

Autogenic drainage for airway clearance in cystic fibrosis

Review information

Review type: Intervention

Review number: 0133

Authors

Pamela McCormack¹, Paul Burnham², Kevin W Southern³

¹Department of Respiratory Physiotherapy, Alder Hey Children's NHS Foundation Trust, Liverpool, UK

²Servicio de Medicina Fisica y Rehabilitacion, Hospital La Paz, Madrid, Spain

³Department of Women's and Children's Health, University of Liverpool, Liverpool, UK

Citation example: McCormack P, Burnham P, Southern KW. Autogenic drainage for airway clearance in cystic fibrosis.

Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD009595. DOI:

10.1002/14651858.CD009595.pub2.

Contact person

Pamela McCormack

Cystic Fibrosis Clinical Specialist Physiotherapist

Department of Respiratory Physiotherapy

Alder Hey Children's NHS Foundation Trust

Eaton Road

Liverpool

L12 2AP

UK

E-mail: pamela.mccormack@alderhey.nhs.uk

Dates

Assessed as Up-to-date: 20 September 2017

Date of Search: 31 August 2017

Next Stage Expected: 23 September 2019

Protocol First Published: Issue 1, 2012

Review First Published: Issue 10, 2017

Last Citation Issue: Issue 10, 2017

What's new

Date	Event	Description

History

Date	Event	Description

Abstract

Background

Autogenic drainage is an airway clearance technique that was developed by Jean Chevallier in 1967. The technique is characterised by breathing control using expiratory airflow to mobilise secretions from smaller to larger airways. Secretions are cleared independently by adjusting the depth and speed of respiration in a sequence of controlled breathing techniques during exhalation. The technique requires training, concentration and effort from the individual. It is important to systematically review the evidence demonstrating that autogenic drainage is an effective intervention for people with cystic fibrosis.

Objectives

To compare the clinical effectiveness of autogenic drainage in people with cystic fibrosis with other physiotherapy airway clearance techniques.

Search methods

We searched the Cochrane Cystic Fibrosis Trials Register, compiled from electronic database searches and handsearching of journals and conference abstract books. We also searched the reference lists of relevant articles and reviews, as well as two trials registers (31 August 2017).

Date of most recent search of the Cochrane Cystic Fibrosis Trials Register: 25 September 2017.

Selection criteria

We identified randomised and quasi-randomised controlled studies comparing autogenic drainage to another airway clearance technique or no therapy in people with cystic fibrosis for at least two treatment sessions.

Data collection and analysis

Data extraction and assessments of risk of bias were independently performed by two authors. The authors assessed the quality of the evidence using the GRADE system. The authors contacted two investigators for further information pertinent to their published studies.

Main results

Searches retrieved 35 references to 21 individual studies, of which seven ($n = 208$) were eligible for inclusion. One study was of parallel design with the remaining six being cross-over in design; participant numbers ranged from 17 to 75. The total study duration varied between four days and two years. The age of participants ranged between seven and 63 years with a wide range of disease severity reported. Six studies enrolled participants who were clinically stable, whilst participants in one study had been hospitalised with an infective exacerbation. All studies compared autogenic drainage to one (or more) other recognised airway clearance technique. Exercise is commonly used as an alternative therapy by people with cystic fibrosis; however, there were no studies identified comparing exercise with autogenic drainage.

The quality of the evidence was generally low or very low. The main reasons for downgrading the level of evidence were the frequent use of a cross-over design, outcome reporting bias and the inability to blind participants.

The review's primary outcome, forced expiratory volume in one second, was the most common outcome measured and was reported by all seven studies; only three studies reported on quality of life (also a primary outcome of the review). One study reported on adverse events and described a decrease in oxygen saturation levels whilst performing active cycle of breathing techniques, but not with autogenic drainage. Six of the seven included studies measured forced vital capacity and three of the studies used mid peak expiratory flow (per cent predicted) as an outcome. Six studies reported sputum weight. Less commonly used outcomes included oxygen saturation levels, personal preference, hospital admissions or intravenous antibiotics. There were no statistically significant differences found between any of the techniques used with respect to the outcomes measured except when autogenic drainage was described as being the preferred technique of the participants in one study over postural drainage and percussion.

Authors' conclusions

Autogenic drainage is a challenging technique that requires commitment from the individual. As such, this intervention merits systematic review to ensure its effectiveness for people with cystic fibrosis. From the studies assessed, autogenic drainage was not found to be superior to any other form of airway clearance technique. Larger studies are required to better evaluate autogenic drainage in comparison to other airway clearance techniques in view of the relatively small number of participants in this review and the complex study designs. The studies recruited a range of participants and were not powered to assess non-inferiority. The varied length and design of the studies made the analysis of pooled data challenging.

Plain language summary

The autogenic drainage breathing technique for helping people with cystic fibrosis to clear mucus from their airways

Background

Cystic fibrosis affects the lungs by producing thick mucus lining the airways. This can lead to infection and inflammation causing lung damage. Physiotherapy can help to keep the airways clear of mucus and there are many methods used to do this, including breathing techniques, manual techniques and mechanical devices. Autogenic drainage is a very controlled technique of breathing which uses different depths and speeds of exhaled breath to move mucus up the airways resulting in a spontaneous or voluntary cough. It can be used without help, but requires training, concentration and effort. We looked at the effect of using autogenic drainage on lung function measurements and quality of life in people with cystic fibrosis, to discover whether using autogenic drainage was better or worse than other existing physiotherapy techniques for clearing the lungs.

Search date

The evidence is current to: 25 September 2017.

Study characteristics

We searched the literature for studies comparing at least two sessions of autogenic drainage with other breathing techniques and devices which help to clear the lungs of mucus. We included seven studies in the review involving 208 people with cystic fibrosis, aged between seven and 63 years of age. People were selected for one physiotherapy treatment or the other randomly. The number of people in the studies ranged from 17 to 75, and had a wide range of disease severity. The studies lasted from four days to two years in total.

Key results

We did not find any clear evidence that autogenic drainage was better than the other techniques for lung function or quality of life in either the short-term or long-term studies. This was also true for our other outcome measures such as hospital admissions, additional antibiotic treatment, exercise tolerance and oxygen saturation, but in one study autogenic drainage was the preferred technique compared to postural drainage and percussion. Exercise was identified as a comparator for airway clearance by the authors of this review but no included studies used it in this way, even though it is often used as an

alternative therapy by people with cystic fibrosis.

Quality of the evidence

Overall, the quality of the evidence from the studies was judged to be mainly low or very low. The main problems for this being the small numbers of participants in each study, the unclear reporting of results in the studies and the study design used. In one study, which was classed as having a high risk of bias due to incomplete results, those taking part had to change physiotherapy technique halfway through the study and there were many who dropped out and did not comply with the postural drainage and percussion treatment arm. Five of the seven studies used research staff to assess results who did not know which technique each person was using and this improved the quality of the evidence and reduced any bias.

Background

Description of the condition

Cystic fibrosis (CF) is a genetic condition which is inherited in an autosomal recessive manner (two carrier parents have a one in four chance of a child with CF). It is more prevalent in Northern European populations (incidence of around one in 3000 births ([Farrell 2008](#))) but less prevalent in populations from outside of Europe ([Farrell 2008](#)). The affected gene codes for the production of a protein that is involved in the movement of salt across cell walls. Infants born with CF often have minimal disease expression in their early weeks of life, but the abnormal salt transport predisposes them to a number of different problems; most commonly salt loss through abnormal sweat production, poor absorption of food through pancreatic dysfunction and airway infection and inflammation through dysfunction of the airway clearance mechanism that normally protects the lungs ([Tiddens 2010](#)).

Abnormal salt transport impacts on the production of airway surface liquid, which potentially disturbs the ability of the cilia to clear the airways ([Boucher 2004](#)). This is an important physiological process, called the mucociliary escalator, for protecting the airways. Disruption of this process makes the airways vulnerable to the unusual infections that characterise CF lung disease. Once established, airway infection and inflammation exacerbate the poor airway clearance. Together with increased production of airway mucus, this leads to a cycle of chronic infection, inflammation and airway damage ([Cantin 2015](#); [Konstan 1997](#)). It is the impact of the CF defect on the airways that is the most significant cause of morbidity and ultimately early death for people with CF ([Tiddens 2010](#)).

Description of the intervention

There is evidence from systematic reviews, including Cochrane Reviews, that exercise and airway clearance are important, even during early stages of the condition, for maintaining respiratory health ([Flume 2009](#)). With more established airway infection, airway clearance techniques are critical to maintaining respiratory function and preventing the deterioration associated with infection and inflammation.

There are a number of different airway clearance techniques (including exercise) that exist and these have been evaluated by other Cochrane Reviews ([Main 2005](#); [McIlwaine 2015](#); [Mckoy 2016](#); [Morrison 2017](#); [Radtke 2015](#); [Warnock 2015](#)). The most traditional technique involves percussion with the individual in several different positions to loosen secretions. Newer strategies involve the use of devices, ranging from simple and cheap airway oscillating devices (AOD), through devices generating positive expiratory pressure (PEP) or Hi-PEP to high frequency chest wall oscillation (HFCWO) devices which have significant cost implications. Other techniques focus more on the individual appreciating and controlling their breathing pattern and using this to augment airway clearance. These techniques include the active cycle of breathing (ACBT) and autogenic drainage (AD), the subject of this review. Exercise is commonly used as an alternative therapy by people with CF.

