favour of oscillatory PEP therapy</td>
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\(^1\)The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval.

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

\(^1\)Small participant numbers

\(^2\)Insufficient power for quality of life comparison

\(^3\)Method of randomisation and allocation concealment unclear, lack of blinding of participants and personnel, no washout period applied

Randomised cross-over trial of ACBT vs Oscillatory PEP therapy (Flutter). Duration of intervention of 4 weeks per ACT.
**BACKGROUND**

**Description of the condition**

Bronchiectasis is a chronic respiratory condition that is defined by a clinical profile of chronic cough with sputum (mucus) production, dyspnoea (uncomfortable breathlessness) and fatigue (Barker 2002; McShane 2013). Several aetiologies of bronchiectasis are known; it may develop secondary to a severe respiratory infection or in association with other conditions, including alpha-1 antitrypsin deficiency, which are characterised by inflammation or impaired mucociliary clearance (mucus transport system), or the cause may be idiopathic (unknown) (Pasteur 2000; Goeminne 2012; Cortese 2016). Bronchiectasis unrelated to cystic fibrosis (CF) has been previously referred to as non-CF bronchiectasis, but a recent consensus agreed that this term undermines the severity, morbidity, and prognosis associated with bronchiectasis not originating from CF (Aliberti 2016); therefore bronchiectasis is now the accepted term to describe this condition. Bronchiectasis originates from a recurring cycle of infection and inflammation, with infection causing chronic inflammation leading to tissue damage and impaired mucociliary clearance (Cole 1986). These pathophysiological (disease) processes increase the risk of further infection, with a cycle of progressive inflammation resulting in structural changes to the airways (Cole 1986; Gaga 1998). The pathophysiology is characterised by a history of recurrent acute exacerbations (flare-ups) (King 2006), which often require hospitalisation. This condition may affect both children and adults (Karadag 2005; Chang 2008; Chang 2010; Pasteur 2010). The global prevalence is not accurately known but estimates from earlier studies have ranged from 0.5 cases per 100,000 in Finland (Säynäjäkangas 1997) to 1106 cases per 100,000 population over an eight-year period in the United States of America (USA) (Seitz 2012). More recently, higher prevalence rates were reported in the UK in 2013, with 566.1 per 100,000 in females and 485.5 per 100,000 in males (Quint 2016), while the prevalence was 3.6 cases per 1000 in 2012 in Catalonia (Monteagudo 2016). In New Zealand, the reported prevalence is 3.7 per 100,000 population, but this varies according to ethnicity (Twiss 2005), and in Australia, the prevalence amongst indigenous children is 1470 per 100,000 (Chang 2002). With increased use of high-resolution computed tomography (HRCT), bronchiectasis is more frequently identified (Weycker 2005; Kwak 2010), and hospitalisation rates associated with bronchiectasis are on the rise, particularly in older individuals (Seitz 2010; Seitz 2012; Ringshausen 2013). The frequency of these respiratory infections is linked to rising morbidity and mortality (Weycker 2005; Martinez-Garcia 2007; Roberts 2010; Goeminne 2012; Chalmers 2014; Goeminne 2014) and is a key predictor of reduced health-related quality of life (HRQOL) in those with bronchiectasis (Martinez-Garcia 2005).

**Description of the intervention**

Current international guidelines for the management of bronchiectasis focus on minimising further damage to the airways by reducing inflammation and infection and optimising airway clearance (Chang 2008; Chang 2010; Pasteur 2010; Chang 2015). To achieve this, recommended approaches incorporate the prescription of antibiotics, anti-inflammatory therapy and mucolytics (mucus loosening agents), together with airway clearance techniques to facilitate sputum clearance (Chang 2008; Chang 2010; Pasteur 2010; Chang 2015). A regular programme of airway clearance therapy has been associated with reduced symptoms of coughing and improved HRQOL (Muralihas 2008). A recent updated review found that compared with no treatment, performing airway clearance techniques (ACTs) was associated with improvement in sputum expectoration (production), lung function and HRQOL (Lee 2013). When undertaken by individuals with stable bronchiectasis, oscillatory PEP therapy (with repetitive vibrations) was associated with greater sputum expectoration and improved disease-specific HRQOL and cough-related QOL compared to no treatment (Lee 2015). Less pulmonary hyperinflation (overinflated) was evident with selected ACTs, including oscillatory PEP therapy (Lee 2013). However, when compared to other ACTs, oscillatory PEP therapy in people with stable bronchiectasis led to equivalent changes in sputum volume, dynamic lung volumes and degree of breathlessness (Lee 2015). Multiple types of ACTs may be applied in individuals with bronchiectasis. Selected techniques have included forms of breathing exercises, forced expirations or controlled coughing, gravity-assisted drainage (GAD) and manual techniques, which often are used in combination and may or may not require the assistance of the therapist for maximal efficacy. Other ACT options for promoting sputum clearance include the application of positive expiratory pressure (PEP) therapy through the use of hand-held devices, which generally do not require the hands-on assistance of a therapist and therefore may facilitate independent treatment.

**How the intervention might work**

The theoretical rationale behind the physiological effects of PEP therapy is that in the presence of small airway obstruction caused by secretion retention, the reduced diameter of the airway lumen (internal space) increases expiratory (exhalation) resistance and encourages airway collapse, which may lead to reduced expiratory flow, insufficient expiration and dynamic hyperinflation (Olsen 2015). PEP therapy has been hypothesised to promote airflow through collateral channels during inspiration to improve ventilation distribution, which allows accumulation of an increased volume of air behind secretions. The pressure gradient across the sputum plug is believed to force secretions centrally towards the larger airways, where expectoration may occur (Falk 1984; Van der Schans 1991). During expiration, the positive pressure gener-
Oberwaldner 1986). In individuals with bronchiectasis, oscillatory PEP therapy is not understood. PEP therapy is applied by inspiriring and expiring through a facemask or mouthpiece for a series of breaths via a one-way valve, followed by forced expiratory manoeuvres (buffling) or a slow expiratory manoeuvre in order to expextorate secretions. PEP therapy may apply low pressure (10 to 25 cmH2O) (Falk 1984; Groth 1985) or high pressure (Hi-PEP) at 40 to 120 cmH2O (Oberwaldner 1986). In contrast to low-pressure PEP therapy, during Hi-PEP, forced expiratory manoeuvres are also performed through the face-mask to prevent dynamic airway collapse during expiration and to facilitate more peripheral secretion clearance (Oberwaldner 1986; Oberwaldner 1991). Forced expiration against a resistive load is thought to direct air from hyperinflated lung units to unobstructed and atelectatic (collapsed) lung units to encourage a homogenised slow expiratory flow.

In comparison, oscillatory PEP therapy offers the combination of PEP and high-frequency oscillations within the airways during exhalation to facilitate secretion clearance. The PEP component is thought to encourage airflow behind secretions, and the oscillation induces vibrations within the airway wall to displace secretions into the airway lumen; repeated accelerations of expiratory airflow favour movement of secretions from the peripheral to the central airways (App 1998; Tambascio 2011). Sputum rheology (mucus flow) may also be altered, with oscillations reducing the viscoelasticity (thickness) of the secretions (Altaus 2009). Several oral devices such as a Flutter valve or Acapella may be used to provide oscillatory PEP therapy.

Comparisons of PEP therapy versus oscillatory PEP therapy have been undertaken in both children and adults with cystic fibrosis (Van Winden 1998; McIlwaine 2001; Newbold 2008). Although oscillatory PEP therapy was associated with a greater decline in lung function and an increased rate of hospitalisation compared with PEP therapy over the longer term in children (McIlwaine 2001), other studies have reported no difference in effects on lung function between the two types of therapy (Van Winden 1998; Newbold 2008). In individuals with bronchiectasis, oscillatory PEP therapy was associated with a greater increase in secretion transport compared with PEP therapy (Tambascio 2011). This mix of results suggests that the various modes of PEP therapy may have differing clinical and physiological effects. For this reason, it may be important to evaluate the distinct effects of each type of PEP therapy.

Why it is important to do this review

Surveys of clinical practice have illustrated considerable variation in the prescription of ACTs, including use of PEP therapy for both adults and children with bronchiectasis, both in a stable clinical state and during an acute exacerbation (O’Neill 2002; Butler 2008; Lee 2008; Johnstone 2013). Selection of ACTs in this population may be influenced by underlying airway pathophysiology, participant compliance and perception of efficacy, as well as by participant resources (Lapin 2002). Of the five studies included in the previous review (Lee 2013), although four applied oscillatory PEP therapy, only a small number of participants (ranging from eight to 20) were included, and the effects were compared with a control condition only. Although the independence of PEP therapy options compared with other treatment options may appeal to both patients and clinicians, the effects of each mode of PEP therapy must be clarified in terms of both physiological and clinical impact when compared with other types of ACTs in individuals with bronchiectasis, to further guide clinical practice.

OBJECTIVES

The primary aim of this review was to determine the effects of any type of PEP therapy compared with other ACTs on HRQOL, rate of acute exacerbations, and incidence of hospitalisation in individuals with stable or an acute exacerbation of bronchiectasis.

Secondary aims included determining the effects of PEP therapy upon physiological outcomes and clinical signs and symptoms compared with other ACTs in individuals with stable or an acute exacerbation of bronchiectasis.

METHODS

Criteria for considering studies for this review

Types of studies
We included randomised controlled trials (RCTs) of both parallel and cross-over design, in which a prescribed mode of PEP therapy was compared with other ACTs in individuals with stable or an acute exacerbation of bronchiectasis.

Types of participants
We included studies of both adults and children with a diagnosis of bronchiectasis of any origin, with the exception of CF. The diagnosis of bronchiectasis was based on a physician diagnosis or on HRCT with any degree of disease severity. We included studies of participants in a stable clinical state and experiencing an acute exacerbation. We classified participants as experiencing an acute exacerbation.
exacerbation if they met the investigators’ definition, or if they had worsening symptoms (increased sputum production, clinical signs of infection or dyspnoea) requiring medical treatment, including antibiotic therapy, and required or didn’t require hospitalisation. We classified participants as stable if they met the investigators’ definition, or if no change were made to medical therapy and stable symptoms persisted over the previous four weeks. We analysed separately studies of participants diagnosed with an acute exacerbation of bronchiectasis and studies of participants in a stable clinical state, as the prescription for treatment and physiological and clinical effects may differ.

We excluded participants diagnosed (on the basis of physician reporting) with concurrent asthma, chronic obstructive pulmonary disease or interstitial lung disease, and those breathing through an artificial airway. Studies of children included participants up to the age of 18 years, and studies of adults included participants older than 18 years. We included studies that incorporated a mix of diagnostic groups only if data on any of the review outcomes could be obtained separately for participants with bronchiectasis.

### Types of interventions

We included trials comparing PEP therapy with other ACTs (which may include a combination of techniques), with PEP therapy applied as a single technique or in conjunction with other recognised ACTs (e.g. oscillatory PEP therapy with active cycle of breathing technique vs active cycle of breathing technique alone). Types of PEP therapy included any of the following options, which were applied for the primary purpose of sputum removal.

- **PEP therapy**, with pressures ranging from 10 to 25 cmH\(_2\)O (Falk 1984; Groth 1985), delivered via mask or mouthpiece (including Bottle PEP) (Campbell 1986).
- **Hi-PEP therapy**, with pressures ranging from 40 to 120 cmH\(_2\)O (Oberwaldner 1986), delivered via mask.
- **Oscillatory PEP therapy**, delivered by a device (e.g. Flutter, Acapella, RC-Cornet, Quaker or Lung Flute) (App 1998; Altaus 2009; Shabari 2011).
- **Minimal PEP therapy** with pressure less than 5 cmH\(_2\)O, delivered via mask or mouthpiece (Venturelli 2012).

We excluded any type of PEP therapy delivered in conjunction with aerosol inhalation.

Comparative ACTs could include any of the following techniques, which could be applied in combination.

- **Gravity-assisted drainage (GAD)**, which uses specific positioning of bronchopulmonary segments to facilitate sputum clearance (Prasad 1993). GAD and manual techniques are often combined as an ACT. Manual techniques, including any combination of percussion, vibration, rib springing, or rib shaking, apply external forces to the chest wall to encourage mobilisation of mucus (Gallon 1992; McCarren 2006).
- **Slow expiration with the glottis open in lateral posture (ELTGOL)**, which uses GAD with slow expirations performed in a lateral decubitus position (Martins 2012).
- **Active cycle of breathing technique (ACBT)**, which utilises a combination of thoracic expansion exercises, breathing control (BC) and the forced expiration technique (FET) to maximise collateral channel ventilation and sputum movement (Pryor 1979), and which may be applied with or without GAD and manual techniques.
- **Autogenic drainage (AD)**, which incorporates breathing of variable volume to generate high expiratory flows while minimising airway collapse (Schini 1989).
- **Exercise performed for the purpose of sputum clearance**, which could include endurance or strength training (Dwyer 2011).
- **High-frequency chest wall oscillation**, which applies external chest wall oscillations at variable frequencies and intensities through an inflatable vest attached to a machine (Warwick 1991).

We included treatments applied over a single session or on a medium-term (one to seven days) or longer-term basis (longer than seven days).

### Types of outcome measures

#### Primary outcomes

- **HRQOL**, measured by disease-specific, generic, or symptom-specific questionnaires, which may or may not have been validated in this population.
- **Rate of, duration of, or time to acute exacerbation of bronchiectasis**, defined according to symptoms, physician diagnosis, or participant diaries.
- **Incidence of hospitalisation for bronchiectasis**.
  - For stable bronchiectasis, this included time to hospitalisation, number of hospital admissions, or number of hospital days.
  - For acute exacerbation of bronchiectasis, this included length of hospital stay, time to re-admission, number of hospital admissions, or number of hospital days.

These could be measured over the short, medium, or longer term according to the time frames previously defined.

#### Secondary outcomes

Secondary outcomes, including physiological outcomes consisted of the following:

- **Sputum volume** (wet and dry weight (g) or volume (mL)). Sputum weight was measured in the short term (within 24 hours of treatment), in the medium term (within one to seven days of treatment) and over the long term (more than seven days of treatment), with successful treatment indicated by an increase in sputum volume.
Measures of mucociliary clearance (e.g. radioaerosol clearance).
- Lung function (e.g. spirometry - forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), forced expiratory flow (FEF), forced expiratory flow at 25% to 75% of pulmonary volume (FEF₂₅₋₇₅), peak expiratory flow rate (PEFR); lung volumes - total lung capacity (TLC), functional residual capacity (FRC), residual volume (RV), inspiratory capacity (IC), TLC/RV ratio.
- Participant symptoms reported on any scale (dyspnoea or breathlessness, fatigue, discomfort), which may or may not have been validated in this population.
- Adverse events (pneumothorax, barotrauma, haemoptysis, bronchospasm, nausea).

Search methods for identification of studies

Electronic searches
We identified trials from the Cochrane Airways Group Specialised Register (CAGR), which is maintained by the information specialist for the Group. The Register contains trial reports identified from several sources:
1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL), through the Cochrane Register of Studies Online (crso.cochrane.org);
2. Weekly searches of MEDLINE Ovid SP 1946 to date;
3. Weekly searches of Embase Ovid SP 1974 to date;
4. Monthly searches of PsycINFO Ovid SP;
5. Monthly searches of CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature);
6. Monthly searches of AMED EBSCO (Allied and Complementary Medicine);
7. Handsearches of the proceedings of major respiratory conferences.

Studies contained in the Trials Register are identified through search strategies based on the scope of Cochrane Airways. Details of these strategies, as well as a list of handsearched conference proceedings, are in Appendix 1. See Appendix 2 for search terms used to identify studies for this review.
We also searched the Physiotherapy Evidence Database (PEDro) using similar terms (Appendix 3).

We conducted a search of the clinical trials registries ClinicalTrials.gov (www.ClinicalTrials.gov) and the World Health Organization (WHO) trials portal (www.who.int/ictrp/en/). We searched all databases from their inception to February 2017, and we imposed no restriction on language of publication.