Jean Chevallier developed AD as an airway clearance technique in 1967 and AD is characterised by the individual with CF understanding and controlling their breathing ([Chevallier 1984](#)). Secretions are cleared by adjusting the rate, depth and location of respiration in a sequence of controlled breathing techniques. The mechanism of mucus clearance rests on two different systems, the effect of the ciliary clearance and the effect of shearing forces induced by the airflow. To create the necessary shearing forces to clear the bronchi from secretions, it is essential to modulate the inspiratory and expiratory airflow. In order to do this, the individual inspires with a deeper than normal breath, described by Chevallier as the functional tidal volume (1.5 to 2 times the size of normal tidal volume), and exhales in a gentle but active way as a sigh. Individuals breathe in with inspiratory pauses through an open glottis, allowing more time for obstructed areas of the lung to fill equally and air to move behind secretions. These secretions are mobilised from the periphery of the lungs to the mouth by adjusting the lung volume at which the individual is performing the AD-style breathing in three distinct phases. In the first phase, known as the 'un-sticking phase', repeated low-lung volume breaths are used within the expiratory reserve volume, i.e. the individual will be instructed to breathe out as far as possible and then to breathe the functional tidal volume. To localize the secretions the three feedback signals (auditive, tactile and proprioceptive) are used, which informs the individual to move to the next phase. In the second phase (collective phase) a mid-volume level of breathing is used, progressing into the inspiratory reserve and secretions are mobilised ready to be expectorated in the third (evacuation) phase using a huff (forced expiration technique) or controlled cough. The aim of breathing in this way is to achieve the highest possible expiratory air flow simultaneously in different generations of the bronchi, keeping bronchial resistance low, and avoiding bronchospasm and dynamic airway collapse. Under these circumstances, the speed of air flow may mobilise secretions by shearing them from the bronchial walls and transporting them from the peripheral to the central airways ([IPG/CF 2009](#)). The use of AD prevents airway collapse during forced expiratory maneuvers and it may consume less energy compared to other airway clearance techniques ([Agostini 2007](#)). In addition to the clinical benefit and

improvement in forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC), a recent study in adults with CF has shown that AD improved inspiratory resistance in all airways except the distal small airways ([Prevotat 2017](#)).

How the intervention might work

The rationale behind airway clearance is simple, that removing infected secretions from the airway will improve ventilatory capacity and reduce direct inflammatory effects on the airway epithelia. There is convincing evidence that such a strategy is important and effective for people with chronic airway infection, but there is a less robust evidence base for those who do not have chronic airway infection and are not usually productive of sputum ([McIllwaine 2014](#)).

Why it is important to do this review

All airway clearance techniques are time-consuming and require effort and commitment from the individual ([Rand 2013](#)). Some techniques have significant cost implications ([Morrison 2017](#)). While AD requires training and support from therapists, it is a popular technique with many people with CF. It allows independence from carers, is recognised to be effective in the modulation of airflow and capable of augmenting the physiological process of the body's mucociliary escalator.

It is important that interventions which have cost implications and are a burden on the time of people with CF are systematically reviewed for evidence of efficacy.

Objectives

To compare the clinical effectiveness of AD in people with CF with other physiotherapy airway clearance techniques.

Methods

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and quasi-RCTs.

Types of participants

Children and adults with CF with a diagnosis based on sweat testing or genetic testing or any combination of these.

Types of interventions

This review will compare AD to all other recognised airway clearance techniques either as a single technique or in combination with other techniques for at least two treatment episodes. In a post hoc change, it was felt that it would be difficult to assess AD in a single treatment episode, therefore such short studies were not included in this review.

Autogenic drainage (AD)

This airway clearance technique was developed by Jean Chevaillier in 1967 and is characterised by breathing control using expiratory airflow to mobilise secretions from smaller to larger airways. Secretions are cleared independently by adjusting the depth and speed of respiration in a sequence of controlled breathing techniques during exhalation ([IPG/CF 2009](#)).

Conventional physiotherapy

Postural drainage and percussion (PD&P) was first introduced for the treatment of CF in the 1950s. Postural drainage (PD) has consisted of placing the individual in a position which allows gravity to assist in draining mucus from the periphery of the lungs centrally. In more recent years modified postural drainage is commonly used, which involves positioning without the use of head-down tilt ([Button 2016](#)). Percussion and vibration manual techniques are used as an adjunct to PD and are directed over the chest wall. Deep breathing, huffing and directed coughing complete the treatment ([Main 2005](#)).

Active cycle of breathing technique (ACBT)

This technique combines breathing control, thoracic expansion exercises and forced expiratory techniques (FET) ([Pryor 1999](#)). Breathing control involves relaxed tidal volume breathing using diaphragmatic control, whereas thoracic expansion exercises focus on active inspiration to increase lung volumes. After one or more cycles of breathing control and thoracic expansion exercises, FET is encouraged from a high-lung volume. The regimen is flexible and can be adapted to suit the individual ([Button 2016](#)). Chest wall manipulation and postural drainage may also be included along with this cycle.

Exercise

Physical exercise that increases minute ventilation leads to the mobilization of pulmonary secretions and enhances airway clearance. Physiological effects of exercise include reduced mechanical impedance of sputum, enhanced expiratory flow rates and inducement of coughing ([Button 2016](#); [Dwyer 2011](#)). Evidence from both short- and long-term studies shows that exercise has a positive effect on lung function and well-being ([Radtke 2015](#)).

Positive expiratory pressure (PEP)

The PEP mask or mouthpiece contains a valve that increases resistance to expiratory airflow. The individual repeats 10 to 15 breaths through the flow resistor, creating positive pressures of 10 to 20 cm H₂O in the airways. The theoretical benefit of PEP therapy lies in its ability to enhance and promote mucus clearance by one or more mechanisms: by preventing small airway collapse through stenting of the airways; or, by enhancing lung recruitment distal to retained secretions using collateral ventilation ([Andersen 1979](#); [Groth 1985](#)); or, by temporarily increasing functional residual capacity ([Mcllwaine 2015](#)).

High-pressure PEP (Hi-PEP)

The Hi-PEP mask physiotherapy employs forced expiratory manoeuvres against the PEP mask's expiratory resistor. An individual performs PEP breathing for eight to 10 cycles using moderately increased tidal breathing before inhaling to total lung capacity and performing a forced expiratory manoeuvre against the stenosis. Sustained expiratory pressures achieved usually range between 40 and 100 cm H₂O ([Oberwaldner 1986](#)).

Oscillatory devices

There are several devices available for augmenting airway clearance.

Cornet®

The Cornet® is a horn-shaped plastic tube which houses a rubber inner hose. Expiration through the Cornet® causes the hose to flex, buckle and unbuckle, causing oscillating positive pressure in the airways which fluctuates rapidly. The mouthpiece can be adjusted to produce the optimal resistance and oscillation ([Pryor 1999](#)).

Flutter®

The Flutter VRP1 device comprises a mouthpiece, a plastic cone, a steel ball and a perforated cover. During exhalation through the device, the tracheobronchial tree undergoes internal vibrations, together with repeated changes of the expiratory airflow against the resistance (PEP component) and oscillations in endobronchial pressure (oscillatory component). This facilitates the mobilisation and loosening of secretions ([Konstan 1994](#); [Pryor 1999](#)).

High frequency chest wall oscillations (HFCWO)

HFCWO delivers external compression pulses to the chest wall through an inflatable vest connected to an air pulse generator. The generator produces an alternating flow of air into, and out of, the vest that rapidly compresses and releases the chest wall within a range of selectable frequencies and pressures. The oscillatory compression imparted to the chest wall has been reported to thin viscous mucus, mobilise secretions and propel mucus to the major airways ([Warwick 1991](#)).

Intrapulmonary percussive ventilation (IPV)

This technique utilizes high frequency oscillatory ventilation to produce endotracheal percussion via the mouth using a device called the Percussionator. Percussive bursts of high-flow respiratory gas are delivered throughout the entire respiratory cycle at high rates. These cause oscillatory airflow which vibrates the airway walls to loosen and mobilize secretions towards the upper airways and oral pharynx ([Homnick 1995](#)).

Acapella

The Acapella combines the principles of high-frequency oscillation and PEP by employing a counterweighted lever and magnet. Exhaled gas passes through a cone, which is intermittently occluded by a plug attached to the lever, producing airflow oscillations. A dial located at the distal end of the device adjusts the proximity of the magnet and counterweighted plug, thereby adjusting the frequency, amplitude, and mean pressure ([Volsko 2003](#)).

Quake® (Thayer Medical, Tucson, Arizona, USA)

This device produces airway oscillation during both inspiration and expiration. The design consists of a manually turned outer barrel which rotates around an inner barrel. Airflow occurs only when vanes within the two barrels line up and is interrupted at regular intervals as the user turns the handle. Percussion is achieved as small bursts of air are inhaled and exhaled through the vanes of the device ([Okeson 2007](#)).

Types of outcome measures

Primary outcomes

1. FEV₁
2. Quality of life (QoL) as measured by any of the scales including:
 - a. Cystic Fibrosis Questionnaire-Revised version (CFQ-R) ([Quittner 2009](#))
 - b. Cystic Fibrosis Quality of Life Questionnaire (CFQoL) ([Gee 2000](#))
 - c. Quality of Well-being (QWB)
 - d. Nottingham Health Profile (NHP)
 - e. any other validated QoL scale

Secondary outcomes

1. Participant preference
2. Exercise tolerance
 - a. six-minute walk test
 - b. shuttle walk test
 - c. cardiopulmonary exercise testing (CPET)

- d. any other validated exercise evaluation
3. Adverse effects (e.g. haemoptysis, bronchospasm, desaturation)
4. Number of admissions to hospital
5. Need for extra treatment
6. Other pulmonary function measurements
 - a. lung clearance index (LCI) (post hoc change)
 - b. FVC
 - c. forced mid-expiratory flow between 25% and 75% of FVC (FEF_{25-75%})
7. Oxygen saturation
 - a. pulse oximeter
 - b. arterial blood gas analysis
8. Sputum weight
9. Survival

Search methods for identification of studies

There was no restriction on language or publication status.

Electronic searches

We identified relevant studies from the Group's Cystic Fibrosis Trials Register by using the term: autogenic drainage.

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

Date of last search of the CF Register: 25 September 2017.

We also searched two online trials registries:

- ClinicalTrials.gov (clinicaltrials.gov) using the key words 'autogenic drainage' and 'forced expiratory techniques', as well as 'autogenic drainage' and 'cystic fibrosis' (date of last search 21 September 2017);
- WHO ICTRP (<http://apps.who.int/trialsearch/>) using the key words "autogenic drainage AND forced expiratory techniques" as well as "autogenic drainage AND cystic fibrosis" (date of last search 31 August 2017).

Searching other resources

We checked the reference lists from the identified studies for further assessment. We also screened the references of all published Cochrane Reviews related to this title.

Data collection and analysis

Selection of studies

Two authors (PM, PB) independently screened the results of the searches for relevant articles based on the title and abstract. They included the studies which either of them identified as relevant and reviewed the full text of those studies. They screened the full text articles to determine the eligibility of the study for inclusion in the review. In case of any disagreement, they planned to consult the third author (KWS), but there were no instances of disagreement. For studies published in languages other than English, the authors planned to seek translation.

Data extraction and management

The authors (PM, PB) independently extracted the data using specifically formulated data extraction forms. The extracted data included characteristics of the participants, information on the study design (type of randomisation, type of allocation concealment, number of participants), aspects of the intervention (details of intervention and control intervention, duration of intervention, frequency of intervention, compliance with intervention, intensity of intervention and details of multifaceted interventions), outcome measures, adverse effects and dropouts.

The authors presented results separately for each comparison of techniques, i.e. AD versus conventional physiotherapy, AD versus ACBT, AD versus PEP, etc. We do not combine all oscillating devices together, instead present separate comparisons for AD versus Flutter® and AD versus Cornet®.

They compared the effect of treatment both in the short term and long term. In a post hoc change, for short-term studies (up to one month), the authors reported outcomes of up to seven days, and from one to four weeks. Likewise, the outcome data for longer-term studies were reported as those measured at one month, three months, six months, 12 months and annually thereafter. The authors also planned to consider any outcome data recorded at other time periods. In a post hoc change, the authors felt that it was difficult to assess the relevance of AD treatment after a single treatment intervention, so did not include these extremely brief studies in the review, setting instead a minimum requirement of two treatment sessions for inclusion.

Assessment of risk of bias in included studies

The authors (PM, PB) independently assessed the risk of bias from the included studies using the approach recommended in

the *Cochrane Handbook of Systematic Reviews of Interventions* (Higgins 2011). They planned to resolve any disagreements by consensus, but this was not necessary. The authors assessed and rated the following domains.

1. Generation of sequence

Low risk of bias: using a computerised random generator, random number tables, coin tossing or any other valid method.

High risk of bias: sequence generation and allocation done by invalid methods such as using odd or even date of birth, or allocation by the judgement of the clinician.

Unclear risk of bias: insufficient information provided about the sequence generation process.

2. Concealment of allocation sequence

Low risk of bias: allocation concealed so that neither the investigators or participants know group assignment at the time of study entry. Valid methods include central randomisation or serially numbered, opaque, sealed envelopes.

High risk of bias: the method of allocation is not concealed (e.g. visible list of random numbers, unsealed or non-opaque envelopes) leading to transparency in group assignments and thereby introducing selection bias.

Unclear risk of bias: insufficient information provided about the concealment of allocation process.

3. Blinding of participants, personnel and outcome assessors

Note: we considered the risk of bias from blinding for the study overall rather than per outcome.

Low risk of bias: either participants or some key study personnel could not or were not blinded, but the outcome assessment was blinded and the non-blinding of others is unlikely to introduce bias.

High risk of bias: no blinding or incomplete blinding and the outcome measurement is likely to be influenced by lack of blinding.

Unclear risk of bias: insufficient information or the study report did not mention it.

4. Incomplete outcome data

Low risk of bias: missing data have been included using appropriate methods such as intention-to-treat analysis.

High risk of bias: authors did not include intention-to-treat analysis for missing data.

Unclear risk of bias: insufficient reporting of attrition or exclusions, no reasons for missing data provided.

5. Selective outcome reporting

Low risk of bias: the published article(s) report(s) primary and secondary outcomes that are of interest to the review in the pre-specified way.

High risk of bias: pre-specified outcomes not reported.

Unclear risk of bias: insufficient information to permit judgement of low or high risk.

6. Other potential threats to validity

Low risk of bias: the study appears to be free of other sources of bias.

High risk of bias: evidence of other potential sources of bias, e.g. there is bias pertaining to the study design (e.g. extreme baseline imbalance).

Unclear risk of bias: insufficient information to assess whether any important risk of bias exist.

Authors previously stated that they would not be allowed to assess the risk of bias in studies in which they were involved, but no such studies were relevant for this review. For studies published in languages other than English, authors fluent in that language would assess the risk of bias or the study would be translated; no such studies were relevant.

Measures of treatment effect

Where possible, for continuous outcomes (FEV₁, QoL, exercise tolerance, number of admissions to hospital, LCI, FVC, FEF_{25-75%}, pulse oximetry, arterial blood gas analysis and sputum weight) using the same unit of measurement, the authors reported the mean difference (MD) and 95% confidence intervals (CIs). They reported the standardised mean difference (SMD) with 95% CIs for continuous outcomes using different units of measurement. For dichotomous outcomes (participant preference, adverse effects, need for extra treatment and survival), the authors planned to report risk ratio (RR) and 95% CIs, however, no such outcomes have been analysed.

Unit of analysis issues

When combining the data from cross-over studies, the authors planned to use the methods recommended by (Elbourne 2002). It is common that the analysis and presentation of results from cross-over studies are often not appropriate or clear, leading to limited data being available for analysis (Nolan 2016). This was true for most of the studies included in this review and since only limited data were available, the authors used only the first-arm data from the studies in order to avoid the carry-over effect (Curtin 2002). As results were not presented from paired analyses for one study (Pfleger 1992), we treated this cross-over study as if it was a parallel study, which is a conservative approach as it does not take into account within-patient correlation.

Cluster-randomised studies are not appropriate for this intervention. Where we have included studies with multiple treatment groups, each comparison is presented in a separate analysis.

Dealing with missing data

The review authors contacted the authors of included studies regarding all missing data. If the study authors had been unavailable or the additional data were insufficient for analysis, the review authors planned to include a

narrative description of the study in the review. The review authors contacted two teams of investigators and obtained additional data ([Mcllwaine 1991](#); [Osman 2010](#)).

Assessment of heterogeneity

For studies which investigated the effect of similar interventions on similar participants and assessed similar outcomes (clinically homogenous), the authors planned to pool the data in a meta-analysis. However, it was not possible to combine data for any outcome measure. If there had been heterogeneity, the authors planned to assess this using the Chi² test and the I² statistic (with CIs) ([Higgins 2003](#)). The authors planned to regard heterogeneity as low if I² was less than 25%, moderate if I² was between 25% and 50% and substantial if I² was over 50%.

Assessment of reporting biases

The review authors planned to use funnel plots to assess any reporting bias if there had been a sufficient number of studies included (a minimum of 10 studies required for the assessment of biases). Had there been asymmetry in the funnel plot, the authors intended to explore the possibility of small study effects and heterogeneity as a cause, as well as outcome reporting bias.

Outcome reporting bias can occur when studies measure outcomes, but do not publish all of them, giving rise to misleading results ([Kirkham 2010](#)). The authors compared the 'Methods' section of each paper to the 'Results' section to ensure all outcomes were reported. If they had suspected outcome reporting bias, they would have contacted the study authors for the data.

Data synthesis

The authors analysed the data using a fixed-effect model, since there was no evidence of substantial heterogeneity between the included studies. If they identify substantial heterogeneity in future updates of the review, they plan to use a random-effects model.

Subgroup analysis and investigation of heterogeneity

We were not able to combine data from multiple studies in an analysis, therefore an assessment of heterogeneity was not possible. In case of moderate to substantial levels of heterogeneity between the included studies, the authors planned to perform the following subgroup analyses:

1. age (paediatric, adolescent and adults as defined by the study investigators);
2. severity of the disease based on lung function (FEV₁ % predicted: above 90%; 70% to 89%; 40% to 69%; under 40%);
3. participants with acute exacerbations in comparison with stable CF.

However, since we were unable to combine data from multiple studies, we have not undertaken any subgroup analysis.

Sensitivity analysis

If the authors had been able to combine studies and had established that some of these studies were judged to have a high risk of bias, in order to test the robustness of their findings they planned to undertake a sensitivity analysis excluding these studies as long as at least two studies would still be combined after any exclusions. However, since we were unable to combine data from multiple studies, we have not undertaken any sensitivity analysis.

Summary of findings table

As a post hoc change, the current author team present summary of findings tables for each comparison of the review. The primary outcomes of the review and the first five secondary outcomes (participant preference, exercise tolerance, adverse effects (e.g. haemoptysis, bronchospasm, desaturation), number of admissions to hospital, need for extra treatment) are presented in the tables and the quality of the evidence for each outcome of each comparison is assessed using GRADE methodology ([Schünemann 2011](#)).

Results

Description of studies

Results of the search

A total of 35 references to 21 individual studies were retrieved through electronic searches. Seven of these studies were considered as eligible for inclusion following screening ([App 1998](#); [Mcllwaine 1991](#); [Mcllwaine 2010](#); [Miller 1995](#); [Osman 2010](#); [Pfleger 1992](#); [Pryor 2010](#)). Of note, the authors have included one study ([App 1998](#)) using a German modification of the AD technique ([David 1991](#)). Whilst the intervention may not have been strictly to the guidance of Jean Chevallier's description using three distinct breathing phases, it was felt the technique used was similar and this study should be included in the evidence. A total of 12 studies were excluded ([Giles 1995](#); [Herrero 2016](#); [Lindemann 1992](#); [NCT01885650](#); [NCT02303808](#); [Reix 2012](#); [Roos 1987](#); [Skopnik 1986](#); [van Ginderdeuren 2001](#); [van Ginderdeuren 2008](#); [van Ginderdeuren 2011](#); [Warwick 1990](#)). Two studies are awaiting classification ([Davies 2012](#); [Vendrusculo 2017](#)).