Searching other resources
We checked reference lists of all primary studies and review articles for additional references. We searched the websites of manufacturers of relevant PEP devices (e.g. Flutter®, Acapella®, RC-Cornet®, Quaker®, Lung Flute®) for trial information.

Data collection and analysis

Selection of studies
Two review authors (AL and AB) independently screened titles and abstracts for inclusion of all potential studies identified as a result of the search and coded them as ‘retrieve’ (eligible or potentially eligible/unclear) or ‘do not retrieve’ (not eligible). We included studies reported as full text, those published as abstract only, and unpublished data when sufficient information was available. We retrieved full-text study reports/publications, and two review authors (AL and AB) independently screened the full text, identified studies for inclusion, and identified and recorded reasons for exclusion of ineligible studies. We resolved disagreements through discussion, or, if required, we consulted a third person (AH). We calculated the degree of agreement between review authors with a kappa statistic. We identified and excluded duplicates and collated multiple reports of the same study, so that each study rather than each report was the unit of interest in the review. We recorded the selection process in sufficient detail to complete a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram (Figure 1) and a ‘Characteristics of included studies’ table (Characteristics of excluded studies).
Figure 1. Study flow diagram.

64 records identified from database searching (2015 - 2017)

16 additional records identified from other sources

57 records after duplicates removed

57 records screened

39 excluded from title and abstract or are ongoing studies or awaiting classification

9 full-text articles excluded
- comparison of two PEP therapies (n = 2)
- mixed disease group (n = 2)
- mixed therapy group (n = 2)
- lack of PEP therapy use (n = 1)
- lack of randomisation (n = 1)
- lack of comparison group (n = 1)

18 full-text articles assessed for eligibility

9 studies included in qualitative analysis

9 studies included in quantitative analysis
Data extraction and management
We used a data collection form that was piloted on at least one study in the review to record study characteristics and outcome data. Two review authors (AL and AB) extracted the following study characteristics from included studies.
- Methods: study design, total duration of study, details of any 'run-in' period, number of study centres and locations, study setting, withdrawals, date of study.
- Participants: number, mean age, age range, gender, severity of condition, diagnostic criteria, baseline lung function, smoking history, inclusion criteria, exclusion criteria.
- Interventions: intervention, comparison, concomitant interventions.
- Outcomes: primary and secondary outcomes specified and collected, time points reported.
- Notes: funding for trial, notable conflicts of interest of trial authors.

Two review authors (AL and AB) independently extracted outcome data from included studies. We noted in the 'Characteristics of included studies' table (Characteristics of included studies) if outcome data were not reported in a useable way. We resolved disagreements by reaching consensus, or by involving a third person (AH). One review author (AL) transferred data into the Review Manager (Review Manager (RevMan)) file. We double-checked that data were entered correctly by comparing data presented in the systematic review with those provided in the study reports. A second review author (AB) performed spot-checks of study characteristics for accuracy against the trial report. We contacted authors of studies to verify extracted data, when necessary, and provided details of missing data when possible.

Assessment of risk of bias in included studies
Two review authors (AL and AB) independently assessed risk of bias for each RCT using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We resolved disagreements by discussion or by involving another review author (AH). We assessed risk of bias according to the following domains.
- Random sequence generation.
- Allocation concealment.
- Blinding of participants and personnel.
- Blinding of outcome assessment.
- Incomplete outcome data.
- Selective outcome reporting.
- Other bias.

We graded each potential source of bias as high, low, or unclear and provided a quote from the study report, together with a justification for our judgement in the 'Risk of bias' table. We summarised 'risk of bias' judgements across different studies for each of the domains listed. We considered blinding separately for different key outcomes when necessary (e.g. for unblinded outcome assessment, risk of bias for rate of hospitalisation may be very different than for a participant-reported symptom scale). When information on risk of bias was related to unpublished data or correspondence with a trialist, we noted this in the 'Risk of bias' table. We graded bias as low, high or unclear, and resolved discrepancies by consensus. We summarised results in a 'Risk of bias' table.

When considering treatment effects, we considered the risk of bias for studies that contributed to this outcome. For randomised cross-over trials, additional considerations for risk of bias included appropriateness of cross-over design, randomisation of treatment order, possibility of carry-over effects, and availability of unbiased data (Higgins 2011).

Assessment of bias in conducting the systematic review
We conducted the review according to the published protocol and reported deviations from it in the 'Differences between protocol and review' section (Differences between protocol and review) of the systematic review.

Measures of treatment effect
We analysed data for each outcome, irrespective of whether participants were stated to drop out (intention-to-treat analysis). We analysed dichotomous data as odds ratios and continuous data as means and standard deviations. We undertook meta-analyses for continuous data only when this was meaningful (i.e. if treatments, participants and the underlying clinical question were similar enough for pooling to make sense). We calculated mean differences (MDs: same metric scale) or standardised mean differences (SMDs: different metric scale) with 95% confidence intervals (95% CIs). We narratively described skewed data reported as medians and interquartile ranges, where available, or medians and 95% confidence intervals.

Unit of analysis issues
We analysed data from HRQOL, symptom questionnaires, lung function, or sputum clearance as continuous or ordinal data. We analysed exacerbation rates or hospitalisations as dichotomous (yes/no) or ratio (frequency, rate) data. We analysed cross-over trials using generic inverse variance methods, when possible. In the event of inadequate washout for a cross-over trial, we included only results from the first phase of the trial, where available. One
study applied independent t-tests for a cross-over trial (Semwal 2015); as raw data were not available, the results were reported narratively. One study applied a Student’s t-test to compare different techniques (Antunes 2001); results were reported narratively.

Dealing with missing data
In the event of missing data, we contacted investigators or study sponsors to verify key study characteristics and to obtain missing numerical outcome data when possible (e.g. when a study was identified as abstract only). When this was not possible, and missing data were related to the intervention, we planned to analyse the impact of including such studies in the overall assessment of results by performing a sensitivity analysis. However, with limited pooling of data, this analysis was not performed.

Assessment of heterogeneity
Where data was able to be pooled, we used the $I^2$ statistic to measure heterogeneity among the trials in each analysis. If we identified substantial heterogeneity ($\geq 50\%$), we would have explored possible causes through prespecified sensitivity analyses. For those studies in which homogeneity was evident, we planned to use a fixed-effect model for analysis. For studies of substantial heterogeneity ($I^2 \geq 50\%$), we used a random-effects model (Deeks 2008). For those with heterogeneity with an $I^2 > 75\%$, results of included studies were presented in a forest plot, but the pooled estimate was suppressed.

Assessment of reporting biases
If we had more than 10 trials, we planned to create a funnel plot and analyse this for small-study and publication biases (Egger 1997). However, a total of only nine trials were identified in this review.

Data synthesis
We analysed separately data from studies related to acute exacerbation compared with studies related to stable bronchiectasis. In addition, we planned to compare studies of low- or Hi-PEP therapy; however no studies using Hi-PEP therapy were included. Studies providing data on oscillatory PEP therapy were analysed separately. Within each group, we planned to pool data that were clinically homogeneous using a fixed-effect model; data that were clinically homogeneous using a random-effects model. However, the differences between interventions and differing units of reporting limited this pooling. We did not pool data that were clinically heterogeneous.

'Summary of findings' table
We created a 'Summary of findings' table using the following outcomes: HRQOL, exacerbation rates, and hospitalisation. We used the five GRADE (Grades of Recommendation, Assessment, Development and Evaluation) considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of a body of evidence as it related to studies that contributed data to the meta-analyses for prespecified outcomes. We used methods and recommendations described in Section 8.5 and Chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011) and GRADEpro software. We justified all decisions to downgrade or upgrade the quality of studies by using footnotes, and we made comments to aid readers’ understanding of the review, when necessary.

Subgroup analysis and investigation of heterogeneity
We planned to carry out the following subgroup analyses:
- Oscillatory PEP therapy vs other ACTs.
- Non-oscillatory PEP therapy vs other ACTs.
- Level of PEP (minimal/low pressure (< 5 cmH2O vs 10 to 25 cm H2O) vs high pressure (40 to 120 cm H2O)).

We used the following outcomes in subgroup analyses:
- HRQOL
- Exacerbation rates.
- Hospitalisation rates.

We used the formal test for subgroup interactions in Review Manager (Review Manager (RevMan)).

Sensitivity analysis
We planned to perform a sensitivity analysis to determine the effects of methodological quality on the pooled estimate by removing studies that were at high or unclear risk of bias for the domains of blinding and incomplete outcome data. We had planned to examine the effects of the method of diagnosing bronchiectasis (physician-based or HRCT). However, insufficient numbers of included studies precluded these analyses.

RESULTS

Description of studies
See Characteristics of included studies, Characteristics of excluded studies and Characteristics of studies awaiting classification for complete details.
Results of the search

The 2017 search of databases (CAGR and Pedro) and clinical trial registries of potential studies and reference checks yielded 81 studies. After removal of duplicates, a total of 57 studies were screened. We excluded 39 studies on the basis of title and abstract, including eight which are currently awaiting classification or are ongoing studies; these were not included in the analysis. A total of 18 full-text studies were assessed for eligibility. We excluded nine studies, as they did not meet the review criteria. We included nine studies in the qualitative analysis. Review authors agreed on 14 out of 18 studies following full-text review (82%), with kappa = 0.90, indicating substantial agreement. In this review, a total of nine studies were included (Figure 1). The full details of excluded studies and those awaiting classification are outlined in Characteristics of excluded studies and Characteristics of studies awaiting classification tables.

Included studies

Design
This review included seven randomised cross-over trials (Antunes 2001; Thompson 2002; Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015) and two randomised controlled trials (Tsang 2003; Altiay 2012).

Participants
The nine included studies involved 213 participants with sample sizes ranging from 10 to 36. Eight studies included clinically stable adult participants (Antunes 2001; Thompson 2002; Patterson 2005; Eaton 2007; Altiay 2012; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015) and one study included adult participants experiencing an acute exacerbation of bronchiectasis (Tsang 2003). Bronchiectasis was diagnosed on the basis of HRCT in six studies (Antunes 2001; Thompson 2002; Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015) and by physician diagnosis in two studies, as per the inclusion criteria (Altiay 2012; Semwal 2015). The study of participants with an acute exacerbation stated inclusion criteria of diagnosis of bronchiectasis of at least one year in duration, with symptoms of cough and sputum production (Tsang 2003). The age range of participants was 46 to 74 years in eight studies (Antunes 2001; Thompson 2002; Tsang 2003; Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015); one study did not report age (Altiay 2012). Of the eight studies in those with stable disease, five reported disease severity according to spirometry, FEV$$_1$$ ranged from 53 to 64% predicted (Antunes 2001; Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015) or 0.67 to 0.7 L (Thompson 2002). In those with an acute exacerbation of bronchiectasis, FEV$$_1$$ ranged from 36 to 49% predicted (Tsang 2003).

Intervention
The duration of each intervention ranged from a single treatment in five studies (Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015), twice over one week (Antunes 2001), daily for four weeks (Altiay 2012) or twice daily for four weeks (Thompson 2002). In those with an acute exacerbation, the frequency was three times per day from day two of admission until day of discharge (Tsang 2003). A washout period of one week was applied in two studies (Guimaraes 2012; Herrero-Cortina 2015), while three studies did not apply a washout period (Antunes 2001; Patterson 2005; Eaton 2007), one study applied a three hour washout (Semwal 2015), and one study did not mention the use of a washout period (Thompson 2002). Outcome measures were only collected throughout the intervention period, with no long-term follow-up beyond the intervention applied in any study. Two studies compared oscillatory PEP therapy (Flutter) to slow inspiration with the glottis open from the FRC to the RV, performed in the lateral decubitus position, with the affected lung in the dependent position (‘L’expiration Lente Totale Glotte Ouverte en Decubitus Lateral’ (ELTGOL) (Guimaraes 2012)) with one study adding chest clapping, vibrocompression and coughing (Antunes 2001). Three studies compared oscillatory PEP therapy (Flutter) to ACBT (Thompson 2002; Eaton 2007; Altiay 2012), with two studies applying ACBT in a seated (Eaton 2007) or a GAD position (Thompson 2002; Eaton 2007) or both. One study compared oscillatory PEP therapy (Flutter) to GAD with BC, deep inspiration, relaxation, and coughing (Tsang 2003). One study applied oscillatory PEP therapy (Acapella) in a GAD position versus ACBT with GAD (Patterson 2005). One study compared minimal PEP therapy to AD and to ELTGOL (Herrero-Cortina 2015). One study compared oscillatory PEP therapy (Acapella) to AD (Semwal 2015).

Outcome measures
Eight studies included a measure of sputum volume or weight, which could be wet or dry, and a measure of spirometry (Antunes 2001; Thompson 2002; Tsang 2003; Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015). Health-related quality of life was assessed using the Short-Form-36 (SF-36) (Altiay 2012) or the Chronic Respiratory Questionnaire (CRQ) (Thompson 2002), while cough-related quality of life was assessed with the Leicester Cough Questionnaire (LCQ) in one study (Herrero-Cortina 2015). Breathlessness was measured using the Borg scale in four studies (Thompson 2002; Eaton 2007; Altiay 2012; Semwal 2015), while the Medical Research Council score for Dyspnoea (Altiay 2012) and the 15-count breathlessness score (Patterson 2005) were each applied in one study. Symptoms of tiredness and discomfort (Eaton 2007) and coughing (Altiay 2012) were assessed in one study each. Lung function was measured in seven studies, with spirometry (Thompson 2002; Tsang 2003;...
Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015), peak expiratory flow (Semwal 2015), and lung volumes included (Guimaraes 2012).

Excluded studies
We excluded a total of 48 studies. Reasons for exclusion of full-text reviewed studies were comparison between two types of PEP therapy (n = 2), mixed disease group from which data related to bronchiectasis could not be extracted (n = 2), mixed therapy group from which data related to PEP therapy could not be extracted (n = 2), lack of PEP therapy use (n = 1), lack of randomisation (n = 1) and lack of comparison group (n = 1). Full details of reasons for exclusion are provided in the Characteristics of excluded studies table. A further six studies are ongoing (Characteristics of ongoing studies) and two are awaiting classification. These will be assessed for eligibility in further updates of this review.

Risk of bias in included studies
Risk of bias was able to be completed for eight studies (Antunes 2001; Thompson 2002; Tsang 2003; Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015). One study was available only in abstract form, therefore all criteria for 'risk of bias' assessment were indicated as unclear (Altiay 2012). An overview of the risk of bias for the domains listed below is outlined in Figure 2.
Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding of participants and personnel (performance bias)</th>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Incomplete outcome data (attrition bias)</th>
<th>Selective reporting (reporting bias)</th>
<th>Other bias</th>
</tr>
</thead>
</table>
Allocation
All studies reported random allocation to groups, but the methods by which this was applied were stated in only four studies (Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015). Five studies stated the use of either sealed, opaque envelopes, or a method of concealment was used for allocation (Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015); three studies did not provide sufficient information to determine the method used (Antunes 2001; Thompson 2002; Tsang 2003).

Blinding
Insufficient information was provided in seven studies regarding the blinding of participants and personnel delivering the interventions (Antunes 2001; Thompson 2002; Eaton 2007; Altiay 2012; Guimaraes 2012; Semwal 2015), while three studies specifically stated the absence of blinding of personnel (Patterson 2005; Tsang 2003) and participants and personnel (Herrero-Cortina 2015). The physical nature of the intervention is likely to impose limits on blinding participants in these studies. One study stated the use of an independent assessor for recording pre and post treatment outcome measures (Patterson 2005). Insufficient data were available to show whether assessors were blinded in other studies (Antunes 2001; Thompson 2002; Tsang 2003; Eaton 2007; Altiay 2012; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015).

No studies reported whether data analysts were blinded to group allocation.

Incomplete outcome data
Three studies stated withdrawal of participants (Antunes 2001; Thompson 2002; Herrero-Cortina 2015). One study outlined that three participants were unable to complete the study and their results were not included in the analysis (Antunes 2001). Thompson stated that of the five participants who withdrew, three dropped out because of an infective exacerbation (two during the oscillatory PEP therapy arm and one during the ACBT arm) and two recorded insufficient data for analysis (Thompson 2002). The third study outlined that two participants dropped out due to acute low back pain and pulmonary exacerbation (Herrero-Cortina 2015). The data of withdrawn participants were not included in analysis in any study (Antunes 2001; Thompson 2002; Herrero-Cortina 2015).

Selective reporting
Three studies were reported on a clinical registry prospectively (Guimaraes 2012; Altiay 2012; Herrero-Cortina 2015). Results were reported for all outcomes at each time point for six studies (Antunes 2001; Thompson 2002; Tsang 2003; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015). With one study reporting only in abstract form, it is possible that not all data were reported in this study (Altiay 2012).

Other potential sources of bias
An adequate washout period of one week was applied in two studies (Guimaraes 2012; Herrero-Cortina 2015). No washout period was applied in three studies (Antunes 2001; Thompson 2002; Patterson 2005), which may have influenced the findings of two studies, with consecutive days of treatment applied in one study (Patterson 2005) and a four-week intervention applied in another study (Thompson 2002). One study used a three-hour washout period between interventions, which may have influenced findings (Semwal 2015). One study did not mention the inclusion of a washout period between interventions (Eaton 2007).

Effects of interventions
See: Summary of findings for the main comparison
See Summary of findings (Summary of findings for the main comparison) for the primary outcome comparisons. We were able to include data from nine studies, in a quantitative and narrative synthesis, with all studies conducted in the adult population (Antunes 2001; Thompson 2002; Tsang 2003; Patterson 2005; Eaton 2007; Guimaraes 2012; Altiay 2012; Herrero-Cortina 2015; Semwal 2015).

Primary outcomes
Health-related quality of life
Three studies examined the effects of PEP therapy compared to other techniques on HRQOL (Thompson 2002; Altiay 2012; Herrero-Cortina 2015). Due to clinical heterogeneity in comparison of treatment techniques, follow-up, and outcome measures, no studies could be combined in meta-analysis. Using oscillatory PEP therapy (Flutter) daily for four weeks improved general health (P = 0.048) based on the SF-36 compared to daily ACBT (Altiay 2012). Minimal PEP, AD, and ELTGOL, when applied for three sessions over one week, all significantly increased (better) cough-related quality of life according to the LCQ total scores, with no difference between minimal PEP therapy and AD (median 0.4 (95% CI 0.1 to 1.2) vs 0.5 (95% CI 0.1 to 0.5)) or minimal PEP therapy and ELTGOL (median 0.4 (95% CI 0.5 to 2.1) vs 0.9 (95% CI 0.1 to 1.2)) (P = 0.60) (Herrero-Cortina 2015). Performing oscillatory PEP therapy (Flutter) compared to ACBT in a GAD position twice daily for four weeks had a similar effect...
on HRQOL for dyspnoea (MD 0.01, 95% CI -0.48 to 0.50; one study, 17 participants, low-quality evidence) (Analysis 1.1), fatigue (MD -0.19, 95% CI -0.82 to 0.45; one study, 17 participants, low-quality evidence) (Analysis 1.2), emotional function (MD -0.06, 95% CI -0.63 to 0.52; one study, 17 participants, low-quality evidence) (Analysis 1.3), mastery (MD -0.10, 95% CI -0.65 to 0.46; one study, 17 participants, low-quality evidence) (Analysis 1.4) and total score (MD -0.09, 95% CI -0.37 to 0.19; one study, 17 participants, low-quality evidence) (Analysis 1.5) (Thompson 2002). The results of all studies are outlined in Table 1.

Rate of exacerbation or time to first exacerbation
No studies reported on the rate of or time to first exacerbation.

Incidence of hospitalisation
No studies reported on the incidence of hospitalisation for those in a stable clinical state.

Secondary outcomes
Sputum volume or weight
Eight studies compared the effects of PEP therapy to other ACTs on sputum yield (Antunes 2001; Thompson 2002; Tsang 2003; Patterson 2005; Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015). Two studies investigating a single session of oscillatory PEP therapy (Acapella or Flutter) compared to GAD with ACBT are presented together, but due to significant clinical heterogeneity, a pooled estimate of results was not calculated. A single session of oscillatory PEP therapy (Acapella) produced a similar sputum weight compared to GAD with ACBT (SMD 0.54 g, 95% CI -0.38 to 1.46 g; 20 participants); while a single session of oscillatory PEP therapy (Flutter) produced less sputum compared to GAD with ACBT (SMD 5.6 g (95% CI 2.91 to 8.29 g; 36 participants) (Analysis 2.1) (Figure 3). Less sputum volume was produced with oscillatory PEP therapy (Flutter) compared to GAD with ACBT (MD 5.1 mL (95% CI 2.24 to 7.96 mL; one study, 36 participants) (Analysis 2.2) (Eaton 2007). There was no difference in sputum weight between oscillatory PEP therapy (Flutter) and ACBT in a seated position (MD -0.3 g (95% CI -1.42 to 0.82 g; one study, 36 participants) (Analysis 3.1) or in sputum volume (MD -0.60 mL, 95% CI -1.87 to 0.67 mL; one study, 36 participants) (Analysis 3.2) (Eaton 2007). A single treatment of oscillatory PEP therapy (Flutter) yielded a lower sputum weight compared to ELTGOL (median 0.15 g (minimum to maximum 0.05 to 0.13 g) versus median 0.38 (minimum to maximum 0.06 to 2.63 g; one study, 10 participants), P < 0.05) (Guimaraes 2012). Less sputum was expectorated during a single treatment of minimal PEP therapy compared to AD (median difference 3.1 g, 95% CI 1.5 to 4.8 g) or ELTGOL (MD 3.6 g, 95% CI 2.8 to 7.1 g; one study, 31 participants) (Herrero-Cortina 2015). However, mean clearance over 24 hours was similar for each of these techniques (P = 0.8) (Herrero-Cortina 2015). A comparison of AD to oscillatory PEP therapy (Acapella) did not yield a difference in sputum volume (mean 16.1 mL (SD 7.9) vs 16.3 mL (10.3), P = 0.92) or sputum weight (mean 15.8 g (5.7) vs 16.2 g (7.9) (P = 0.85) immediately post treatment (Semwal 2015). Comparing four sessions of oscillatory PEP therapy (Flutter) to ELTGOL, there was no significant difference in average sputum dry weight per session (0.28 g (SD 0.28) vs 0.16 g (0.06), P < 0.05 or wet weight (7.2 g (SD 2.3) vs 6.3 g (0.7), P > 0.05) (Antunes 2001). Four weeks of twice daily oscillatory PEP therapy compared to ACBT with GAD did not increase sputum weight (median difference 7.64 g, P = 0.77) (Thompson 2002). When applied during an acute exacerbation, oscillatory PEP therapy (Flutter) and GAD yielded a similar sputum weight on day two of admission (MD favouring GAD 19.86 g, 95% CI 7.95 to 47.67 g; one study, 10 participants) (Analysis 4.1), day four of admission (MD 22.46 favouring GAD, 95% CI -10.71 to 55.63 g; one study, 10 participants) (Analysis 4.2) or day of discharge (MD favouring GAD, 21.03 g 95% CI -11.29 to 53.35 g; one study, 10 participants) (Analysis 4.3) (Tsang 2003). The results of all studies are outlined in Table 2.

Figure 3. Forest plot of comparison: Oscillatory PEP therapy vs ACBT with GAD (single session), Sputum weight (g)
Sputum clearance

No studies reported on sputum clearance using radioaerosol clearance.

Lung function

Eight studies compared the effects of PEP therapy to other ACTs on measures of lung function (Antunes 2001; Thompson 2002; Tsang 2003; Patterson 2005; Altiay 2012; Guimaraes 2012; Herrero-Cortina 2015; Semwal 2015). None could be combined in meta-analysis due to clinical heterogeneity. A single treatment session of oscillatory PEP therapy (Acapella) and ACBT with GAD yielded a similar effect on FEV1, FVC and PEF % predicted (Patterson 2005). There was no difference in lung function (FEV1, FVC, FEF25–75) at treatment conclusion between minimal PEP therapy and ELTGOL or minimal PEP therapy and AD (P > 0.05) (Herrero-Cortina 2015). Similarly, a single session of oscillatory PEP therapy (Acapella) compared to AD did not change PEFR immediately following treatment (176.1 L/min (72.6) vs 179.1 L/min (72.6), P = 0.87) (Semwal 2015). There was no difference in PEFR between oscillatory PEP therapy (Flutter) vs ELTGOL between four occasions of treatment (P > 0.05) (Antunes 2001). One session of oscillatory PEP therapy (Flutter) had a similar effect to ELTGOL on change in FEV1 (median 1.6 L (minimum to maximum -6.8 to 21.4) vs median 2.2 L (-20.2 to 20.9)), change in FVC (median 2.44 L (minimum to maximum -3.9 to 8.1) vs median 0.96 L (-11.8 to 22.1)), change in FEV1/FVC (median 0.7 L (minimum to maximum -11.3 to 19.6) vs median 0 L (-8.6 to 10.6)), change in FEF25–75 (median 4.5 L (minimum to maximum -21.4 to 160) vs median 6 L (-90.51 to 236)), change in IC (median 3.49 L (minimum to maximum -28.47 to 33.78) vs median 2.65 L (-15.65 to 27.66), change in TLC (median -18.27 L (minimum to maximum -42.83 to -6.43) vs median 9.66 L (-40.03 to -1.96)), change in FRC (median -25.81 L (minimum to maximum -52.02 to -5.14) vs median -14.48 L (-55.65 to -3.6)), change in RV (median -29.55 L (minimum to maximum -54.66 to -8.86) vs median -18.72 L (-71.85 to -10.73) or change in RV/TLC ratio (median -5.21 L (minimum to maximum -22.81 to 27.59) vs median -8.48 L (-25.46 to 113.04)) (Guimaraes 2012). Four weeks of treatment with oscillatory PEP therapy (Flutter) compared to ACBT with GAD did not affect PEFR for the morning session (median difference -2.5 L/min, P = 0.38) or the evening session (median -2.72 (95% CI -6.95 to 1.52), P = 0.30) (Thompson 2002). Four weeks of daily ACBT or oscillatory PEP therapy (Flutter) did not yield a difference in FEV1 or FVC between techniques (Altiay 2012). During an acute exacerbation, there was no difference in FEV1 post treatment between oscillatory PEP therapy (Flutter) and GAD on day two of admission (MD 0.12 L (95% CI -0.32 to 0.56 L)) (Analysis 4.4), day four (MD 0.15 L (95% CI -0.27 to 0.57 L)) (Analysis 4.5) or day of discharge (MD 0.12 L (95% CI -0.52 to 0.76 L)) (Tsang 2003). Similarly, there was no difference between these interventions for FVC on day two of admission (MD -0.22 L (95% CI -0.81 to 0.37 L)) (Analysis 4.7), Day four of admission (MD 0.2 L (95% CI -0.48 to 0.88 L)) (Analysis 4.8) or day of discharge (MD 0.12 L (95% CI -0.52 to 0.76 L)) (Analysis 4.9). Equivalent results were evident for PEFR for day two (MD 22.2 L/min (95% CI -48.88 to 93.28 L/min)) (Analysis 4.10), day four (MD 22.6 L/min (95% CI -40.69 to 85.89 L/min)) (Analysis 4.11) and day of discharge (MD 23.2 L/min (95% CI -39.56 to 85.96 L/min)) (Analysis 4.12) (Tsang 2003). The results of all studies are outlined in Table 3.

Symptoms

A single session of oscillatory PEP therapy (Flutter), when compared to ACBT with GAD, generated a similar level of fatigue (MD -0.3, 95% CI -0.35 to 0.95) (Analysis 2.3). However, using the Flutter was more tiring compared to ACBT alone (MD 0.7, 95% CI 0.15 to 1.25) (Analysis 3.3) (Eaton 2007). There was no difference in discomfort level between the Flutter compared to ACBT alone (MD 0.40, 95% CI -0.12 to 0.92) (Analysis 3.4), or between Flutter and ACBT combined with GAD (MD -0.3, 95% CI -0.82 to 0.22) (Analysis 2.4) (Eaton 2007). Similarly, there was no difference in dyspnoea (Borg score) between oscillatory PEP therapy (Acapella) and AD (mean 1.8 (SD 1.1) vs 1.8 (1.2), P = 1.00) (Semwal 2015) or in a comparison of oscillatory PEP therapy (Flutter) vs ACBT or ACBT with GAD (Eaton 2007). The 15-count breathlessness score did not differ between a single session of oscillatory PEP therapy (Acapella) and ACBT with GAD (Patterson 2005). Four weeks of daily oscillatory PEP therapy (Flutter) compared to ACBT had a similar effect on the degree of dyspnoea (Borg score), and symptoms of cough and feelings of weakness when compared to ACBT (Altiay 2012). Four weeks of twice daily oscillatory PEP therapy (Flutter) generated similar levels of breathlessness following morning therapy session (MD 0.13, 95% CI -0.078 to 0.34), P = 0.36 and evening sessions (median difference -0.04, P > 0.99) (Thompson 2002). The results of all studies are outlined in Table 4.

Adverse events

One study reported the occurrence of nausea in one participant when using oscillatory PEP therapy (Flutter) (Thompson 2002). No other reports of adverse events were made from other studies; it is unknown if any adverse events occurred in these studies.

DISCUSSION

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Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis (Review)
Summary of main results

This review compared the effects of PEP therapy to other forms of ACTs in individuals with bronchiectasis. Results from nine studies of 213 individuals were mixed. In individuals with stable bronchiectasis, data from a small number of studies illustrated that PEP therapy offered similar effects on HRQOL, cough-related quality of life and symptoms of breathlessness as other ACTs. Short and medium-term use of PEP therapy offered no greater advantage in sputum expectoration compared to other types of techniques, irrespective of clinical disease state. No difference in effects on measures of lung function were evident between PEP therapy and other ACTs. According to the GRADE criteria, all review outcomes were rated as low-quality. Future, longer term studies are required to confirm the magnitude of effect on HRQOL, exacerbation frequency, and hospitalisation rates. Further information is needed regarding the effect of PEP therapy during an acute exacerbation of bronchiectasis.

Overall completeness and applicability of evidence

Key clinical features of bronchiectasis are cough, fatigue, and breathlessness (King 2006); for this reason, a reduction in these symptoms is beneficial. It is therefore encouraging that minimal PEP therapy, AD, and ELTGOL lead to improvement in cough-related quality of life, even when used for a short duration (Herrero-Cortina 2015). This is despite each of these techniques differing in their underlying rationale. The proposed physiological basis for ELTGOL is the promotion of two-phase gas-liquid interaction to facilitate mucociliary clearance (Guimaraes 2012), while the proposed primary mechanism of oscillatory PEP therapy involves a splinting effect on the airways to improve collateral ventilation and altering sputum rheology (Tambascio 2011). In contrast, AD relies on the generation of shearing forces induced by airflow at different lung volumes to loosen and mobilise secretions (Schno 1989). This suggests that, regardless of the type of technique, use of either PEP therapy, AD, or ELTGOL may lead to more efficient expectoration in the short term. However, with a lack of sustained improvement following the washout period between treatment techniques, improvement in this domain of quality of life may only be able to be maintained with regular treatment.