The process of the search and study selection is documented in the PRISMA diagram ([Figure 1](#)).

Included studies

Study characteristics

One randomised study was of parallel design ([Pryor 2010](#)). The remaining six studies were of cross-over design; in five

of these a two-arm design was used ([App 1998](#); [Mcllwaine 2010](#); [Miller 1995](#); [Osman 2010](#); [Pfleger 1992](#)) and in one study a three-arm design was used ([Mcllwaine 1991](#)). A washout period was described in three of these studies, varying in length between one week ([App 1998](#); [Miller 1995](#)) and one month ([Mcllwaine 1991](#)). A total of 208 participants were randomised with participant numbers varying between studies; 17 participants in the smallest study ([App 1998](#)) and 75 participants in the largest study ([Pryor 2010](#)). The total study duration varied between four days ([Miller 1995](#)) and two years ([Mcllwaine 2010](#)). The majority of studies, six in total, were single-centre studies; three were based in the UK ([Miller 1995](#); [Osman 2010](#); [Pryor 2010](#)), two in Canada ([Mcllwaine 1991](#); [Mcllwaine 2010](#)) and one in Austria ([Pfleger 1992](#)). The remaining study was a multicentre study based in Germany ([App 1998](#)).

Participants

One study was conducted in children ([Mcllwaine 2010](#)), two in adults ([Osman 2010](#); [Pryor 2010](#)) and four in both adults and children ([App 1998](#); [Mcllwaine 1991](#); [Miller 1995](#); [Pfleger 1992](#)). The age of participants ranged between seven years and 63 years. The gender of participants was reported in six of the studies with a ratio of 108 males to 79 females ([App 1998](#); [Mcllwaine 2010](#); [Miller 1995](#); [Osman 2010](#); [Pfleger 1992](#); [Pryor 2010](#)). The inclusion criteria in one study was a hospital admission with an infective pulmonary exacerbation ([Osman 2010](#)), whereas in the remaining six studies participants were clinically stable. One study did not report any measure of disease severity of the included participants ([App 1998](#)). Lung function at baseline was described in three studies: one study reported a wide range in FVC (38% to 117%) ([Mcllwaine 1991](#)); one measured FEV₁ in litres with a range of 1.9 L to 2.6 L ([Pryor 2010](#)); and one study reported a mean FEV₁ of 38% ([Osman 2010](#)). Four studies reported Shwachman scores as a measure of disease severity and each study reported participants with a wide range of scores ([Mcllwaine 1991](#); [Mcllwaine 2010](#); [Miller 1995](#); [Pfleger 1992](#)).

Interventions

Each of the seven studies varied in their treatment comparisons. Three studies compared AD to PEP ([Mcllwaine 1991](#); [Pfleger 1992](#); [Pryor 2010](#)), three studies compared AD to PD&P or just PD ([Mcllwaine 1991](#); [Mcllwaine 2010](#); [Miller 1995](#)), two studies compared AD to Flutter® ([App 1998](#); [Pryor 2010](#)), one study compared AD to the Cornet® ([Pryor 2010](#)), two studies compared AD to ACBT ([Miller 1995](#); [Pryor 2010](#)) and one study compared participants' normal airway clearance technique (which included AD) to HFCWO ([Pryor 2010](#)).

In three studies, the duration of each treatment arm was less than seven days ([Miller 1995](#); [Osman 2010](#); [Pfleger 1992](#)). In the remaining studies, the duration of each treatment arm ranged from four weeks to one year ([App 1998](#); [Mcllwaine 1991](#); [Mcllwaine 2010](#); [Pryor 2010](#)).

Outcomes measured

Lung function, specifically FEV₁, was the most common outcome measure used and was included in each of the seven studies. Six of the seven studies also measured FVC and three of the studies used FEF_{25-75%} as an outcome ([Mcllwaine 1991](#); [Mcllwaine 2010](#); [Miller 1995](#)). Six studies reported sputum weight or volume ([App 1998](#); [Mcllwaine 1991](#); [Mcllwaine 2010](#); [Miller 1995](#); [Osman 2010](#); [Pfleger 1992](#)). Less commonly used outcomes were oxygen saturation ([Miller 1995](#); [Osman 2010](#)), participant preference ([Mcllwaine 1991](#); [Mcllwaine 2010](#); [Miller 1995](#); [Osman 2010](#)), QoL measures ([Mcllwaine 1991](#); [Osman 2010](#); [Pryor 2010](#)), hospital admissions or intravenous antibiotic therapy ([Mcllwaine 2010](#); [Pryor 2010](#)). LCI has not been measured in any of the studies to date.

Excluded studies

A total of 10 studies were excluded ([Giles 1995](#); [Herrero 2016](#); [Lindemann 1992](#); [Reix 2012](#); [Roos 1987](#); [Skopnik 1986](#); [van Ginderdeuren 2001](#); [van Ginderdeuren 2008](#); [van Ginderdeuren 2011](#); [Warwick 1990](#)). The authors felt it was difficult to assess the relevance of a single treatment session using AD and consequently excluded three studies using this criteria ([Giles 1995](#); [Herrero 2016](#); [Lindemann 1992](#)). One study had not been completed when the abstract was published and no further associated abstracts or papers were found despite correspondence with the study team ([Roos 1987](#)). In three studies the authors considered the intervention not appropriate for this review ([Reix 2012](#); [van Ginderdeuren 2001](#); [Warwick 1990](#)). Two studies evaluated inhalation rather than AD ([van Ginderdeuren 2008](#); [van Ginderdeuren 2011](#)) and in the final study there was no evidence of randomisation ([Skopnik 1986](#)).

Studies awaiting classification

Two studies are listed as 'awaiting classification' ([Davies 2012](#); [Vendrusculo 2017](#)). One is an RCT of parallel design ([Davies 2012](#)). It is a single-centre study based in the UK comparing participants' usual airway clearance technique (including AD) to airway clearance using an oscillating device in hospitalised participants (aged 16 years and over) admitted with a pulmonary infection and FEV₁ of 15% predicted or over. The primary outcome measure is the mean % change in FEV₁; ad secondary outcome measures include wet weight of sputum expectorated in 24 hours, length of time to next course of intravenous antibiotics and the rate of change of C-reactive protein. The second is an RCT of cross-over design ([Vendrusculo 2017](#)). It compares cardiopulmonary exercise testing with and without the use of an airway clearance technique (including AD) prior to the test. It is not clear in either of these studies how many participants were using AD and whether we will be able to obtain the specific data for these participants.

Risk of bias in included studies

We used the approach for assessing the risk of bias in included studies recommended by Cochrane ([Higgins 2011](#)) and described above ([Assessment of risk of bias in included studies](#)).

The 'Risk of bias graph' illustrates the proportion of studies with each of the judgements for each entry in the tool ([Figure 2](#)), whilst the 'Risk of bias summary' presents the review authors' judgements in a cross-tabulation of study by entry ([Figure 3](#)). Further details can be found in the risk of bias sections of the tables describing the [Characteristics of included studies](#).

Allocation (selection bias)

Sequence generation

In four of the seven included studies, the authors failed to specify how the randomisation sequence was generated. These papers stated that participants had been randomly assigned to different treatment groups, but did not clearly define the means of doing so; hence the risk of bias for sequence generation was unclear in these studies ([App 1998](#); [Mcllwaine 1991](#); [Miller 1995](#); [Pfleger 1992](#)). Three studies employed computer randomisation to determine treatment allocation ([Mcllwaine 2010](#); [Osman 2010](#); [Pryor 2010](#)), thus their risk of bias due to the sequence generation was deemed to be low.

Allocation concealment

None of the included studies discussed allocation concealment and we judged all to have an unclear risk of bias ([App 1998](#); [Mcllwaine 1991](#); [Mcllwaine 2010](#); [Miller 1995](#); [Osman 2010](#); [Pfleger 1992](#); [Pryor 2010](#)).

Blinding (performance bias and detection bias)

The airway clearance techniques being compared require the individual's participation and, on occasion, the use of manual techniques or mechanical devices. It is not possible to blind by design and, in this respect, all of the included studies were deemed to carry a similarly low risk of bias. Conversely, the extent to which the lack of blinding may have had an effect is unclear, particularly on the reporting of subjective outcomes such as individual preference ([Mcllwaine 1991](#); [Miller 1995](#)) or QoL ([Mcllwaine 1991](#); [Osman 2010](#); [Pryor 2010](#)). It is feasible, however, to blind the individuals collecting data or assessing outcomes to the allocated treatment group.

Five studies identified that some or all of the outcome assessors had been blinded and were, therefore, considered to carry a low risk of bias in this respect ([Mcllwaine 1991](#); [Mcllwaine 2010](#); [Osman 2010](#); [Pfleger 1992](#); [Pryor 2010](#)). In two studies the clinical assessment was carried out by a CF physician blind to the physiotherapy technique being performed ([Mcllwaine 1991](#); [Mcllwaine 2010](#)). In another, both the physician and the pulmonary function technician had been blinded ([Mcllwaine 2010](#)). Two papers stated that a blinded, independent investigator or observer had assessed one or more of the outcome measures ([Osman 2010](#); [Pfleger 1992](#)). Only one paper, however, noted that both the data collection and the statistical analysis had been performed by blinded observers ([Pryor 2010](#)). Two studies did not discuss the issue of blinding of outcome assessors and, thus, their risk of bias was deemed unclear ([App 1998](#); [Miller 1995](#)).