The degree of breathlessness was not greater with PEP therapy compared to other techniques, including ACBT with GAD (Thompson 2002; Patterson 2005; Eaton 2007; Altiay 2012; Semwal 2015). Although not specifically stated, this may be related to the approach with these techniques, with the inclusion of sessions of breathing control (Thompson 2002). However, for those experiencing fatigue, use of oscillatory PEP with a Flutter may be less tiring compared to ACBT in a seated position (Eaton 2007). The reason for this is unclear, with both techniques undertaken in a seated position. It is possible that a greater degree of breathing control was incorporated into the performance of ACBT, but in the absence of a specific description of the PEP therapy, this finding should be interpreted with caution. The lack of difference in disease-specific HRQOL between oscillatory PEP therapy and ACBT with GAD (Thompson 2002) suggests that any type of ACT may offer equal benefit in HRQOL. Evaluating the effects of ACTs on HRQOL is difficult with a treatment duration of only four weeks; a longer length of time of six or 12 months is required to fully evaluate treatment effect. With reports of greater preference for independent techniques such as oscillatory PEP therapy (Eaton 2007), longer term studies which factor in adherence would provide a clearer indication of the effect on HRQOL. In addition, alternative options for evaluating HRQOL have now been developed for bronchiectasis and which specifically consider all clinical symptoms which are of importance to people with this condition (Quittner 2015). Including this tool as an outcome measure in future studies of PEP therapy and other ACTs may provide more definitive information. Experiencing less pain with oscillatory PEP therapy is likely to influence adherence. However, with this study only available in abstract form and the lack of detail in location of pain (Altiay 2012), this finding requires further clarification. Using PEP therapy compared to GAD during an acute exacerbation offers no additional advantage in the duration of hospital stay. With the lack of studies including exacerbation rates and hospitalisation rates, there is a need for further long-term research which incorporate these clinically important outcomes.

The effect on sputum expectoration is variable, with some single treatments with oscillatory PEP therapy (either Flutter or Acapella) producing less sputum expectoration compared to GAD with ACBT or with AD or ELTGOL (Eaton 2007; Guimaraes 2012; Herrero-Cortina 2015), while other studies found no difference in the use of oscillatory PEP therapy and ACBT, with or without GAD, AD, or GAD with chest clapping and vibrocompression and coughing (Antunes 2001; Thompson 2002; Tsang 2003; Patterson 2005; Eaton 2007; Semwal 2015), irrespective of clinical state. Reasons for these contrasting findings are likely to be related to the differences in treatment approaches as well as the duration of treatment sessions. Greater sputum expectoration in a single session or with four weeks of daily treatment with ACBT and GAD compared to oscillatory PEP therapy was achieved only when the selection of GAD positions was based on HRCT results (Eaton 2007), rather than right and left lateral decubitus positions or two positions based on unknown criteria (Antunes 2001; Thompson 2002; Patterson 2005). This may be an important factor when choosing between PEP therapy and ACBT with GAD and the approach adopted in position selection. The addition of chest clapping and vibrocompression offered no greater advantage over oscillatory PEP therapy (Antunes 2001). However, as ACBT and GAD are perceived to be more time-consuming (Eaton 2007), the degree of interference in daily life may be an important clinical consideration. If GAD is not included, equivalent benefits for
sputum production were achieved with ACBT in a seated position or oscillatory PEP therapy (Flutter). This illustrates the role of patient preference, with oscillatory PEP therapy a well accepted and preferable technique to patients with bronchiectasis (Thompson 2002; Patterson 2005; Eaton 2007). The greater sputum weight immediately post treatment achieved with ELTGOL over oscillatory PEP therapy (Flutter) or minimal PEP highlight that the components of ELTGOL may be of greater advantage. In one study of ELTGOL, participants performed slow expirations with an open glottis from FRC to RV in a lateral decubitus positions while oscillatory PEP therapy was undertaken in a seated position also for 15 minutes (Guimaraes 2012). Herrero-Cortina 2015 applied ELTGOL and compared this to minimal PEP therapy, with each session lasting 40 minutes. However, with the difference in sputum weight in one study being only 0.23 g (Guimaraes 2012) and in the second 3.6 g (Herrero-Cortina 2015), the clinical significance of these findings is unclear. However, it should be noted that differing approaches to sputum expectoration were applied between these two studies. Prior to any intervention, a series of five minutes of voluntary coughing was administered to all participants to clear central airway secretions (Guimaraes 2012); this approach was not used in the study conducted by Herrero-Cortina 2015. Although clearance of central secretions prior to commencing ACTs may provide a more accurate estimate of the effectiveness of a specific ACT upon sputum expectoration and could avoid an overestimation of the impact of the technique, it is a challenge to directly image the airways and determine whether secretions are originating from peripheral or central airways. Further studies could employ similar methods to allow direct comparison of techniques. The lack of difference in sputum clearance over a 24 hour period between ELTGOL and minimal PEP therapy may be related to a slower action timing for minimal PEP therapy in sputum clearance, with only 28% of sputum cleared during the physiotherapy session compared to 42% for ELTGOL (Herrero-Cortina 2015). The amount of pressure applied in PEP therapy may also influence sputum expectoration. Minimal PEP generated pressure of 1 cmH2O rather than 10 to 25 cmH2O reached with PEP therapy or oscillatory PEP therapy (Falk 1984; Darbee 2004). This may be insufficient to promote airflow through collateral ventilation and allow an increased volume of air behind secretions which supports sputum movement towards the larger airways (Falk 1984; Van der Schans 1991). This degree of pressure may account for the contrasting findings between studies comparing AD and PEP therapy. Comparing AD and oscillatory PEP therapy, a similar sputum volume is achieved after four weeks of treatment (Semwal 2015), while a single session of minimal PEP therapy yielded less expectoration during a physiotherapy session (Herrero-Cortina 2015). Although exacerbations of bronchiectasis are characterised by an increase in sputum production, both oscillatory PEP therapy and GAD appear to be equally effective (Tsang 2003); this emphasises the value in considering patient preference for technique in this clinical state. A confounding factor is the difference between studies in the measurement of sputum expectoration, with five studies using wet weight/volume (Thompson 2002; Tsang 2003; Eaton 2007; Herrero-Cortina 2015; Semwal 2015), one study using dry weight (Guimaraes 2012), one using wet and dry weight (Antunes 2001) and one not stated (Patterson 2005). Wet volume may be influenced by an individual’s reluctance to expectorate, saliva contamination and the swallowing of secretions (Williams 1994). Contamination with saliva may be corrected by drying sputum and measuring dry weight (Boucher 2010), which may lend more support to studies which have applied this technique. Hydration levels will also influence sputum volume and has been identified as a mode of supporting airway clearance and sputum expectoration (Wilkinson 2014). In the absence of commentary about hydration levels in the studies included in this review, it is difficult to determine its contribution.

That oscillatory PEP therapy has similar effects after a single session of treatment on measures of spirometry as other techniques (ranging from ACBT with GAD, AD, and ELTGOL in clinically stable participants (Patterson 2005; Eaton 2007; Guimaraes 2012; Semwal 2015)) is not surprising. Single sessions of treatment offer little opportunity to make a substantial change in spirometry, even when experiencing an acute exacerbation. Similar effects were noted for minimal PEP therapy compared to ELTGOL or AD (Herrero-Cortina 2015). Even the use of four sessions of treatment or four weeks of treatment of either oscillatory PEP therapy or ACBT with GAD or GAD with chest clapping and compression suggested there was no greater advantage or detriment between techniques in measures of spirometry or peak expiratory flow rates (Antunes 2001; Thompson 2002; Alsiy 2012). The lack of advantage of oscillatory PEP therapy over GAD during an acute exacerbation upon spirometry measurements may be influenced by concurrent medical therapy administered as part of exacerbation management for all patients (Tsang 2003). For this reason, the opportunity to identify a difference between techniques on measures of FEV1, FVC is limited. The same degree of reduction in FRC, RV, and TLC with oscillatory PEP therapy as ELTGOL indicates that both types of ACTs reduce pulmonary hyperinflation (Guimaraes 2012), a feature of bronchiectasis (Koulouris 2003). The splinting effect of the oscillatory PEP therapy is believed to stabilise airways during expiration to avoid dynamic collapse and favour pulmonary deflation (Calverley 2005; Guimaraes 2012). This suggests that issues affecting patient compliance, such as preference for techniques, practical considerations, and cost are of greater importance and significance in selecting a technique. Similar findings were evident in a single session or up to three months of treatment with PEP therapy compared to other techniques in individuals with cystic fibrosis (McIlwaine 2015). Other measurements of lung function such as the lung clearance index, a measure of abnormal ventilation distribution, may provide more detailed information about the effects of specific ACTs on lung function (Horsley 2009). With ventilation heterogeneity a clini-
The physiological effects of bronchiectasis depend on the degree of disease severity, including the number of lobes affected, not specified in any study. Bronchiectasis severity can be determined by HRCT scan scoring (Bhalla 1991) or a combination of clinical signs and symptoms (Chalmers 2014). Knowledge of the severity of disease and the presence and degree of airway hyperresponsiveness does influence the selection of ACTs in cystic fibrosis (Volsko 2013); this may be equally important in bronchiectasis. The range of intervention durations between studies (from single sessions to four weeks) makes it difficult to generalise the findings to broader clinical practice, which reflects the long-term use of ACTs (Butler 2008; Lee 2008; O’Neill 2002), regardless of the chosen intervention. With a single study of PEP therapy during an acute exacerbation, further research is required to determine the impact of PEP therapy during this clinical state.

A key factor is the consideration of patient preference. Adherence to treatment is increasingly recognised as important in bronchiectasis (McCullough 2014), with poor adherence influencing the rate of acute exacerbations. Adherence to ACT is associated with a higher burden of treatment and worsening respiratory symptoms (McCullough 2014). In people with bronchiectasis, adherence decision-making involves patient evaluation of the advantages and disadvantages of adhering to treatment (McCullough 2014a). Five studies included in the current review reported a preference for PEP therapy compared to ACBT with or without GAD or AD (Thompson 2002; Tsang 2003; Patterson 2005; Eaton 2007; Semwal 2015); in view of similar effects on selected physiological outcomes, patient preference for a technique may be an important clinical consideration, particularly if this influences adherence rates in the longer term. In studies of individuals with cystic fibrosis (Elkins 2006; McIlwaine 2015) and in some studies in the current review (Tsang 2003; Eaton 2007), the independence, ease of use, and perception of effectiveness have been reported to be higher with PEP therapy. While no studies in the current review have considered participant adherence and its influence on clinical outcomes of PEP therapy over other techniques, these may be important outcomes in future research.

Quality of the evidence

The quality of the nine studies included in this review is mixed, with small sample sizes and often unclear or high risk of bias for blinding of participants and of outcome assessors. Differing intervention duration and different comparative airway clearance techniques limited meta-analysis. Little information on the primary outcomes of interest of quality of life, rate of acute exacerbations, and incidence of hospitalisations were available. While blinding of participants is difficult to achieve in cross-over trials, which was the design of seven out of nine included studies, inclusion of assessor blinding and therapist blinding were not consistently undertaken. The absence of an adequate washout period within studies, particularly for those which applied treatment techniques on the same or consecutive days, may have influenced the short-term outcomes.

Review outcomes were rated as low quality (all outcomes) using the GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) system. Imprecision was increased by the small number of included studies and participants, with one study contributing to each outcome.
Potential biases in the review process

This review was based on a published protocol (Lee 2015a). A broad search which incorporated handsearching of conference abstracts and trial registries was undertaken, with the inclusion of studies published only in the abstract form. Limited information was available from one paper (Altiay 2012), despite contacting the authors, with details only as reported in abstract form. Therefore, the ability to accurately assess the included data were limited. Two review authors independently extracted data and resolved disagreements via discussion. These two review authors independently rated the risk of bias.

Agreements and disagreements with other studies or reviews

The findings of this review are similar to a previously published review of the effects of oscillatory PEP therapy compared to other ACTs in individuals with stable bronchiectasis (Lee 2015). Oscillatory PEP therapy resulted in similar sputum expectoration as ACBT with GAD and, compared to other ACTs, had comparable impact on dynamic lung volumes, gas exchange, and breathlessness.

AUTHORS’ CONCLUSIONS

Implications for practice

There appears to be similar benefits and effects of PEP therapy (oscillatory and non-oscillatory) to other ACTs in terms of HRQOL, sputum expectoration, lung function, and impact on symptoms. PEP therapy was not superior to any other ACT in the short and long term. The quality of the evidence however, was low, and therefore, these findings should be interpreted with caution. Additional information is required to establish the clinical value of PEP therapy compared to other ACTs on exacerbation rates and incidence of hospitalisation, both outcomes which influence disease progression in bronchiectasis. The effect of PEP therapy during an acute exacerbation of bronchiectasis requires further clarification.

Implications for research

The longer term effect of PEP therapy compared to other ACTs in people with bronchiectasis has not been established and larger scale studies are required to fully evaluate the effects of this therapy on HRQOL, symptoms, hospitalisation rates, and exacerbation frequency. Future trials should ensure that outcome assessors are blinded to the intervention and, in the case of cross-over trials, an adequate washout period between interventions is applied.

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REFERENCES

References to studies included in this review

Altiay 2012  {published data only}

Antunes 2001  {published data only}

Eaton 2007  {published data only}

Guimaraes 2012  {published data only}
NCT01300403. Physiological effects of expiration with the glottis open in lateral posture (ELTGOL) and flutter valve in patients with bronchiectasis [Acute physiological effects of expiration with the glottis open in lateral posture (ELTGOL) and flutter valve in dynamic and static pulmonary volumes of patients with bronchiectasis]. clinicaltrials.gov/show/ NCT01300403 (first received 18 February 2011).
References to studies excluded from this review

Herrero-Cortina 2015 [published data only]


NCT01854788. Three airway clearance techniques in non cystic fibrosis bronchiectasis [A comparative study of three airway clearance techniques with different autonomy degrees in non cystic fibrosis bronchiectasis: randomized cross-over trial]. clinicaltrials.gov/show/NCT01854788 (first received 8 August 2012).


Patterson 2005 [published data only]

Semwal 2015 [published data only]

Thompson 2002 [published data only]


Tsang 2003 [published data only]

References to studies excluded from this review

Ambrosino 1995 [published data only]


Amit 2012 [published data only]

Andrejak 2013 [published data only]

Barbagallo 2012 [published data only]

Cecins 1999 [published data only]

Cegla 1993 [published data only]

Chakrovorty 2011 [published data only]

Conway 1992 [published data only]

Feng 1998 [published data only]

Figueroirodo 2012 [published data only]

Furumoto 2008 [published data only]
Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis (Review)

Landau 1973 [published data only]

Lavery 2011 [published data only]

Maa 2007 [published data only]

Mandal 2012 [published data only]

Marques 2012 [published data only]

Messens 1973 [published data only]

Morgan 1999 [published data only]


Murray 2009 [published data only]

Naraparaju 2010 [published data only]

NCT00452114 [published data only]
NCT00452114. In-exsufflator cough assist device in patients with symptomatic bronchiectasis [A randomized,
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controlled study evaluating the effectiveness of the inexsufflator cough assist device in patients with symptomatic bronchiectasis. clinicaltrials.gov/ct2/show/NCT00452114 (first received 22 March 2007).

Newall 2005 [published data only]

Nicolini 2013 [published data only]

Osadnik 2014 [published data only]
Osadnik C, Stuart-Andrew C, Ellis S, Thompson B, McDonald CF, Holland AE. Positive expiratory pressure via mask does not improve ventilation inhomogeneity more than huffing or coughing in individuals with stable chronic obstructive pulmonary disease and chronic sputum expectoration. Respiration 2014;87:38–44.

Patterson 2004 [published data only]

Patterson 2007 [published data only]

Pryor 1979 [published data only]

Punithavathi 2014 [published data only]

Richmond 2016 [published data only]

Santamaria 1998 [published data only]

Senthil 2015 [published data only]

Shabari 2011 [published data only]

Silva 2015 [published data only]

Su 2012 [published data only]

Sunderram 2000 [published data only]

Svenningsen 2014 [published data only]
NCT02282202. Evaluation of oscillatory positive expiratory pressure (oPEP) in bronchiectasis and COPD. clinicaltrials.gov/show/NCT02282202 (first received 24 October 2014).

Syed 2009 [published data only]

Tambascio 2011 [published data only]
Tambascio J, De Souza LT, Lisboa RM, Passarelli RDCV, Souza HCD, Gastaldi AC. The influence of flutter®VRP1 components on respiratory secretion transport of patients


**Tambascio 2014 [published data only]**
NCT01209546. Study of the effect of flutter VRP1 (PEP and oscillating high frequency) [Study of the effect of flutter VRP1 in patients with bronchiectasis]. clinicaltrials.gov/show/NCT01209546 (first received 12 June 2010).


**Valente 2004 [published data only]**

**Venturelli 2012 [published data only]**
NCT00700388. Efficacy of temporary positive expiratory pressure (TPEP) in chronic hypersecretion (UNIKO) [Multicentre controlled trial on efficacy of TPEP device in adult patients with chronic hypersecretion]. clinicaltrials.gov/show/NCT00700388 (first received 17 June 2008).


**Vishteh 2011 [published data only]**

References to studies awaiting assessment

**Fazzi 2010 [published data only]**

**NCT03013452 [published data only]**
NCT03013452. Oscillating PEP vs autogenic drainage in people with bronchiectasis (oPEP vs AD) [A randomised controlled trial of long term airway clearance with oscillating positive end expiratory pressure device versus autogenic drainage in people with bronchiectasis]. clinicaltrials.gov/show/NCT03013452 (first received 1 January 2017).

References to ongoing studies

**ACTRN12614001233617 [published data only]**
ACTRN12614001233617. Does the bubblepositive expiratory pressure (PEP) device improve secretion clearance compared to the active cycle of breathing technique (ACBT) or no intervention (control) in people with noncystic fibrosis bronchiectasis?. www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=367418&isReview=true (first received 12 November 2014).

**NCT01929356 [published data only]**

**NCT02324855 [published data only]**
NCT02324855. Long term airway clearance therapy in non cystic fibrosis bronchiectasis: a randomized controlled trial. clinicaltrials.gov/ct2/show/NCT02324855 (first received 1 December 2014).

**NCT02411981 [published data only]**
NCT02411981. Effect of chest physiotherapy (CPT) on lung clearance index (LCI) in non cystic fibrosis (CF) bronchiectasis [Short term effects of chest physiotherapy on ventilation inhomogeneity in non–CF bronchiectasis]. clinicaltrials.gov/ct2/show/NCT02411981 (first received 3 April 2015).

**NCT02509637 [published data only]**
NCT02509637. Acute effects of a flutter device and chest wall compression on respiratory system impedance in bronchiectasis patients. clinicaltrials.gov/NCT02509637 (first received 3 July 2015).

**NCT02906826 [published data only]**

Additional references

**Aliberti 2016**

**Altaus 2009**

**App 1998**

**Barker 2002**


**Bhalla 1991**


**Boucher 2010**


**Butler 2008**


**Calverley 2005**


**Campbell 1986**


**Chalmers 2014**


**Chang 2002**


**Chang 2008**


**Chang 2010**


**Chang 2015**


**Cole 1986**


**Cortese 2016**


**Darbee 2004**


**Deeks 2008**


**Dwyer 2011**


**Egger 1997**


**Elkins 2006**


**Falk 1984**


**Gaga 1998**


**Gallon 1992**

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Goeminne 2012  

Goeminne 2014  

Groth 1985  

Higgins 2011  

Horsley 2009  

Johnstone 2013  

Karadag 2005  

King 2006  

Koulouris 2003  

Kwak 2010  

Lapin 2002  

Lee 2008  

Lee 2013  

Martinez-Garcia 2005  

Martinez-Garcia 2007  

Martins 2012  

McCarron 2006  

McCullough 2014  

McCullough 2014a  

McIlwaine 2001  
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**Van Winden 1998**

**Volsko 2013**

**Warwick 1991**

**Weycker 2005**

**Wilkinson 2014**

**Williams 1994**

**References to other published versions of this review**

**Lee 2015a**

* Indicates the major publication for the study
## CHARACTERISTICS OF STUDIES

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

**Altiay 2012**

| Methods | Randomised cross-over trial  
Study setting: Turkey  
Study duration: 4 weeks |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Participants</td>
<td>36 adults (mean age not reported) with stable bronchiectasis</td>
</tr>
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</table>
| Interventions | Intervention 1: Active cycle of breathing technique, daily for 4 weeks  
Intervention 2: Oscillatory PEP therapy (Flutter), daily for 4 weeks |
| Outcomes | Symptoms of cough  
Borg dyspnoea score and Medical Research Council dyspnoea score  
Health-related quality of life: Short form-36  
Spirometry (FEV₁ and FVC) |
| Notes | Study available in abstract form only; no further information available from authors despite requests  
No study sponsor |

### Risk of bias

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<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
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<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Not specified</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
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</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>Unclear risk</td>
<td>Not specified</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Unclear risk</td>
<td>Not specified</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Unclear risk</td>
<td>Not specified</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Not specified</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Not specified</td>
</tr>
</tbody>
</table>
**Antunes 2001**

| Methods | Randomised cross-over trial  
Study setting: medical department, Brazil  
Study duration: 4 weeks (1 week per therapy) |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>13 adults (mean age 59 years) with stable bronchiectasis, diagnosis confirmed by clinical history and radiological findings (chest x-ray and HRCT, number of lobes affected, and severity not reported), mean FEV₁ 60% predicted</td>
</tr>
</tbody>
</table>
| Interventions | Intervention 1: two treatment sessions in one week of oscillatory PEP therapy (Flutter), performed in a seated position for 20 minutes, with coughing incorporated into the routine, followed by 30 minutes of rest  
Intervention 2: two treatment sessions in one week of conventional respiratory therapy, consisting of postural drainage with right and left lateral decubitus for 10 minutes on each side, with chest clapping and vibrocompression and coughing |
| Outcomes | Sputum volume (dry and wet weight) (g) during session  
Respiratory rate before and after treatment  
Expiratory flow rate (L/min) before and after treatment |
| Notes | No washout period between interventions  
Before control and intervention sessions, 10 minutes of inhalation bronchodilator therapy (ipratropium bromide and/or fenoterol) was administered  
No adverse events.  
No study sponsor |

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
| Random sequence generation (selection bias) | Unclear risk | Stated that participants are randomised, but mode of randomisation was unclear  
Quote “patients were randomly divided in two groups according to the technique…”  
Insufficient information was provided |
| Allocation concealment (selection bias) | Unclear risk | Comment: nothing is stated regarding concealment of allocation of participants to treatment order  
Insufficient information was provided |
| Blinding of participants and personnel (performance bias) All outcomes | Unclear risk | No information was provided  
Comment: Participants and therapist(s) were not likely to be blinded to group allocation. This may have influenced outcome measures of spirometry, respiratory rate, and sputum volume (dry weight) |
### Antunes 2001 (Continued)

<table>
<thead>
<tr>
<th></th>
<th>Risk</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No information was provided. Comment: Outcome assessor(s) were not likely to be blinded to group allocation. As outcomes were objectively measured (spirometry, sputum dry weight, respiratory rate), it is likely they were resistant to issues with blinding.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Quote: &quot;Thirteen patients took part in the study, 3 patients did not conclude the study...The results are from 10 patients that concluded the study&quot;. All data for participants who completed the study was provided.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Protocol was not available, but all specified outcomes were reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No washout period between interventions, which could have affected outcomes. Insufficient information provided.</td>
</tr>
</tbody>
</table>

### Eaton 2007

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Randomised cross-over trial. Study setting: physiotherapy department, New Zealand. Study duration: 3 days</td>
</tr>
<tr>
<td>Participants</td>
<td>36 adults (mean age 62 years) with stable bronchiectasis with chronic productive cough, diagnosis confirmed by HRCT (number of lobes affected and severity not reported), mean FEV\textsubscript{1} 57.8% predicted</td>
</tr>
<tr>
<td>Interventions</td>
<td>Intervention 1: one day of active cycle of breathing technique (ACBT), with thoracic expansion exercises, breathing control, and forced expiratory technique in seated position for maximum of 30 minutes. Intervention 2: one day of ACBT as previously described, performed in gravity-assisted drainage position for maximum of 30 minutes. Intervention 3: oscillatory PEP therapy (Flutter), no further details provided</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Sputum wet weight (g) and volume (mL), collected during treatment and 30 minutes post treatment, with total volume and weight also recorded. Borg dyspnoea score pre and post treatment. Spirometry (FEV\textsubscript{1}, FVC). Patient-reported tiredness, discomfort with technique (7-point Likert scale).</td>
</tr>
<tr>
<td>Notes</td>
<td>No washout period between interventions. No adverse events reported. No study sponsor.</td>
</tr>
<tr>
<td>Bias</td>
<td>Authors’ judgement</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
</tr>
</tbody>
</table>
| Blinding of participants and personnel (performance bias) | Unclear risk | No information was provided
Comment: Participants and therapist(s) were not likely to be blinded to group allocation. This may have influenced outcome measures of sputum volume and weight, dyspnoea, and participant-reported tiredness and discomfort |
| Blinding of outcome assessment (detection bias) | Unclear risk | No information was provided
Comment: Outcome assessor(s) were not likely to be blinded to group allocation. This was unlikely to affect objective measures of gas exchange or spirometry, but could affect sputum volume and weight, dyspnoea scores, and participant-reported tiredness and discomfort |
| Incomplete outcome data (attrition bias)       | Unclear risk       | Comment: All participants completed the study, but data were not available for all reported outcomes                                                                                   |
| Selective reporting (reporting bias)           | High risk          | No report of spirometry measures or gas exchange included in results. Outcomes for Borg dyspnoea summarised in text
All other measures outlined. No protocol was available.                                                   |
| Other bias                                     | Unclear risk       | No mention of washout period between interventions (consecutive days) and this may have influenced outcomes. Insufficient information provided |
### Guimaraes 2012

| Methods | Randomised cross-over trial  
Study setting: medical department, Brazil  
Study duration: 24 days |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>10 adults (mean age 56 years) with stable bronchiectasis, with a persistent productive cough, diagnosis confirmed by HRCT (number of lobes affected and severity not reported), mean FEV$_1$ 53% predicted</td>
</tr>
</tbody>
</table>
| Interventions | Intervention 1: single session of oscillatory PEP therapy (Flutter), performed in a seated position for 15 minutes (breathing from total lung capacity until cough occurred), followed by 5 minutes coughing  
Intervention 2: single session of L-expiration Lente Totale Glotte Ouverte en Decubitus Lateral, with affected lung in the dependent position and the participant performing slow expirations with the glottis open from functional residual capacity to residual volume |
| Outcomes | Sputum dry weight (g)  
Spirometry (FEV$_1$, FVC, FEV$_1$/FVC, FEF$_{25-75%}$)  
Static lung volumes (IC, VC, TLC, FRC, RV, RV/TLC, IC/TLC)  
All measurements were recorded immediately following completion of the intervention |
| Notes | 1 week washout period between interventions  
Salbutamol and a series of 5 minutes of voluntary coughing were administered prior to commencing interventions  
No adverse events  
No study sponsor |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Quote: “Patients were submitted to the two interventions in a random order. Block randomisation sequences were created by a researcher not involved with recruitment, selection and assessments”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Quote: “Sealed opaque envelopes containing patients’ assignments were opened at the time of first treatment”</td>
</tr>
</tbody>
</table>
| Blinding of participants and personnel (performance bias)  
All outcomes | Unclear risk | No information was provided. Comment: Participants and treating therapist(s) were not likely to be blinded to group allocation. This may have influenced outcome measures (spirometry, static lung volumes, and sputum dry weight) |
Guimaraes 2012  (Continued)

| Blinding of outcome assessment (detection bias) | Unclear risk | No information was provided
| All outcomes | Comment: Outcome assessor(s) were not likely to be blinded to group allocation. As outcomes were objectively measured (spirometry, static lung volumes, and sputum dry weight), it is likely they were resistant to issues with blinding |

| Incomplete outcome data (attrition bias) | Low risk | Quote: “All individuals tolerated and completed the steps in this study” Complete data were available for reported outcomes |
| All outcomes | |

| Selective reporting (reporting bias) | Low risk | Protocol was available and all specified outcomes were reported |

| Other bias | Low risk | Adequate washout period was included. Quote: “Measurement of static lung volumes were conducted before the spirometry to avoid any residual effect of dynamic compression of the airways in the plethysmography results” Comment: Attempts were made to minimise the impact of multiple measures of lung function |

Herrero-Cortina 2015

| Methods | Randomised cross-over trial |
| Study setting: tertiary hospital, Spain |
| Study duration: one session per treatment, applied on non-consecutive days |

| Participants | 31 adults (mean age 60 years) with stable bronchiectasis for previous 6 weeks, with mean daily sputum production > 15 ml, diagnosis confirmed by HRCT (number of lobes affected and severity not reported), mean FEV1 63% predicted |

| Interventions | Intervention 1: single session of autogenic drainage, with breathing from lower lung volumes in the expiratory reserve volume through to higher lung volumes into the inspiratory reserve volume with an open glottis. Pauses were permitted between manoeuvres as necessary with spontaneous coughing. Total session time of 40 minutes, performed at same time of day |
| Intervention 2: single session of L-expiration Lente Totale Glotte Ouverte en Decubitus Lateral, with the participant performing slow expirations with the glottis open from functional residual capacity to end expiratory reserve volume in both lateral positions. Pauses were permitted between manoeuvres as necessary with spontaneous coughing. Total session time of 40 minutes, performed at same time of day |
| Intervention 3: single session of minimal PEP therapy, generating a pressure of 1 cmH₂O during breathing manoeuvres. Position used during this treatment was not stated. Pauses |
were permitted between manoeuvres as necessary with spontaneous coughing. Total session time of 40 minutes, performed at same time of day

| Outcomes                  | Sputum wet weight (g) during treatment and over 24 hours following treatment  
|                          | Spirometry (FEV\(_1\), FVC, FEF\(_{25-75\%}\))  
|                          | Cough-related quality of life (Leicester Cough Questionnaire)  
|                          | Measurements for spirometry and cough-related quality of life were recorded immediately following intervention completion

| Notes                     | 1 week washout period between interventions  
|                          | No study sponsor

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Quote: “Block randomisation was computer generated by an independent investigator”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Quote: “The allocation was concealed”</td>
</tr>
<tr>
<td>Comment: Although details of the allocation concealment method were not given, this was considered sufficient for low risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Quote: “The same physiotherapist supervised/assisted each session to ensure treatment standardisation. Due to the nature of the intervention, neither participants nor physiotherapist were blinded to the intervention”</td>
</tr>
</tbody>
</table>
| Blinding of outcome assessment (detection bias) All outcomes | Unclear risk        | No information was provided  
| Comment: Outcome assessor(s) were not likely to be blinded to group allocation. As some outcomes were objectively measured (spirometry, sputum wet weight), it is likely they were resistant to issues with blinding |
| Incomplete outcome data (attrition bias) All outcomes | Low risk           | Quote: “Two patients dropped out of the study due to acute low back pain and pulmonary exacerbation”  
| Comment: data were available for all participants who completed the study |
| Selective reporting (reporting bias)    | Low risk           | Protocol was available and all specified outcomes were reported                         |
### Herrero-Cortina 2015 (Continued)

**Other bias** | Low risk  
---|---  

*Quote:* “There were no statistical differences in the total LCQ score and lung function between baseline of Session 1 and the end of the two washout periods, indicating no carryover effect.”  
*Comment:* the washout period between interventions appeared to be adequate

### Patterson 2005

**Methods**  
Randomised cross-over trial  
Study setting: respiratory clinic, Northern Ireland  
Study duration: 2 days

**Participants**  
20 adults (mean age 58 years) with stable bronchiectasis, productive of 1/2 egg cup of sputum per day, diagnosis confirmed by HRCT (number of lobes affected and severity not reported), mean FEV₁ 64% predicted

**Interventions**  
Intervention 1: Active cycle of breathing technique (ACBT) with thoracic expansion exercises, breathing control and forced expiration in two predetermined gravity-assisted drainage (GAD) positions with percussion and/or vibration. Treatment duration was either a maximum of 30 minutes (15 minutes per position), participant no longer expectorating sputum or participant was too fatigued to continue treatment  
Intervention 2: Oscillatory PEP therapy (Acapella) completed in two predetermined GAD positions. Treatment consisted of breathing control, 10 breaths through the Acapella, inhaling to 3/4 maximum breathing capacity, 2 to 3 second breath hold, active exhalation to functional residual capacity and cough or forced expiration in set cycle