Incomplete outcome data (attrition bias)

Participant dropout was the primary reason for incomplete outcome data. Only a single study lasting four days had no withdrawals and all participants were analysed in the groups to which they were assigned ([Miller 1995](#)). Reasons for withdrawals were described for the remaining studies and, with the exception of one paper ([Mcllwaine 2010](#)), were judged to have a low risk of bias in this respect.

In addition to the Miller study, only one other paper explicitly carried out an intention-to-treat analysis for the primary outcome of FEV₁ ([Pryor 2010](#)). However, 13 participants in the Pryor study did not like the intervention to which they had been allocated and withdrew from the study; it is unclear whether these participants were included in the intention-to-treat group. The use of an intention-to-treat analysis was unclear for the remainder of the included studies ([App 1998](#); [Mcllwaine 1991](#); [Mcllwaine 2010](#); [Osman 2010](#); [Pfleger 1992](#)).

All six studies reporting withdrawals gave reasons for these ([App 1998](#); [Mcllwaine 1991](#); [Mcllwaine 2010](#); [Osman 2010](#); [Pfleger 1992](#); [Pryor 2010](#)). Withdrawal rates ranged from 3.3% of participants ([Osman 2010](#)) to an overall attrition of 44.4% in the case of the longest study ([Mcllwaine 2010](#)). It should be pointed out that in the Mcllwaine study withdrawals at the end of the first year comprised 13.9% of the participants, but attrition increased to 33.3% of those remaining for the second year of the study ([Mcllwaine 2010](#)). The reason for this increase following the crossing over to the alternate treatment was related to a large number of participants not returning for the PD&P arm of the study due to a preference to continue with AD. This, together with the strong cross-over effect of a further seven participants who continued with the study whilst incorporating AD into PD&P, biased the second arm of the study.

Selective reporting (reporting bias)

As the study protocols were unavailable, selective reporting was assessed by comparing the outcomes listed in the 'Methods' section with those of the 'Results' section from each study.

Two studies were considered as having a high risk of selective reporting ([Mcllwaine 2010](#); [Pryor 2010](#)). In one study, relevant baseline characteristics such as FVC and Huang scores were omitted and adherence, which had been closely monitored throughout, was not reported ([Mcllwaine 2010](#)). Similarly, the duration of hospital admissions was recorded but not reported. The Huang scoring system is applied pre- and post-treatment to evaluate the therapeutic response to the intervention being studied, taking into account 20 separate items; 10 clinical, five radiographic and five pulmonary function parameters. The lower the score, the more severe the disease ([Huang 1981](#)). In the second study, lung function and BMI data were not reported at the six-month time frame as had been stated in the 'Methods' for the study ([Pryor 2010](#)).

We judged one study to have an unclear risk of selective reporting ([App 1998](#)). In this study blood oxygen saturation levels were recorded during the study but were not commented on in the paper. As there is no published data available to reflect whether this parameter changed over the course of the study or as a result of any intervention received, the risk of selective reporting is deemed to be unclear ([App 1998](#)).

In the four remaining studies, all outcomes described in the 'Methods' section were reported in the 'Results' section, thus there is a low risk of bias from selective reporting associated with these studies ([Mcllwaine 1991](#); [Miller 1995](#); [Osman 2010](#); [Pfleger 1992](#)).

Other potential sources of bias

In one cross-over study, those carrying out AD were asked to perform AD breathing exercises during the inhalation of their pre-treatment nebuliser ([Miller 1995](#)). However, those performing ACBT were asked to breathe normally during the nebulisation period, potentially introducing bias in the form of an "extra" eight minutes of treatment time for the AD group. No statistically significant differences were found between the two treatment groups for any of the outcomes measured. Despite this, the risk of bias was deemed to be high as the stated treatment time for the two groups was unequal, favouring the AD group.

Out of six cross-over studies, only three of them reported washout periods between treatment arms; these varied between one week ([App 1998](#); [Miller 1995](#)) and one month ([Mcllwaine 1991](#)). The ideal length of washout periods is unknown, but the risk of bias due to carryover effects is certainly higher in short-term studies lacking any washout period ([Pfleger 1992](#); [Osman 2010](#)) and of less significance in long-term studies lasting two years ([Mcllwaine 2010](#)). However, in the case of those participating in a four-day cross-over study during an acute respiratory exacerbation, a washout period is likely to be impractical due to rapid clinical improvements during a hospital admission ([Osman 2010](#)).

One study was supported by Hill-Rom (manufacturer of the oscillating VEST®) and a grant from the Robert Luff Foundation ([Osman 2010](#)). This may be considered as a source of bias. Although Hill-Rom provided devices and equipment for the study, they did not participate in the design, collection, analysis, interpretation of data or in the writing of the manuscript. Thus, the risk of bias was deemed to be unclear.

Effects of interventions

Autogenic drainage versus conventional physiotherapy

Two studies (54 participants) reported on this comparison of AD versus PD&P ([Mcllwaine 1991](#); [Mcllwaine 2010](#)).

Primary outcomes

1. FEV₁

Both studies measured FEV₁ ([Mcllwaine 1991](#); [Mcllwaine 2010](#)), but only data from the later study were available for our analysis ([Mcllwaine 2010](#)). In this study, the rate of decline in FEV₁ % predicted for each participant was determined over the one-year study period. At the 12-month time point, our analysis found no statistically significant difference between AD and PD&P, MD -1.12 (95% CI -2.64 to 0.40) (very low quality evidence) ([Analysis 1.1](#)). In the earlier Mcllwaine study, lung function was measured as % change from baseline for each of three two-month treatment periods using AD, PEP and PD&P (results for the AD versus PEP arm are reported below). There were no statistically significant changes in FEV₁/FVC between the AD and PD&P treatment periods ([Mcllwaine 1991](#)).

2. QoL

Questionnaires incorporating a Likert scale 0 - 10 were used to gauge comfort, level of control and degree of interruption in their daily life (very low quality evidence). Participants subjectively reported AD to be superior to PD&P ([Mcllwaine 1991](#)). In the later study, the participants subjectively felt that AD "worked the best" and the authors reflected that, collectively, AD gave the participants more independence and a greater amount of freedom in performing their physiotherapy treatment when compared to PD&P ([Mcllwaine 2010](#)).

Secondary outcomes

1. Participant preference

The later Mcllwaine study reported a preference for AD by all participants in the study, with many participants refusing to go back to performing PD&P (very low quality evidence) ([Mcllwaine 2010](#)).

2. Exercise tolerance

Neither study reported on this outcome ([Mcllwaine 1991](#); [Mcllwaine 2010](#)).

3. Adverse effects

Neither study reported on this outcome ([Mcllwaine 1991](#); [Mcllwaine 2010](#)).

4. Number of admissions

Only the later study reported on this outcome and provided data to enter into our analysis ([Mcllwaine 2010](#)). The authors did not specify the number of separate individuals admitted to hospital for pulmonary exacerbations, although they did state that the total number of hospitalisations per group by the 12-month time point (13 for the AD group, 16 for the PD&P group) (very low quality evidence). The published paper reported that mean number of hospital admissions was not significantly lower in the AD group compared to the PD&P group; however, in contrast, our analysis shows the mean number of hospital admissions during the first year of the study was significantly lower

in the AD group, MD -0.24 (95% CI -0.42 to -0.06) ([Analysis 1.2](#)). The reason for this statistical discrepancy remains unclear and as we have been unable to further clarify this with the authors of the article, these results should be interpreted with caution.

5. Need for extra treatment

The later Mcllwaine study described 16 hospitalisations for pulmonary exacerbations in the PD&P group compared to 13 in the AD group in the first year of the study (there were 18 participants in each group), but the authors did not specify the number of separate individuals from each group who were hospitalised. The investigators did report that no participants received home intravenous antibiotic treatment (very low quality evidence) ([Mcllwaine 2010](#)).

6. Pulmonary function measurements

a. LCI

This outcome was not measured in either study ([Mcllwaine 1991](#); [Mcllwaine 2010](#)).

b. FVC

Both studies measured FVC ([Mcllwaine 1991](#); [Mcllwaine 2010](#)), but only data from the later study were available for our analysis ([Mcllwaine 2010](#)). In this study, the change in FVC % predicted was determined over the 12-month study period and analysed as a parallel study with no statistically significant changes being reported between the treatment methods. In contrast to the published paper, our analysis shows statistical significance in favour of AD, MD 1.88 (95% CI 0.68 to 3.08) ([Analysis 1.3](#)). The reason for this statistical discrepancy remains unclear and as we have been unable to clarify with the authors of the article, these results should be interpreted with caution. In the earlier Mcllwaine study, FVC was measured as % change from baseline for each two-month treatment period using AD and PD&P and there were no significant changes found between the treatment methods ([Mcllwaine 1991](#)).

c. FEF_{25-75%}

Both studies measured FEF_{25-75%} ([Mcllwaine 1991](#); [Mcllwaine 2010](#)), but only data from the later study were available for our analysis ([Mcllwaine 2010](#)). In this study, the change in FEF_{25-75%} predicted was determined over the 12-month study period and analysed as a parallel study with no statistically significant changes being reported between the treatment methods. In contrast to the published paper, our analysis shows statistical significance in favour of PD&P, MD -7.54 (95% CI -10.39 to -4.69) ([Analysis 1.4](#)). Once again, the reason for this statistical discrepancy remains unclear and as we have been unable to further clarify this with the authors of the article, these results should be interpreted with caution. In the earlier Mcllwaine study, FEF_{25-75%} was measured as % change from baseline for each two-month treatment period using AD and PD&P and there were no significant changes found between the treatment methods ([Mcllwaine 1991](#)).