**Outcomes**  
Spirometry (FEV₁, FVC, PEF) pre and post treatment (10 minutes after completion)  
15-count breathlessness score pre and post treatment (10 minutes after completion)  
Sputum weight (g) during treatment and 30 minutes post treatment

**Notes**  
Prior to intervention, 1 day of 40 minutes training session was completed, to determine appropriate GAD position by auscultation, selection of correct Acapella device (green for participants able to sustain expiratory flow > 15 L/min for at least 3 seconds, blue for participants with an expiratory flow < 15 L/min), determination of the correct Acapella settings and training in ACBT and Acapella  
Each intervention was performed at the same time on 2 consecutive days. Short and/or long acting bronchodilators and steroids where applicable were administered 1 hour prior to treatment  
No washout period between interventions  
No study sponsor

## Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>

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**Patterson 2005**  (Continued)

<table>
<thead>
<tr>
<th>Random sequence generation (selection bias)</th>
<th>Low risk</th>
<th>Quote: “Treatment order was determined by a concealed computerised randomisation procedure”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Quote: “Treatment order was determined by a concealed computerised randomisation procedure”</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Quote: “The same physiotherapist administered all treatment sessions. Comment: It is likely that neither participants or treating therapist(s) were blinded to the intervention”</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Quote: ”an independent assessor conducted pre and post treatment...measures of spirometric lung function, pulse oximetry and 15-count breathlessness score. It is not clear if the independent assessor was blinded to treatment order. It is likely that some outcome measures were resistant to issues with blinding (spirometry, SpO2), but other measures (dyspnoea score) may not have been resistant”</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>Quote: “All twenty patients...completed the study” Not all outcomes were provided</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Outcome related to breathlessness score was not provided. All other outcomes were provided</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Comment: treatments were performed on consecutive days, which allowed for no washout period</td>
</tr>
</tbody>
</table>

**Semwal 2015**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised cross-over trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study setting: respiratory or medicine clinic, India</td>
<td></td>
</tr>
<tr>
<td>Study duration: 1 day</td>
<td></td>
</tr>
</tbody>
</table>

| Participants | 30 adults (mean age of males 46 years, mean age of females 49 years) with stable bronchiectasis, with history of productive cough, diagnosis not confirmed by HRCT, mean FEV1 not reported |
### Interventions

**Intervention 1:** Autogenic drainage. Participant seated and instructed to breathe at different lung volumes starting from low lung volumes, with a series of 10 to 20 breaths at low volumes until secretions were audible on auscultation. Participants then instructed to breathe at tidal volumes for a further 10 to 12 breaths, then breathe at vital capacity followed by cough. Treatment duration was 20 to 30 minutes.

**Intervention 2:** Oscillatory PEP therapy (Acapella) completed in unspecified position. Treatment consisted of 10 to 12 breaths through the Acapella, with a 2 to 3 second breath hold and exhalation. Cough or huff was performed every 10 breaths. Treatment duration was 20 to 30 minutes depending on participant requirements.

### Outcomes

- PEF, immediately post and 10 minutes after treatment
- Borg score for breathlessness, immediately post and 10 minutes after treatment
- Sputum wet weight (g), immediately post and 10 minutes after treatment

### Notes

- Washout period of 3 hours between techniques
- No study sponsor

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Comment: Title of paper indicated randomised cross-over trial. No information provided on nature of randomisation process</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Quote: “The patients were recruited for either the chest physiotherapy technique Acapella or Autogenic Drainage via concealed envelope method” Comment: While limited detail was provided, the use of concealed envelopes indicated a low risk of bias</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>No information was provided Comment: Participants and treating therapist(s) were not likely to be blinded to group allocation. This may have influenced outcome measures (spirometry, breathlessness, SpO\textsubscript{2}, and sputum wet weight).</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No information was provided Comment: Outcome assessor(s) were not likely to be blinded to group allocation. As outcomes were objectively measured (spirometry, breathlessness, SpO\textsubscript{2}, and sputum wet weight), it is likely they were resistant to issues with blinding</td>
</tr>
</tbody>
</table>
### Semwal 2015 (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Quote: “The total of thirty completed the study”. Comment: Data were available for all 30 participants for each arm of the study</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Although no protocol was available, all outcomes were reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Comment: Treatments were performed within three hours of each other, which was a limited washout period for this type of intervention</td>
</tr>
</tbody>
</table>

### Thompson 2002

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised cross-over trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study setting</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Study duration</td>
<td>8 weeks</td>
</tr>
</tbody>
</table>

| Participants                 | 22 adults (median age ranging from 59 to 68 years), with stable bronchiectasis and diagnosis confirmed by HRCT (number of lobes affected and severity not reported), with median FEV\textsubscript{1} ranging from 0.67 to 0.70 L |

| Interventions                | Intervention 1: Active cycle of breathing technique (ACBT) in a gravity-assisted drainage (GAD) positioning, performed twice daily at home until no further sputum was expectorated. GAD was used as necessary throughout |
|------------------------------| Intervention 2: Oscillatory PEP therapy (Flutter), with the device tilted until maximum vibrations were felt within the chest to loosen the secretions with forced expiratory technique, performed twice daily at home until no further sputum was expectorated |

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Sputum weight (g) daily</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Spirometry (PEFR, FEV\textsubscript{1}, FVC) pre and post intervention</td>
</tr>
<tr>
<td></td>
<td>Dyspnoea score (Borg scale) pre and post intervention</td>
</tr>
<tr>
<td></td>
<td>Health-related quality of life (Chronic Respiratory Questionnaire) at baseline and post 4 weeks intervention</td>
</tr>
</tbody>
</table>

| Notes                        | Report of nausea in one participant when using the Flutter, no other adverse events reported |
|------------------------------| No report of washout period between interventions |
|                              | Study sponsor: Frenchay Respiratory Research Fund |

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
| Random sequence generation (selection bias) | Unclear risk       | Quote: “ACBT and the Flutter were each used unassisted at home for 4 weeks in a
<table>
<thead>
<tr>
<th><strong>Thompson 2002 (Continued)</strong></th>
<th><strong>Comment:</strong> nothing was stated beyond the fact that the study was randomised</th>
<th><strong>Insufficient information provided</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allocation concealment (selection bias)</strong></td>
<td><strong>Unclear risk</strong></td>
<td><strong>Comment:</strong> Nothing was stated regarding concealment of assignment of participants to treatment order. <strong>Insufficient information provided</strong></td>
</tr>
<tr>
<td><strong>Blinding of participants and personnel (performance bias)</strong></td>
<td><strong>Unclear risk</strong></td>
<td><strong>Quote:</strong> “Before the ACBT arm each patient had a refresher session with the physiotherapist”, “Before the Flutter arm they were instructed to tilt the device until maximum vibrations were felt within the chest”. <strong>Comment:</strong> It was likely that neither participants or treating therapist(s) were blinded to the intervention, which may have affected outcome measures of (spirometry, sputum weight, dyspnoea and HRQOL scores)</td>
</tr>
<tr>
<td><strong>All outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blinding of outcome assessment (detection bias)</strong></td>
<td><strong>Unclear risk</strong></td>
<td><strong>Quote:</strong> “Patients recorded the daily weight of sputum produced, PEFR and breathlessness scores”** Comment:** As participants were unlikely to be blinded to the intervention and were collecting some outcome measures, this may have affected these outcomes measures. It was not stated that personnel were blinded to other outcomes of spirometry and HRQOL scores, which may have affected these outcome measures.</td>
</tr>
<tr>
<td><strong>All outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Incomplete outcome data (attrition bias)</strong></td>
<td><strong>High risk</strong></td>
<td><strong>Quote:</strong> “Five of the 22 patients recruited to the study were withdrawn”. <strong>Complete data were available for reported outcomes</strong></td>
</tr>
<tr>
<td><strong>All outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Selective reporting (reporting bias)</strong></td>
<td><strong>Low risk</strong></td>
<td><strong>Although no protocol was available, all specified outcomes were reported</strong></td>
</tr>
<tr>
<td><strong>Other bias</strong></td>
<td><strong>Unclear risk</strong></td>
<td><strong>No washout period between intervention, which may have had impact on findings. Insufficient information provided</strong></td>
</tr>
</tbody>
</table>
**Methods**

Randomised controlled trial  
Study setting: Hong Kong  
Study duration: from day 2 of admission until day of discharge (mean ranging from 6.2 to 7.2 days)

**Participants**

15 adults (mean age ranging from 67 to 74 years), with acute exacerbation of bronchiectasis (presenting with symptoms of persistent cough and sputum production), diagnosis of bronchiectasis stated only as being of at least 1 year in duration, mean FEV\(_1\) ranging from 36.1 to 48.5% predicted

**Interventions**

Intervention 1: two gravity-assisted drainage (GAD) positions, with position choice based on chest radiographs and auscultation. Breathing control every 3 minutes consisting of 5 slow, deep inspiratory breaths followed by relaxed expiration and a voluntary cough and normal relaxed breathing, repeated for 15 minutes  
Intervention 2: Oscillatory PEP therapy (Flutter) in a seated position. Angle of inclination set for maximal resonance of the chest wall. Cycle consisted of every 3 minutes, 5 deep breaths, expired through the Flutter, followed by a voluntary cough and breathing control, repeated for 15 minutes  
Each intervention was to be completed 3 times daily (one supervised, two unsupervised), with coughing as necessary to expectorate sputum

**Outcomes**

Spirometry (FEV\(_1\), FVC, PEFR) pre and post intervention on days 2, 4, and day of discharge  
Sputum wet weight (g) during 15 minutes intervention, 15 minutes post intervention and at 24 hours post intervention on days 2, 4 and day of discharge

**Notes**

No reports of adverse events  
No study sponsor

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
| Random sequence generation (selection bias)      | Unclear risk        | Quote: “patients recruited were randomised into...groups by drawing lots”  
Comment: nothing was stated beyond use of this method, it was not clear if this was sufficiently robust  
Insufficient information provided |
| Allocation concealment (selection bias)          | Unclear risk        | Comment: Nothing was stated regarding concealment of assignment of participants  
Insufficient information provided |
| Blinding of participants and personnel (performance bias) All outcomes | High risk | Quote: “All protocols were carried out once per day, under the supervision of the same physiotherapist”  
Comment: This suggested that treating therapist(s) was not blinded to group |
**Tsang 2003 (Continued)**

<table>
<thead>
<tr>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Unclear risk</th>
<th>No information was provided. Comment: Outcome assessor(s) were not likely to be blinded to group allocation. As outcomes were objectively measured (spirometry, static lung volumes, and sputum dry weight), it is likely they were resistant to issues with blinding.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Data were provided for all participants. Complete data were available for most outcomes.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Although no protocol was available, all specified outcomes were reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No evidence of other bias</td>
</tr>
</tbody>
</table>

ACBT - active cycle of breathing technique; cmH2o - centimetres of water pressure; FEV1 - forced expiratory volume in one second; FEF25−75% - forced expiratory ratio in 25-75% of expiration; FVC - forced vital capacity; FRC - functional residual capacity; g - grams; GAD - gravity-assisted drainage; HRCT - high resolution computed tomography; IC - inspiratory capacity; IC/TLC - ratio of inspiratory capacity over total lung capacity; L - litres; LCQ - Leicester Cough Questionnaire; L/min - litres per minute; mL - millilitres; PEP - positive expiratory pressure; PEF - peak expiratory flow; PEFR - peak expiratory flow rate; RV - residual volume; RV/TLC - ratio of residual volume over total lung capacity; SpO2 - percutaneous oxygen saturation; TLC - total lung capacity; VC - vital capacity.

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambrosino 1995</td>
<td>Mixed disease sample, data for bronchiectasis not available (via correspondence with study author)</td>
</tr>
<tr>
<td>Amit 2012</td>
<td>Two types of PEP therapy compared</td>
</tr>
<tr>
<td>Andrejak 2013</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Barbagallo 2012</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Cecins 1999</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Study</td>
<td>Description</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Cegla 1993</td>
<td>Mixed disease sample, data for bronchiectasis not available (via correspondence with study authors)</td>
</tr>
<tr>
<td>Chakrovorty 2011</td>
<td>No inclusion of individuals with bronchiectasis</td>
</tr>
<tr>
<td>Conway 1992</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Feng 1998</td>
<td>No comparison group</td>
</tr>
<tr>
<td>Figueiredo 2012</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Furumoto 2008</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Gastaldi 2011</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Goldemir 2013</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Goldman 2004</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Jao 2010</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Kaminska 1988</td>
<td>Not randomised</td>
</tr>
<tr>
<td>Kubal 2013</td>
<td>Not randomised</td>
</tr>
<tr>
<td>Kurz 1997</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Landau 1973</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Lavery 2011</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Maa 2007</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Mandal 2012</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Marques 2012</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Messens 1973</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Morgan 1999</td>
<td>Mixed disease group with data for individuals with bronchiectasis unable to be extracted</td>
</tr>
<tr>
<td>Murray 2009</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Naraparaju 2010</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>NCT00452114</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Newall 2005</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Study (Year)</td>
<td>Details</td>
</tr>
<tr>
<td>-------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Nicolini 2013</td>
<td>Data for PEP group (from mix of airway clearance techniques) not able to be extracted</td>
</tr>
<tr>
<td>Osadnik 2014</td>
<td>No inclusion of individuals with bronchiectasis</td>
</tr>
<tr>
<td>Patterson 2004</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Patterson 2007</td>
<td>Data for usual airway clearance group (mix of techniques) not able to be individually extracted per technique</td>
</tr>
<tr>
<td>Pryor 1979</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Punithavathi 2014</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Richmond 2016</td>
<td>No comparison group</td>
</tr>
<tr>
<td>Santamaria 1998</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Senthil 2015</td>
<td>PEP therapy combined with another technique</td>
</tr>
<tr>
<td>Shabari 2011</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Silva 2015</td>
<td>Comparison of two types of oscillatory PEP therapy</td>
</tr>
<tr>
<td>Su 2012</td>
<td>Positive pressure therapy not meeting the definition applied in this review</td>
</tr>
<tr>
<td>Sunderram 2000</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Svenningsen 2014</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Syed 2009</td>
<td>No PEP therapy included</td>
</tr>
<tr>
<td>Tambascio 2011</td>
<td>Comparison of Oscillatory PEP therapy and PEP therapy</td>
</tr>
<tr>
<td>Tambascio 2014</td>
<td>No use of PEP therapy</td>
</tr>
<tr>
<td>Valente 2004</td>
<td>No comparison group (non-PEP ACT)</td>
</tr>
<tr>
<td>Venturelli 2012</td>
<td>Mixed disease sample, data for bronchiectasis not available (via correspondence with study author)</td>
</tr>
<tr>
<td>Vishteh 2011</td>
<td>Not randomised</td>
</tr>
</tbody>
</table>
### Characteristics of studies awaiting assessment [ordered by study ID]

**Fazzi 2010**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised cross-over trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>20 participants with stable bronchiectasis</td>
</tr>
<tr>
<td>Interventions</td>
<td>T-PEP (1 cmH(_2)O) vs PEP therapy (mask) (20 cmH(_2)O)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Distribution of ventilation (radioaerosol measurements)</td>
</tr>
<tr>
<td>Notes</td>
<td>Identified in 2015 search. Further information required to confirm appropriateness</td>
</tr>
</tbody>
</table>

**NCT03013452**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Individuals with bronchiectasis (confirmed by HRCT, sputum production most days of the year, stable chronic therapy in the last 4 weeks, FEV(_1) = 70% predicted, aged 18 to 80 years)</td>
</tr>
<tr>
<td>Interventions</td>
<td>Autogenic drainage daily for 15 minutes each day, for 1 month vs Aerobika oPEP device daily for 15 minutes each day for 1 month</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Lung clearance index, Total score on Quality of Life - Bronchiectasis, Score on respiratory domain on Quality of Life - Bronchiectasis, FEV(_1), FVC</td>
</tr>
<tr>
<td>Notes</td>
<td>Identified in 2017 search. Further information required to confirm appropriateness</td>
</tr>
</tbody>
</table>

### Characteristics of ongoing studies [ordered by study ID]

**ACTRN12614001233617**

<table>
<thead>
<tr>
<th>Trial name or title</th>
<th>Does the bubble-positive expiratory pressure (PEP) device improve secretion clearance compared to the active cycle of breathing technique (ACBT) or no intervention (control) in people with non-cystic fibrosis bronchiectasis?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>Participants</td>
<td>Diagnosis of bronchiectasis confirmed by HRCT, daily sputum production, ability to perform airway clearance technique</td>
</tr>
<tr>
<td>Interventions</td>
<td>Bubble-positive expiratory pressure (PEP) device (10-20 cm H(_2)O) vs Active cycle of breathing technique (ACBT)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Sputum weight, acceptability and perceived benefit of Bubble PEP therapy</td>
</tr>
<tr>
<td>Starting date</td>
<td>05/01/2015</td>
</tr>
</tbody>
</table>
ACTRN12614001233617  (Continued)

Contact information  mary.santos@sesiabs.health.nsw.gov.au
Notes  Identified in 2015 search. Further information required to confirm appropriateness

NCT01929356

Trial name or title  Chest Physiotherapy and Lung Function in Primary Ciliary Dyskinesia
Methods
Participants  Diagnosis of primary ciliary dyskinesia, aged 6-60 years
Interventions  Chest physiotherapy with PEP (positive expiratory pressure) device
Outcomes  FEV1, Lung clearance index, multiple breath washout
Starting date  October 2013
Notes  Identified in 2015 search. Further information required to confirm appropriateness

NCT02324855

Trial name or title  Long-term Airway Clearance Therapy in Non-cystic Fibrosis Bronchiectasis
Methods
Participants  Chronic sputum production, two confirmed exacerbations in previous year, ability to understand and perform airway clearance therapy, clinically stable
Interventions  Usual medical care vs usual medical care and oscillatory PEP therapy
Outcomes  Leicester cough questionnaire, Quality of life - Bronchiectasis, exacerbation frequency, lung function, exercise capacity, inflammatory markers
Starting date  October 2015
Notes  Identified in 2015 search. Further information required to confirm appropriateness
### NCT02411981

**Trial name or title**
Effects of Chest Physiotherapy (CPT) on Lung Clearance Index (LCI) in Non Cystic Fibrosis (CF) Bronchiectasis

**Methods**

**Participants**
Diagnosis of non-cystic fibrosis bronchiectasis, clinically stable

**Interventions**
Autogenic drainage

**Outcomes**
Lung clearance index, FEV\(_1\), FEV\(_{25-75}\)\%, sputum weight

**Starting date**
April 2013

**Contact information**

**Notes**
Identified in 2015 search. Further information required to confirm appropriateness

### NCT02509637

**Trial name or title**
Acute Effects of a Flutter Device and Chest Wall Compression on Respiratory System Impedance in Bronchiectasis Patients

**Methods**
Randomised controlled trial

**Participants**
Diagnosis of bronchiectasis (by HRCT and confirmed clinically), aged 30 to 80 years

**Interventions**
Oscillatory PEP therapy (Flutter) vs Chest compression intervention

**Outcomes**
Respiratory system impedance, difficulty in expectorating sputum, dry and wet weight of sputum, oxygen saturation, dyspnoea, acceptability and tolerance, adhesiveness of expectorated sputum

**Starting date**
August 2015

**Contact information**

**Notes**
Identified in 2016 search. Further information required to confirm appropriateness

### NCT02906826

**Trial name or title**
Adherence to Airway Clearance. Novel Approaches to Improving Adherence

**Methods**

**Participants**
Diagnosis of bronchiectasis, confirmed by HRCT or chest radiograph, aged 6 to 12 years, previous use of PEP therapy, clinically stable, willingness to adhere to treatment

**Interventions**
No monitoring of adherence vs monitoring of adherence of use of PEP therapy
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Rate of adherence to prescribed therapy, FEV₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting date</td>
<td>August 2016</td>
</tr>
<tr>
<td>Contact information</td>
<td><a href="mailto:mmcilwaine@cw.bc.ca">mmcilwaine@cw.bc.ca</a></td>
</tr>
<tr>
<td>Notes</td>
<td>Identified in 2017 search. Further information required to confirm appropriateness</td>
</tr>
</tbody>
</table>
## DATA AND ANALYSES

### Comparison 1. Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks)

<table>
<thead>
<tr>
<th>Outcome or subgroup 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>1 CRQ Dyspnoea score</td>
<td>1</td>
<td></td>
<td>Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>2 CRQ Fatigue score</td>
<td>1</td>
<td></td>
<td>Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>3 CRQ Mastery score</td>
<td>1</td>
<td></td>
<td>Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>4 CRQ Emotional function score</td>
<td>1</td>
<td></td>
<td>Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>5 CRQ Total score</td>
<td>1</td>
<td></td>
<td>Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>

### Comparison 2. Oscillatory PEP therapy vs ACBT with GAD (single session)

<table>
<thead>
<tr>
<th>Outcome or subgroup 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>1 Sputum weight (g)</td>
<td>2</td>
<td></td>
<td>Std. Mean Difference (Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>2 Sputum volume (ml)</td>
<td>1</td>
<td></td>
<td>Std. Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>3 Fatigue</td>
<td>1</td>
<td></td>
<td>Std. Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>4 Discomfort</td>
<td>1</td>
<td></td>
<td>Std. Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>

### Comparison 3. Oscillatory PEP therapy vs ACBT (single session)

<table>
<thead>
<tr>
<th>Outcome or subgroup 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>1 Sputum weight (g)</td>
<td>1</td>
<td></td>
<td>Std. Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>2 Sputum volume (ml)</td>
<td>1</td>
<td></td>
<td>Std. Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>3 Fatigue</td>
<td>1</td>
<td></td>
<td>Std. Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>4 Discomfort</td>
<td>1</td>
<td></td>
<td>Std. Mean Difference (Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>
### Comparison 4. Oscillatory PEP vs GAD during acute exacerbation

<table>
<thead>
<tr>
<th>Outcome or subgroup 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>1 Sputum weight (over 24 hours) Day 2 of admission</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>2 Sputum weight (over 24 hours) Day 4 of admission</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>3 Sputum weight (over 24 hours) Day of Discharge</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>4 FEV1 (Day 2 of admission)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>5 FEV1 (Day 4 of admission)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>6 FEV1 (Day of Discharge)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>7 FVC (Day 2 of admission)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>8 FVC (Day 4 of admission)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>9 FVC (Day of Discharge)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>10 PEFR (Day 2 of admission)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>11 PEFR (Day 4 of admission)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>12 PEFR (Day of Discharge)</td>
<td>1</td>
<td></td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>Totals not selected</td>
</tr>
</tbody>
</table>

---

### Analysis 1.1. Comparison 1 Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks), Outcome 1 CRQ Dyspnoea score.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 1 Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks)

Outcome: 1 CRQ Dyspnoea score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Mean Difference (SE)</th>
<th>Mean Difference (IV, Fixed, 95% CI)</th>
<th>Mean Difference (IV, Fixed, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thompson 2002</td>
<td>0.01 (0.25)</td>
<td>0.01 [-0.48, 0.50]</td>
<td>0.01 [-0.48, 0.50]</td>
</tr>
</tbody>
</table>

-1 -0.5 0 0.5 1

Favours Oscillatory PEP  Favours ACBT with GAD

---

Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis (Review)  
Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
### Analysis 1.2. Comparison 1: Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks), Outcome 2: CRQ Fatigue score.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 1 Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks)

Outcome: 2 CRQ Fatigue score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Mean Difference (SE)</th>
<th>Mean Difference (IV, Fixed 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thompson 2002</td>
<td>-0.19 (0.3214)</td>
<td>-0.19 [-0.82, 0.44]</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP vs ACBT with GAD

### Analysis 1.3. Comparison 1: Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks), Outcome 3: CRQ Mastery score.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 1 Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks)

Outcome: 3 CRQ Mastery score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Mean Difference (SE)</th>
<th>Mean Difference (IV, Fixed 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thompson 2002</td>
<td>-0.1 (0.2806)</td>
<td>-0.10 [-0.65, 0.45]</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP vs ACBT with GAD
### Analysis 1.4. Comparison 1 Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks), Outcome 4 CRQ Emotional function score.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 1 Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks)

Outcome: 4 CRQ Emotional function score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Mean Difference (SE)</th>
<th>Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thompson 2002</td>
<td>-0.06 (0.2908)</td>
<td>-0.06 [-0.63, 0.51]</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

Favours ACBT with GAD

### Analysis 1.5. Comparison 1 Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks), Outcome 5 CRQ Total score.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 1 Oscillatory PEP therapy (Flutter) vs ACBT with GAD (4 weeks)

Outcome: 5 CRQ Total score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Mean Difference (SE)</th>
<th>Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thompson 2002</td>
<td>-0.09 (0.1429)</td>
<td>-0.09 [-0.37, 0.19]</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

Favours ACBT with GAD
### Analysis 2.1.  Comparison 2 Oscillatory PEP therapy vs ACBT with GAD (single session), Outcome 1 Sputum weight (g).

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 2 Oscillatory PEP therapy vs ACBT with GAD (single session)

Outcome: 1 Sputum weight (g)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Std. Mean Difference (SE)</th>
<th>IV(Random,95% CI)</th>
<th>Std. Mean Difference</th>
<th>IV(Random,95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaton 2007</td>
<td>5.6 (1.37)</td>
<td>5.60 [2.91, 8.29]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patterson 2005</td>
<td>0.54 (0.47)</td>
<td>0.54 [-0.38, 1.46]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP Favours ACBT and GAD

### Analysis 2.2.  Comparison 2 Oscillatory PEP therapy vs ACBT with GAD (single session), Outcome 2 Sputum volume (ml).

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 2 Oscillatory PEP therapy vs ACBT with GAD (single session)

Outcome: 2 Sputum volume (ml)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental N</th>
<th>Control N</th>
<th>Std. Mean Difference (SE)</th>
<th>IV(Fixed,95% CI)</th>
<th>Std. Mean Difference</th>
<th>IV(Fixed,95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaton 2007</td>
<td>36</td>
<td>0</td>
<td>5.1 (1.46)</td>
<td>5.10 [2.24, 7.96]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP Favours ACBT and GAD
### Analysis 2.3. Comparison 2 Oscillatory PEP therapy vs ACBT with GAD (single session), Outcome 3 Fatigue.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 2 Oscillatory PEP therapy vs ACBT with GAD (single session)

Outcome: 3 Fatigue

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Std. Mean Difference (SE)</th>
<th>Std. Mean Difference</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaton 2007</td>
<td>0.3 (0.33)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

Favours ACBT and GAD

### Analysis 2.4. Comparison 2 Oscillatory PEP therapy vs ACBT with GAD (single session), Outcome 4 Discomfort.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 2 Oscillatory PEP therapy vs ACBT with GAD (single session)

Outcome: 4 Discomfort

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Std. Mean Difference (SE)</th>
<th>Std. Mean Difference</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaton 2007</td>
<td>-0.3 (0.267)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

Favours ACBT and GAD
### Analysis 3.1. Comparison 3 Oscillatory PEP therapy vs ACBT (single session), Outcome 1 Sputum weight (g).

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 3 Oscillatory PEP therapy vs ACBT (single session)

Outcome: 1 Sputum weight (g)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Std. Mean Difference (SE)</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaton 2007</td>
<td>-0.3 (0.57)</td>
<td>[-1.42, 0.82]</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

### Analysis 3.2. Comparison 3 Oscillatory PEP therapy vs ACBT (single session), Outcome 2 Sputum volume (ml).

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 3 Oscillatory PEP therapy vs ACBT (single session)

Outcome: 2 Sputum volume (ml)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Std. Mean Difference (SE)</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaton 2007</td>
<td>-0.6 (0.65)</td>
<td>[-1.87, 0.67]</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

---

Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis (Review)

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### Analysis 3.3.  Comparison 3 Oscillatory PEP therapy vs ACBT (single session), Outcome 3 Fatigue.

**Review:** Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

**Comparison:** 3 Oscillatory PEP therapy vs ACBT (single session)

**Outcome:** 3 Fatigue

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Std. Mean Difference (SE)</th>
<th>Std. Mean Difference (SE)</th>
<th>Std. Mean Difference (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaton 2007</td>
<td>0.7 (0.283)</td>
<td></td>
<td>0.70 [0.15, 1.25]</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP  
Favours ACBT

### Analysis 3.4.  Comparison 3 Oscillatory PEP therapy vs ACBT (single session), Outcome 4 Discomfort.

**Review:** Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

**Comparison:** 3 Oscillatory PEP therapy vs ACBT (single session)

**Outcome:** 4 Discomfort

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Std. Mean Difference (SE)</th>
<th>Std. Mean Difference (SE)</th>
<th>Std. Mean Difference (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaton 2007</td>
<td>0.4 (0.267)</td>
<td></td>
<td>0.40 [-0.12, 0.92]</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP  
Favours ACBT
Analysis 4.1. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 1 Sputum weight (over 24 hours) Day 2 of admission.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 4 Oscillatory PEP vs GAD during acute exacerbation

Outcome: 1 Sputum weight (over 24 hours) Day 2 of admission

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[g]</td>
<td>N</td>
<td>Mean(SD)[g]</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>45.34 (26.48)</td>
<td>5</td>
<td>25.48 (17.47)</td>
</tr>
</tbody>
</table>

-100 -50 0 50 100
Favours Oscillatory PEP Favours GAD

Analysis 4.2. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 2 Sputum weight (over 24 hours) Day 4 of admission.

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 4 Oscillatory PEP vs GAD during acute exacerbation

Outcome: 2 Sputum weight (over 24 hours) Day 4 of admission

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[g]</td>
<td>N</td>
<td>Mean(SD)[g]</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>36.35 (35.67)</td>
<td>5</td>
<td>13.89 (12.64)</td>
</tr>
</tbody>
</table>

-100 -50 0 50 100
Favours Oscillatory PEP Favours GAD
### Analysis 4.3. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 3 Sputum weight (over 24 hours) Day of Discharge.

**Review:** Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

**Comparison:** 4 Oscillatory PEP vs GAD during acute exacerbation

**Outcome:** 3 Sputum weight (over 24 hours) Day of Discharge

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>5</td>
<td>21.03 [ -11.29, 53.35 ]</td>
<td></td>
</tr>
</tbody>
</table>

### Analysis 4.4. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 4 FEV1 (Day 2 of admission).

**Review:** Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

**Comparison:** 4 Oscillatory PEP vs GAD during acute exacerbation

**Outcome:** 4 FEV1 (Day 2 of admission)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>5</td>
<td>0.12 [ -0.32, 0.56 ]</td>
</tr>
</tbody>
</table>
Analysis 4.5. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 5 FEV1 (Day 4 of admission).

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 4 Oscillatory PEP vs GAD during acute exacerbation

Outcome: 5 FEV1 (Day 4 of admission)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsang 2003</td>
<td>0.79 (0.44)</td>
<td>0.64 (0.18)</td>
<td>0.15 [-0.27, 0.57]</td>
<td></td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

Analysis 4.6. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 6 FEV1 (Day of Discharge).

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 4 Oscillatory PEP vs GAD during acute exacerbation

Outcome: 6 FEV1 (Day of Discharge)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsang 2003</td>
<td>1.19 (0.68)</td>
<td>1.07 (0.28)</td>
<td>0.12 [-59.48, 59.72]</td>
<td></td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP
Analysis 4.7. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 7 FVC (Day 2 of admission).

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 4 Oscillatory PEP vs GAD during acute exacerbation

Outcome: 7 FVC (Day 2 of admission)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[L]</td>
<td>N</td>
<td>Mean(SD)[L]</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>0.92 (0.42)</td>
<td>5</td>
<td>1.14 (0.52)</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP  Favours GAD

Analysis 4.8. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 8 FVC (Day 4 of admission).