7. Oxygen saturation

Neither study reported on this outcome ([Mcllwaine 1991](#); [Mcllwaine 2010](#)).

8. Sputum weight

Only the earlier study measured sputum weight ([Mcllwaine 1991](#)). The paper reported that the net weight of sputum produced during AD was significantly greater ($P < 0.01$) than that produced during PD&P, but data were not reported in sufficient detail to enter into our analysis ([Mcllwaine 1991](#)). It was noted that sputum production whilst using AD was relatively consistent over the two-month study period.

9. Survival

Neither study reported on this outcome ([Mcllwaine 1991](#); [Mcllwaine 2010](#)).

Autogenic drainage versus spontaneous cough

One study (14 participants) used cough alone in a comparison with AD ([Pfleger 1992](#)).

Primary outcomes

1. FEV₁

There were no significant differences in FEV₁ % predicted between AD and cough alone when measured at 30 minutes post physiotherapy, MD 3.00% (95% CI -11.08 to 17.08) (very low quality evidence) ([Analysis 2.1](#)) ([Pfleger 1992](#)).

2. QoL

The study did not report on this outcome ([Pfleger 1992](#)).

Secondary outcomes

1. Participant preference

The study did not report on this outcome ([Pfleger 1992](#)).

2. Exercise tolerance

The study did not report on this outcome ([Pfleger 1992](#)).

3. Adverse effects

No adverse effects were reported in this study (very low quality evidence) ([Pfleger 1992](#)).

4. Number of admissions

The study did not report on this outcome ([Pfleger 1992](#))

5. Need for extra treatment

The study did not report on this outcome ([Pfleger 1992](#))

6. Pulmonary function measurements*a. LCI*

This outcome was not measured in this study ([Pfleger 1992](#)).

b. FVC

There were no significant differences in FVC % predicted between the treatment groups when measured at 30 minutes post physiotherapy, MD 4.00% (95% CI -10.83 to 18.83) ([Analysis 2.2](#)) ([Pfleger 1992](#)).

c. FEF_{25-75%}

Pfleger did not report on this outcome ([Pfleger 1992](#)).

7. Oxygen saturation

The study did not report on this outcome ([Pfleger 1992](#)).

8. Sputum weight

Pfleger compared cough alone with AD and Hi-PEP alone and in combination (Hi-PEP results not reported here). It was reported that all four forms of physiotherapy used in this study produced significantly more sputum than spontaneous coughing alone ($P < 0.001$) and our statistical analysis corroborates this, MD 18.33 g (95% CI 3.11 to 33.55) ([Analysis 2.3](#)). However, sputum production with AD alone was the lowest and differed significantly from that of the other physiotherapy treatment groups ([Pfleger 1992](#)).

9. Survival

The study did not report on this outcome ([Pfleger 1992](#)).

Autogenic drainage versus active cycle of breathing technique

Two studies (48 participants) reported on this comparison ([Miller 1995](#); [Pryor 2010](#)). Although 75 participants were included overall in the Pryor study, only 15 were randomised to each of the five treatment groups; therefore the study only contributes 30 participants to this pair-wise comparison ([Pryor 2010](#)).

Primary outcomes**1. FEV₁**

Both studies reported on FEV₁, but data were only available from one study for FEV₁ (L) for our analysis ([Pryor 2010](#)). Pryor reported data at three time points over the 12-month period of the study - at the start, at six months and at 12 months ([Pryor 2010](#)). At the 12-month time point, our analysis found no statistically significant difference between the AD and ACBT groups, MD 0.70 L (95% CI -0.09 to 1.49) (very low quality evidence) ([Analysis 3.1](#)). Pryor also reported FEV₁ % predicted and overall observed a significant deterioration in FEV₁ % predicted over the 12-month period for the entire cohort (-1.8% predicted; $P = 0.02$), stating this decline was within the international average at the time of the study ([Pryor 2010](#)). However, recruitment was challenging for this long-term study, meaning it was underpowered to detect such a change. Consequently, the results obtained may have over or underestimated any decline in lung function identified by the original authors.

Miller (18 participants) measured lung function prior to and following each physiotherapy treatment over the four-day period of the study, but FEV₁ was not reported specifically ([Miller 1995](#)). The paper stated that taken overall, pulmonary function tests showed no significant difference between the two methods.

2. QoL

Health-related QoL was measured in one study using the Short Form-36 (Medical Outcomes Trust, Boston, USA), analysing the physical and mental domains of the participants (low quality evidence) ([Pryor 2010](#)). There were no significant differences in the physical domain between the groups, though the paper observed that overall there was a trend towards deterioration over time reported ($P = 0.05$). Similarly, in the mental domain there were no significant differences found amongst the groups but there was a significant deterioration over time reported ($P = 0.002$).

Pryor also analysed data for the four domains of dyspnoea, fatigue, emotion and mastery in the Chronic Respiratory Questionnaire (CRQ) ([Guyatt 1987](#)); but found no significant differences in any domain, although there was a significant improvement in dyspnoea ($P = 0.01$) reported over time in the group as a whole ([Pryor 2010](#)).

Secondary outcomes**1. Participant preference**

Miller reported that nine participants preferred AD, eight participants preferred ACBT, and one participant had no preference ([Miller 1995](#)). They went on to qualify that those who preferred AD to ACBT tended to be those who displayed a greater concentration and compliance with treatment. During the course of the Pryor study, 13 participants withdrew as they did not like the regimen to which they had been randomised and either reverted to their original

preferred option or chose a different regimen; the intervention each participant was using was not identified ([Pryor 2010](#)). The quality of the evidence from both these studies was very low.

2. Exercise tolerance

The modified shuttle test was reported in one study (30 participants), but no data were available for our analysis ([Pryor 2010](#)). No significant difference was found between AD and ACBT (low quality evidence).

3. Adverse effects

Miller described a decrease in oxygen saturation levels whilst performing ACBT in the moderate to severe group of participants, but not during any AD sessions ([Miller 1995](#)). The authors did not quantify the extent but did report that in three participants, one episode was observed and in a fourth participant two episodes were reported (both morning and afternoon ACBT sessions) (very low quality evidence).

4. Number of admissions

Neither study reported on this outcome ([Miller 1995](#); [Pryor 2010](#)).

5. Need for extra treatment

In the Pryor study, some participants in each of the regimens required intravenous antibiotics during the course of the study; the median number of courses per group ranged from 1.0 to 1.5 (low quality evidence) ([Pryor 2010](#)). The number of participants and allocated treatment arm was not specified.

6. Pulmonary function measurements

a. LCI

This outcome was not measured in either study ([Miller 1995](#); [Pryor 2010](#)).

b. FVC

Neither study reported this outcome in sufficient detail to enter into our analysis, but both studies reported there was no statistically significant difference between the two methods ([Miller 1995](#); [Pryor 2010](#)). However, Miller reported that more participants demonstrated an improved FVC with ACBT than AD ([Miller 1995](#)).

c. FEF_{25-75%}

This outcome was reported in one study (18 participants), but not in sufficient detail for inclusion in our analysis ([Miller 1995](#)). The investigators stated that more participants had an improved FEF_{25-75%} with AD than with the ACBT.

7. Oxygen saturation

Oxygen saturation levels were reported in one study (18 participants), but no data were available for our analysis ([Miller 1995](#)). There was no difference found in mean saturation levels of oxygen between the treatment methods over the four study days. However, four participants with moderate to severe disease decreased their oxygen saturation levels during the morning ACBT session, and one also demonstrating a decrease in the afternoon session. Participants maintained their oxygen saturation levels during AD sessions.

8. Sputum weight

Sputum weight was an outcome used in one study (18 participants), but no data were available for our analysis ([Miller 1995](#)). Sputum was collected and weighed during one hour following physiotherapy treatment. There was no significant difference found between the AD and ACBT groups.

9. Survival

One participant died during the course of the Pryor study and the allocated treatment arm was not specified; however, the investigators stated that the death was unlikely to have been caused by any intervention under evaluation ([Pryor 2010](#)).

Autogenic drainage versus positive expiratory pressure

A total of three studies (62 participants) reported on this comparison ([Mcllwaine 1991](#); [Pfleger 1992](#); [Pryor 2010](#)). Although 75 participants were included overall in the Pryor study, only 15 were randomised to each of the five treatment groups; therefore the study only contributes 30 participants to this pair-wise comparison ([Pryor 2010](#)). Two studies compared AD with PEP ([Mcllwaine 1991](#); [Pryor 2010](#)) and one study compared AD to Hi-PEP ([Pfleger 1992](#)).

Primary outcomes

1. FEV₁

All three studies (62 participants) reported on FEV₁ as an outcome, but used different units of measurement and we were unable to combine any data ([Mcllwaine 1991](#); [Pfleger 1992](#); [Pryor 2010](#)).

Pryor reported FEV₁ (L) at the start and end of the 12-month study period ([Pryor 2010](#)). At the 12-month time point, our analysis found no statistically significant difference between the AD and PEP groups, MD 0.62 L (95% CI -0.30 to 1.54) (low quality evidence) ([Analysis 4.1](#)).

Pryor also reported FEV₁ % predicted and, overall, observed a significant deterioration in FEV₁ % predicted over the 12-month period for the entire cohort (-1.8% predicted; P = 0.02), stating this decline was within the international average at the time of the study ([Pryor 2010](#)). However, recruitment was challenging for this long-term study, meaning it was underpowered to detect such a change. Consequently, the results obtained may have over or underestimated any

decline in lung function identified by the original authors. Pflieger reported FEV₁ % predicted was measured repeatedly before, during and after physiotherapy treatments over the five-day study period (Pflieger 1992); our analysis found no statistically significant difference between AD and Hi-PEP at 30 minutes following physiotherapy, MD 2.00% predicted (95% CI -12.45 to 16.45) (Analysis 4.2). Finally, in the three-arm study, Mcllwaine measured FEV₁ % predicted at the outset and at the beginning and end of each of the three two-month study periods; investigators reported no significant difference in FEV₁/FVC when each group performed either AD or PEP, but no data were available for our analysis (Mcllwaine 1991).