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 4 Oscillatory PEP vs GAD during acute exacerbation

Outcome: 8 FVC (Day 4 of admission)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[L]</td>
<td>N</td>
<td>Mean(SD)[L]</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>1.26 (0.72)</td>
<td>5</td>
<td>1.06 (0.29)</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP  Favours GAD
**Analysis 4.9. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 9 FVC (Day of Discharge).**

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 4 Oscillatory PEP vs GAD during acute exacerbation

Outcome: 9 FVC (Day of Discharge)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[L]</td>
<td>N</td>
<td>Mean(SD)[L]</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>1.19 (0.68)</td>
<td>5</td>
<td>1.07 (0.28)</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

Favours GAD

---

**Analysis 4.10. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 10 PEFR (Day 2 of admission).**

Review: Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

Comparison: 4 Oscillatory PEP vs GAD during acute exacerbation

Outcome: 10 PEFR (Day 2 of admission)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[L]</td>
<td>N</td>
<td>Mean(SD)[L]</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>136 (70.17)</td>
<td>5</td>
<td>113.8 (35.59)</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP

Favours GAD
### Analysis 4.11. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 11 PEFR (Day 4 of admission).

**Review:** Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

**Comparison:** 4 Oscillatory PEP vs GAD during acute exacerbation

**Outcome:** 11 PEFR (Day 4 of admission)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[L]</td>
<td>N</td>
<td>Mean(SD)[L]</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>131.4 (54.38)</td>
<td>5</td>
<td>108.8 (47.5)</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP  
Favours GAD

### Analysis 4.12. Comparison 4 Oscillatory PEP vs GAD during acute exacerbation, Outcome 12 PEFR (Day of Discharge).

**Review:** Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis

**Comparison:** 4 Oscillatory PEP vs GAD during acute exacerbation

**Outcome:** 12 PEFR (Day of Discharge)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)[L]</td>
<td>N</td>
<td>Mean(SD)[L]</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>5</td>
<td>141.2 (49.65)</td>
<td>5</td>
<td>118 (51.59)</td>
</tr>
</tbody>
</table>

Favours Oscillatory PEP  
Favours GAD
## ADDITIONAL TABLES

### Table 1. Individual study outcomes for HRQOL

<table>
<thead>
<tr>
<th>Study name</th>
<th>Number of participants</th>
<th>Comparison</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thompson 2002</td>
<td>17</td>
<td>Oscillatory PEP therapy vs ACBT with GAD</td>
<td><strong>Disease-specific QOL</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dyspnoea domain: MD 0.01 (95% CI -0.48 to 0.50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fatigue domain: MD -0.19 (95% CI -0.82 to 0.45)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Emotional function domain: MD -0.06 (95% CI -0.63 to 0.52)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mastery domain: MD -0.10 (95% CI -0.65 to 0.46)</td>
</tr>
<tr>
<td>Altiay 2012</td>
<td>36</td>
<td>Oscillatory PEP therapy vs ACBT (daily for 4 weeks)</td>
<td>Improved general health on SF-36 (P = 0.048) with PEP therapy</td>
</tr>
<tr>
<td>Herrero-Cortina 2015</td>
<td>31</td>
<td>Minimal PEP therapy vs AD Minimal PEP therapy vs ELTGOL</td>
<td><strong>Cough-related quality of life (LCQ)</strong> median 0.4 (95% CI 0.1 to 1.2) vs 0.5 (95% CI 0.1 to 0.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Day 2: MD 19.86 g (95% CI -7.95 to 47.67) Day 4: MD 22.46 g (95% CI -10.71 to 55.63) Day of discharge: MD 21.03 g (95% CI -11.29 to 53.35)</td>
</tr>
</tbody>
</table>

ACBT - active cycle of breathing technique; AD - autogenic drainage; CI - confidence interval; ELTGOL - L’expiration Lente Totale Glotte Ouverte en Decubitus Lateral; LCQ - Leicester cough questionnaire; MD - mean difference; PEP - positive expiratory pressure; QOL - quality of life; SF-36 - short form 36.

### Table 2. Individual study outcomes for sputum yield

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Comparison</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antunes 2001</td>
<td>10</td>
<td>Oscillatory PEP therapy (Flutter) vs ELTGOL</td>
<td>dry weight (MD 0.28 g (SD 0.28) vs 0.16 g (0.06)), P &gt; 0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>wet weight (MD 7.2 g (SD 2.3) vs 6.3 g (0.7)), P &gt; 0.05</td>
</tr>
<tr>
<td>Thompson 2002</td>
<td>17</td>
<td>Oscillatory PEP therapy (Flutter) vs ACBT with GAD</td>
<td>median difference 7.64 g, P = 0.77</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>10</td>
<td>Oscillatory PEP therapy (Flutter) vs GAD</td>
<td>Day 2: MD 19.86 g (95% CI -7.95 to 47.67) Day 4: MD 22.46 g (95% CI -10.71 to 55.63) Day of discharge: MD 21.03 g (95% CI -11.29 to 53.35)</td>
</tr>
</tbody>
</table>
Table 2. Individual study outcomes for sputum yield  (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Comparison</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patterson 2005</td>
<td>20</td>
<td>Oscillatory PEP therapy (Acapella) vs ACBT with GAD</td>
<td>MD 0.54 g (95% CI -0.39 to 1.46)</td>
</tr>
<tr>
<td>Eaton 2007</td>
<td>36</td>
<td>Oscillatory PEP therapy (Flutter) vs ACBT</td>
<td>MD 0.3 g (95% CI -1.42 to 0.82) MD -5.6 g (95% CI -10.1 to -1.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oscillatory PEP therapy (Flutter) vs ACBT with GAD</td>
<td></td>
</tr>
<tr>
<td>Guimaraes 2012</td>
<td>10</td>
<td>Oscillatory PEP therapy (Flutter) vs ELTGOL</td>
<td>median 0.15 g (minimum to maximum 0.05 to 0.13 g) vs 0.38 g (0.06 to 2.63 g)</td>
</tr>
<tr>
<td>Herrero-Cortina 2015</td>
<td>31</td>
<td>Minimal PEP therapy vs AD</td>
<td>median difference 3.1 g (95% CI 1.5 to 4.8 g)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimum PEP therapy vs ELTGOL</td>
<td>median difference 3.6 g (95% CI 2.8 to 7.1 g)</td>
</tr>
<tr>
<td>Semwal 2015</td>
<td>30</td>
<td>Oscillatory PEP therapy vs AD</td>
<td>mean 15.8 g (SD 5.7) vs 16.2 g (7.9)</td>
</tr>
</tbody>
</table>

ACBT - active cycle of breathing technique; AD - autogenic drainage; CI - confidence interval; ELTGOL - L’expiration Lente Totale Glotte Ouverte en Decubitus Lateral; g - grams; GAD - gravity assisted drainage; MD - mean difference; PEP - positive expiratory pressure; SD - standard deviation.

Table 3. Individual study outcomes for lung function

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Comparison</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antunes 2001</td>
<td>10</td>
<td>Oscillatory PEP therapy (Flutter) vs ELTGOL</td>
<td>Day 1 PEFR: mean 405 L/min (SD 157) vs 439 L/min (175) Day 2 PEFR: 434 L/min(150) vs 417 L/min (134) Day 3 PEFR: 428 L/min(166) vs 419 L/min (157) Day 4 PEFR: 456 L/min(159) vs 462 L/min (185)</td>
</tr>
<tr>
<td>Thompson 2002</td>
<td>17</td>
<td>Oscillatory PEP therapy (Flutter) vs ACBT with GAD</td>
<td>PEFR morning: median difference -2.5 L/min, P = 0.38 PEFR evening: median difference -2.72 L/min (95% CI -6.95 to 1.52), P = 0.30</td>
</tr>
<tr>
<td>Tsang 2003</td>
<td>10</td>
<td>Oscillatory PEP therapy (Flutter) vs GAD</td>
<td>Day 2 FEV₁: MD 0.12 L (95% -0.32 to 0.56) Day 4 FEV₁: MD 0.15 L (95% CI -0.27 to 0.57)</td>
</tr>
</tbody>
</table>
### Table 3. Individual study outcomes for lung function (Continued)

| Patterson 2005 | 20 | Oscillatory PEP therapy (Acapella) vs ACBT with GAD | Day of discharge FEV<sub>1</sub>: (MD 0.12 L (95% CI -0.52 to 0.76)  
Day 2 FVC: MD -0.22 L (95% CI -0.81 to 0.37)  
Day 4 FVC: MD 0.2 L (95% CI 0.48 to 0.88)  
Day of discharge: FVC MD 0.12 L (95% CI -0.52 to 0.76)  
Day 2 PEFR: MD 22.2 L/min (95% CI -48.88 to 93.28)  
Day 4 PEFR: MD 22.6 L/min (95% CI -40.69 to 85.89)  
Day of discharge PEFR: MD 23.2 L/min (95% CI -39.56 to 85.96) |
| Altiay 2012 | 36 | Oscillatory PEP therapy (Flutter) vs ACBT | No difference between techniques, MD NR |
| Guimaraes 2012 | 10 | Oscillatory PEP therapy (Flutter) vs ELTGOL | FEV<sub>1</sub>: median 1.6 L (minimum to maximum -6.8 to 21.4) vs 2.2 L (-20.2 to 20.9)  
FVC: median 2.44 L (minimum to maximum -3.9 to 8.1) vs 0.96 L (-11.8 to 22.1)  
FEV<sub>1</sub>/FVC: median 0.7 L (minimum to maximum -11.3 to 19.6) vs 0.0 L (-8.6 to 10.6)  
FEF<sub>25-75</sub>: median 4.5 L (minimum to maximum -21.4 to 160.0) vs 6.0 (-90.51 to 236)  
Change in IC: median 3.5 L (minimum to maximum 28.5 to 33.8) vs 2.7 (-15.7 to 27.7)  
Change in TLC: median -18.3 L (minimum to maximum -42.4 to -6.4) vs 9.7 (-40.0 to -1.9)  
Change in FRC: median -25.8 L (minimum to maximum -52.0 to -5.1) vs -14.5 L (-55.7 to -3.6)  
Change in RV: median 62.9 L (minimum to maximum -54.7 to -8.9) vs 18.7 L (-71.9 to -10.7)  
Change in RV/TLC ratio (median -5.2, range -12.6 to 2.9) |
Table 3. Individual study outcomes for lung function  (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Comparison</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herrero-Cortina 2015</td>
<td>31</td>
<td>Minimal PEP therapy vs ELTGOL</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;, FVC, FEF&lt;sub&gt;25–75&lt;/sub&gt; remain unchanged between techniques, MD NR, P &gt; 0.05</td>
</tr>
<tr>
<td>Semwal 2015</td>
<td>30</td>
<td>Oscillatory PEP therapy (Acapella) vs AD</td>
<td>PEFR: mean 176.1 L/min (SD 72.6) vs 179.1 (72.6), P = 0.87</td>
</tr>
</tbody>
</table>

ACBT - active cycle of breathing technique; AD - autogenic drainage; ELTGOL - L’expiration Lente Totale Glotte Ouverte en Decubitus Lateral; FEF<sub>25–75</sub> - forced expiratory flow at 25 to 75% of forced vital capacity; FEV<sub>1</sub> - forced expiratory volume in one second; FRC - functional residual capacity; FVC - forced vital capacity; GAD - gravity assisted drainage; IC - inspiratory capacity; L - litres; L/min - litres per minute; MD - mean difference; NR - not reported; PEFR - peak expiratory flow rate; PEP - positive expiratory pressure; RV - residual volume; SD - standard deviation; TLC - total lung capacity.

Table 4. Individual study outcomes for symptoms

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of participants</th>
<th>Comparison</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thompson 2002</td>
<td>17</td>
<td>Oscillatory PEP therapy (Flutter) vs ACBT with GAD</td>
<td>Borg dyspnoea scale morning: MD 0.13 (95% CI -0.078 to 0.34), P = 0.36 Borg dyspnoea scale evening: median difference -0.04, P &gt; 0.99</td>
</tr>
<tr>
<td>Patterson 2005</td>
<td>20</td>
<td>Oscillatory PEP therapy (Acapella) vs ACBT with GAD</td>
<td>15-count breathlessness score: MD NR</td>
</tr>
<tr>
<td>Eaton 2007</td>
<td>36</td>
<td>Oscillatory PEP therapy (Flutter) vs ACBT with GAD</td>
<td>Fatigue: MD -0.3 points (95% CI -0.35 to 0.95) Discomfort: MD -0.3 points (95% CI -0.82 to 0.22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oscillatory PEP therapy (Flutter) vs ACBT</td>
<td>Fatigue: MD 0.7 points (95% CI 0.15 to 1.25) Discomfort: MD 0.40 points (95% CI -0.12 to 0.92)</td>
</tr>
<tr>
<td>Altiay 2012</td>
<td>36</td>
<td>Oscillatory PEP therapy (Flutter) vs ACBT</td>
<td>Borg and Medical Research Council scores: no difference between techniques, MD NR</td>
</tr>
<tr>
<td>Semwal 2015</td>
<td>30</td>
<td>Oscillatory PEP therapy (Acapella) vs AD</td>
<td>mean 1.8 (SD 1.1) vs 1.8 (1.2), P = 1.00</td>
</tr>
</tbody>
</table>

ACBT - active cycle of breathing technique; AD - autogenic drainage; CI - confidence interval; GAD - gravity assisted drainage; MD - mean difference; NR - not reported; PEP - positive expiratory pressure.
APPENDICES

Appendix 1. Sources and search methods for the Cochrane Airways Group Specialised Register (CAGR)

MEDLINE search strategy used to identify trials for the CAGR

Bronchiectasis search
1. exp Bronchiectasis/
2. bronchiect$.mp.
3. bronchoect$.mp.
4. kartagener$.mp.
5. (ciliary adj3 dyskinesia).mp.
6. (bronchial$ adj3 dilat$).mp.
7. or/1-6

Filter to identify RCTs
1. exp "clinical trial [publication type]"/
2. (randomised or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. Animals/
10. Humans/
11. 9 not (9 and 10)
12. 8 not 11

The MEDLINE strategy and RCT filter are adapted to identify trials in other electronic databases.

Appendix 2. Search strategy to identify relevant trials from the CAGR

#1 BRONCH:MISC1
#2 MeSH DESCRIPTOR Bronchiectasis Explode All
#3 bronchiect*
#4 #1 or #2 or #3
#5 MeSH DESCRIPTOR Positive-Pressure Respiration Explode All
#6 positive* NEAR expirat*
#7 PEP:ti,ab
#8 Hi-PEP:ti,ab
#9 *PEP:ti,ab
#10 VRP1
#11 flutter*
#12 acapella*
#13 cornet*
#14 quake*
#15 resistance* NEAR breath*
#16 desitin*
#17 scandipharm*
#18 flute*

Positive expiratory pressure therapy versus other airway clearance techniques for bronchiectasis (Review)

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Appendix 3. Search terms used in PEDro database

'bronchiectasis',
'Kartegener'
'Agammaglobulinaemia'.

CONTRIBUTIONS OF AUTHORS

Initiated the protocol: AL
Developed the protocol: AL, AB, and AH.
 Undertook literature search and retrieved papers: AL
Screened retrieved papers against eligibility criteria: AL and AB.
Appraised quality of papers: AL and AB.
Extracted data: AL and AB.
Wrote to study authors for additional information: AL.
Entered data into RevMan: AL.
Performed analysis: AL.
Wrote review: AL, reviewed manuscript: AB and AH.
Served as guarantor of the review: AL.

DECLARATIONS OF INTEREST

AL: none known.
AB: none known.
AH: none known.

SOURCES OF SUPPORT
Internal sources

- The authors declare that no such funding was received for this systematic review, Other.

External sources

- The authors declare that no such funding was received for this systematic review, Other.

**Differences between protocol and review**

The term non-cystic fibrosis bronchiectasis has been altered to bronchiectasis, to align with recent recommendations.