2. QoL

Pryor (n = 30) evaluated QoL as an outcome using the Short Form-36 and CRQ (low quality evidence) (Pryor 2010). For the Short Form-36 there were no significant differences in the physical domain between the two groups, but overall the paper reported that there was a significant trend towards deterioration over time; similarly, in the mental domain there were no significant differences found, but there was a significant deterioration reported over time. For the CRQ there were no significant differences found for dyspnoea, fatigue, emotion or mastery between the two groups. Overall, there was a significant improvement in dyspnoea (P = 0.01) reported over time in the group as a whole (Pryor 2010).

Secondary outcomes

1. Participant preference

During the course of the Pryor study (n = 30), 13 participants withdrew as they did not like the regimen to which they had been randomised and either reverted to their original preferred option or chose a different regimen (low quality evidence). The intervention each was using at the time was not identified (Pryor 2010).

2. Exercise tolerance

The modified shuttle test was reported in one study (30 participants), but no data were available for our analysis (Pryor 2010). No significant difference was reported between AD and PEP.

3. Adverse effects

None of the studies reported on this outcome (Mcllwaine 1991; Pflieger 1992; Pryor 2010).

4. Number of admissions

None of the studies reported on this outcome (Mcllwaine 1991; Pflieger 1992; Pryor 2010).

5. Need for extra treatment

Pryor reported some participants in each of the regimens required intravenous antibiotics during the course of the study. The number of participants and allocated treatment arm was not specified (Pryor 2010). The median number of courses per group ranged from 1.0 to 1.5, though statistical analysis was not carried out due to the small numbers and scattered nature of the data (low quality evidence).

6. Pulmonary function measurements

a. LCI

This outcome was not measured in any study (Mcllwaine 1991; Pflieger 1992; Pryor 2010).

b. FVC

All three studies (62 participants) measured FVC, but data were only available from one study for FVC % predicted which was measured 30 minutes following physiotherapy (Pflieger 1992). Our analysis found no statistically significant difference between the AD and Hi-PEP groups, MD 1.00% (95% CI -13.45 to 15.45) (Analysis 4.3). There were no significant changes in FVC found in either of the remaining studies when using AD or PEP (Mcllwaine 1991; Pryor 2010).

c. FEF_{25-75%}

One study (18 participants) reported FEF_{25-75%}, but not in sufficient detail to include in our analysis; the investigators reported no statistically significant changes between AD and PEP (Mcllwaine 1991).

7. Oxygen saturation

None of the studies reported on this outcome (Mcllwaine 1991; Pflieger 1992; Pryor 2010).

8. Sputum weight

Two studies (32 participants) used sputum weight as an outcome (Mcllwaine 1991; Pflieger 1992). Data were only available from one study (14 participants) for our analysis (Pflieger 1992). The review authors estimated this data from a bar chart in the published article, demonstrating that AD showed the lowest sputum production and PEP the highest (Pflieger 1992). Our analysis of sputum weight following physiotherapy treatment showed a numerical advantage to PEP, but found no statistically significant differences between the AD and PEP groups, MD -15.00 g (95% CI -35.46 to 5.46) (Analysis 4.4). This, however, contrasts with the published paper, which states statistical significance in favour of PEP (Pflieger 1992). The data extracted were approximate and measured from the graph of sputum production, so this probably accounts for the discrepancy with the results in the published paper.

In one of the three published abstracts relating to the Mcllwaine study (presented at the 17th European Cystic Fibrosis Conference), the authors reported the net weight of sputum obtained was significantly greater (P < 0.01)

with AD compared to PEP, but the remaining two abstracts do not state this ([McIlwaine 1991](#)). The unpublished paper which we obtained from the authors does not fully clarify the matter and we will attempt to address these discrepancies in a future update. However, it was noted that sputum production whilst using AD was relatively consistent over the two-month study period.

9. Survival

One participant died during the course of the Pryor study and the allocated treatment arm was not specified; however, the investigators stated that the death was unlikely to have been caused by any intervention under evaluation ([Pryor 2010](#)).

Autogenic drainage versus Cornet®

One study (30 participants) reported on this comparison ([Pryor 2010](#)). Although 75 participants were included overall in the Pryor study, only 15 were randomised to each of the five treatment groups; therefore the study contributes 30 participants ([Pryor 2010](#)).

Primary outcomes

1. FEV₁

Pryor reported FEV₁ (L) data at the start and end of the 12-month study period that was available to enter into our analysis ([Pryor 2010](#)). At the 12-month time point our analysis found no statistically significant difference between the AD and Cornet® groups, MD 0.74 L (95% CI -0.07 to 1.55) (moderate quality evidence) ([Analysis 5.1](#)). Pryor also reported FEV₁ % predicted and, overall, observed a significant deterioration in FEV₁ % predicted over the 12-month period for the entire cohort (-1.8% predicted; P = 0.02), stating this decline was within the international average at the time of the study ([Pryor 2010](#)). However, recruitment was challenging for this long term study, meaning it was underpowered to detect such a change. Consequently, the results obtained may have over or underestimated any decline in lung function identified by the original authors.

2. QoL

Pryor used the Short Form-36 questionnaire and the CRQ and found no significant difference in the domains between the two groups (low quality evidence) ([Pryor 2010](#)). The results of the CRQ reported minimal clinically important differences (improvements) in dyspnoea in the AD group, but not the Cornet® group over the 12-month study period. However, there was an overall significant improvement in dyspnoea (P = 0.01) reported over time in the entire cohort.

Secondary outcomes

1. Participant preference

During the course of the Pryor study, 13 out of 75 participants withdrew as they did not like the regimen to which they had been randomised and either reverted to their original preferred option or chose a different regimen (low quality evidence) ([Pryor 2010](#)). The intervention each was using at the time was not identified.

2. Exercise tolerance

Pryor measured exercise tolerance using the Modified Shuttle Test and no significant difference was found between AD and Cornet® groups ([Pryor 2010](#)). No detailed data were available for our analysis.

3. Adverse effects

Pryor did not report this outcome ([Pryor 2010](#)).

4. Number of admissions

Pryor did not report this outcome ([Pryor 2010](#)).

5. Need for extra treatment

Pryor reported that some participants in each of the regimens required intravenous antibiotics during the course of the study ([Pryor 2010](#)). The median number of courses per group ranged from 1.0 to 1.5, though statistical analysis was not carried out due to the small numbers and scattered nature of the data (low quality evidence). The number of participants and allocated treatment arm was not specified.

6. Pulmonary function measurements

a. LCI

Pryor did not report this outcome ([Pryor 2010](#)).

b. FVC

Pryor reported no significant difference in FVC (L) between AD and Cornet®, but no detailed data were available for our analysis ([Pryor 2010](#)).

c. FEF_{25-75%}

This outcome was not reported in this study ([Pryor 2010](#)).

7. Oxygen saturation

The study only reported oxygen saturation levels at baseline in the participant demographics ([Pryor 2010](#)).

8. Sputum weight

This outcome was not reported ([Pryor 2010](#)).

9. Survival

One participant died during the course of the Pryor study and the allocated treatment arm was not specified; however, the investigators stated that the death was unlikely to have been caused by any intervention under evaluation ([Pryor 2010](#)).

Autogenic drainage versus Flutter®

Two studies (47 participants) reported on this comparison ([App 1998](#); [Pryor 2010](#)). Although 75 participants were included overall in the Pryor study, only 15 were randomised to each of the five treatment groups; therefore the study only contributes 30 participants to this pair-wise comparison ([Pryor 2010](#)).

Primary outcomes

1. FEV₁

Both studies reported data for FEV₁ (L) which we could enter into our analysis ([App 1998](#); [Pryor 2010](#)). App recorded lung function before and after four weeks of treatment using each study intervention ([App 1998](#)). Only the first-arm data from this cross-over study were used as the authors felt there would be a carryover effect into the second arm of the study. There was no statistical difference found between AD and Flutter® at one month, MD 0.10 L (95% CI -0.95 to 1.15) ([App 1998](#)) or at 12 months MD 0.21 L (95% CI -0.64 to 1.06) (low quality evidence) ([Pryor 2010](#)) ([Analysis 6.1](#)). Pryor also reported FEV₁ % predicted and, overall, observed a significant deterioration in FEV₁ % predicted over the 12-month period for the entire cohort (-1.8% predicted; P = 0.02), stating this decline was within the international average at the time of the study ([Pryor 2010](#)). However, recruitment was challenging for this long-term study, meaning it was underpowered to detect such a change. Consequently, the results obtained may have over or underestimated any decline in lung function identified by the original authors.

2. QoL

One study measured QoL using the Short Form-36 questionnaire and the CRQ ([Pryor 2010](#)). Investigators found no significant difference in the domains between the two groups (low quality evidence). However, the latter questionnaire reported an overall significant improvement in dyspnoea (P = 0.01) over time in the group as a whole.

Secondary outcomes

1. Participant preference

During the course of one study, 13 out of 75 participants withdrew as they did not like the regimen to which they had been randomised and either reverted to their original preferred option or chose a different regimen (low quality evidence) ([Pryor 2010](#)). The intervention each was using at the time was not identified.

2. Exercise tolerance

The modified shuttle test was reported in one study (30 participants) and no significant difference was found between AD and Flutter®. No detailed data were available for our analysis ([Pryor 2010](#)).

3. Adverse effects

Neither study reported on this outcome ([App 1998](#); [Pryor 2010](#)).

4. Number of admissions

Neither study reported on this outcome ([App 1998](#); [Pryor 2010](#)).

5. Need for extra treatment

One study reported some participants in each of the regimens required intravenous antibiotics during the course of the study (low quality evidence) ([Pryor 2010](#)). The median number of courses per group ranged from 1.0 to 1.5, though statistical analysis was not carried out due to the small numbers and scattered nature of the data. The number of participants and allocated treatment arm was not specified. The second study reported that two participants required intravenous antibiotic treatment (one from from each group) for an acute exacerbation and were withdrawn from the study. We are unable to present these data in the graphs as the paper did not clarify which treatment group the participants were in when they required the antibiotics ([App 1998](#)).

6. Pulmonary function measurements

a. LCI

This outcome was not measured in either study.

b. FVC

Both studies measured FVC ([App 1998](#); [Pryor 2010](#)), but only one study (17 participants) provided data for our analysis ([App 1998](#)). There was no statistical difference found between AD and Flutter® at one month, MD -0.30 L (95% CI -1.50 to 0.90) ([Analysis 6.2](#)). Pryor reported no significant difference in FVC between AD and Flutter® ([Pryor 2010](#)).

c. FEF_{25-75%}

Neither study reported on this outcome ([App 1998](#); [Pryor 2010](#)).

7. Oxygen saturation

In both studies oxygen saturation levels were only reported at baseline as part of the participant demographics ([App 1998](#);

[Pryor 2010](#)).

8. Sputum weight

Only one study (17 participants) reported on this outcome with data we could use in our analysis ([App 1998](#)). There was no statistical difference found in sputum weight between AD and Flutter® at one month, MD -0.90 g (95% CI -3.52 to 1.72) ([Analysis 6.3](#)).

9. Survival

One participant died during the course of one study and the allocated treatment arm was not specified; however, the investigators stated that the death was unlikely to have been caused by any intervention under evaluation ([Pryor 2010](#)).

Autogenic drainage versus high frequency chest wall oscillation

One study reported on this comparison ([Osman 2010](#)). However, as a consequence of the investigators grouping several interventions (AD, Flutter®, PEP and PD&P) as "usual airway clearance techniques" when comparing them to HFCWO we have limited data. After contacting Leyla Osman, additional raw data was obtained which identified eight participants using AD alone as their 'normal' airway clearance technique as a comparison to HFCWO. This study was performed over four consecutive days alternating two treatment techniques. Due to the study design it was felt inappropriate to present this data in the analysis given the carry-over effect.

Primary outcome

1. FEV₁

There was no significant change found in FEV₁ % predicted after either HFCWO or usual airway clearance techniques compared to baseline ([Osman 2010](#)).

2. QoL

Perceived efficacy and comfort of each airway clearance techniques and the incidence of urinary leakage during treatment were measured using 10 cm visual analogue scales (VAS). There was no significant difference in self-reported comfort and urinary leakage after either HFCWO or usual airway clearance techniques. Participants scored perceived efficacy of their usual airway clearance techniques significantly higher than for HFCWO ([Osman 2010](#)).

Secondary outcomes

1. Participant preference

Of the 29 participants who completed the study, 17 (55%) expressed a preference for their usual airway clearance technique over HFCWO ([Osman 2010](#)).

2. Exercise tolerance

This outcome was not reported in this study ([Osman 2010](#)).

3. Adverse effects

One participant was withdrawn due to a hypoglycaemic episode. It is not clear in which treatment arm of the study this event occurred ([Osman 2010](#)).

4. Number of admissions

Inclusion criteria for participants in the Osman study included hospitalisation with an infective pulmonary exacerbation ([Osman 2010](#)).

5. Need for extra treatment

All 29 participants were already receiving intravenous antibiotics as part of their medical management as inpatients during the course of this study ([Osman 2010](#)).

6. Pulmonary function measurements

Osman did not report on LCI, FVC or FEF_{25-75%} ([Osman 2010](#)).

7. Oxygen saturation

There was no significant change found in oxygen saturation levels after either HFCWO or usual airway clearance techniques compared to baseline, but no information was provided for the comparison between groups ([Osman 2010](#)).

8. Sputum weight

Significantly more sputum was expectorated with usual airway clearance techniques than with HFCWO during both a single treatment session and over a 24-hour period, MD 4.4 g and 6.9 g respectively (P < 0.001) ([Osman 2010](#)).

9. Survival

This outcome was not reported in this study ([Osman 2010](#)).

Discussion

Summary of main results

The aim of this review was to determine the effectiveness of AD, particularly the impact on lung function and QoL in people with CF compared to other airway clearance techniques or no physiotherapy. Single-treatment studies were excluded

because the short-term outcomes measured were not of relevance to people with CF.

We identified seven studies eligible for inclusion in this review; six were published as full papers and one as an abstract only. The authors of the abstract have kindly provided the full report of that study ([Mcllwaine 1991](#)). The included studies compared AD to one or more recognised airway clearance techniques including PEP, ACBT, conventional physiotherapy (PD&P) and oscillatory devices (Flutter®, Cornet® and HFCWO). These techniques have been evaluated by other reviews ([Main 2005](#); [Mcllwaine 2015](#); [Mckoy 2016](#); [Morrison 2017](#)).

A total of 208 participants were randomised in the seven studies (numbers ranging from 17 to 75). The length of individual studies varied from four days to two years. Six studies enrolled clinically stable people with CF and one enrolled participants experiencing an exacerbation of their chest condition. Due to the heterogeneity of the studies, data analysis was not possible for most outcomes.

In terms of primary outcome measures, FEV₁ was reported in all seven included studies. Changes in FEV₁ were not significantly different for AD compared to other airway clearance techniques. The rate of decline in FEV₁ in participants using AD over the course of a year-long parallel study was comparable to that of a group using a variety of airway clearance techniques (ACBT, PEP, Cornet® and Flutter®) ([Pryor 2010](#)). However, recruitment was challenging for this long-term study which meant it was underpowered to detect such a change and consequently any results may have under or overestimated any decline in lung function identified by the original authors.

Three of the seven studies measured the impact of airway clearance on health-related QoL, but only one study used validated scales ([Pryor 2010](#)). Measures of QoL such as dyspnoea in the AD group were comparable with those observed in the other treatment groups ([Pryor 2010](#)). Similarly, when using a non-validated Likert scale, there was evidence to suggest that AD, together with PEP treatment modalities, may be seen as preferable to PD&P in terms of QoL measures ([Mcllwaine 1991](#)). One study compared AD and a variety of other airway clearance techniques to HFCWO and reported no significant difference in comfort and urinary leakage ([Osman 2010](#)). Participants in this study scored perceived efficacy of their usual airway clearance techniques, including AD, significantly higher than for HFCWO ([Osman 2010](#)).

Personal preference was assessed in two studies where participants were older children or adults ([Mcllwaine 2010](#); [Miller 1995](#)). Participants in one study preferred AD over PD&P ([Mcllwaine 2010](#)), but the second study showed no difference between AD and ACBT ([Miller 1995](#)). Personal preference is associated with greater adherence to therapy, but is also subject to variability over the course of a lifetime ([Flume 2009](#)). A transient fall in oxygen saturation levels was reported for ACBT in one study but not for AD ([Miller 1995](#)).

With respect to other secondary outcomes, one study assessed exercise tolerance ([Pryor 2010](#)). Investigators found no significant differences between the treatment groups ([Pryor 2010](#)). Analysis of the data from a single long-term study of people with CF with stable disease which compared AD to PD&P demonstrated a reduced number of mean (SD) hospital admissions over 12 months in the 12 to 18 years age group undertaking AD (1.00 (0.32) versus 0.76 (0.18)) resulting in MD -0.24 (95% CI -0.42 to -0.06). In contrast, this was reported as non-significant by the study investigators ([Mcllwaine 2010](#)). Six of the seven included studies reported FVC and three of the studies reported FEF_{25-75%}; results of these outcome measures showed AD was not significantly different to any of the other treatments under investigation in either short- or long-term studies. One study suggested better sputum production with AD ([Mcllwaine 1991](#)), but not consistently compared to other techniques ([Pfleger 1992](#)). It is difficult to assess the impact of sputum production on people with CF, particularly those with mild disease. These studies describe wet weight of sputum which can be unreliable taking into account underestimating due to swallowing sputum or overestimating due to inclusion of saliva.

There is no evidence that AD is superior to other airway techniques when considering the primary and secondary outcomes assessed in the review.

Overall completeness and applicability of evidence

The literature includes representation from both adults and children (range seven to 63 years); five out of seven studies included participants under the age of 16. Studies recruited participants with mild to severe disease. Three cross-over studies were considered short term (less than seven days duration). A further three cross-over studies and one of parallel design were considered long term and ranged from eight weeks to two years.

The literature is relevant and representative of the majority of airway clearance techniques currently available to people with CF; three studies compared AD to PD&P, two studies used AD versus ACBT as a comparison, three studies compared AD to PEP and a total of four studies compared AD to an oscillating device - one study compared AD to the Cornet®, two studies compared it to Flutter®, and one study compared AD to HFCWO. There were no studies comparing AD to acapella, intrapulmonary percussive ventilation (IPV) or Quake® devices; or to exercise.

The applicability of the available evidence needs to be considered in light of the fact that some of the studies were undertaken 18 years ago. General improvements in clinical condition of people with CF need to be taken into account as there have been well-documented improvements in respiratory condition.

It should also be noted that the most recent national annual CF registry reports cite exercise as one of the most frequently used primary or secondary forms of airway clearance amongst both adult and paediatric populations ([CFF 2015](#); [New Zealand CF Association 2013](#); [UK CF Trust 2015](#)). Whilst this is not necessarily representative of current international practice outside the aforementioned countries, it is, nonetheless, a form of treatment which is likely to be available to the majority of people with CF. In this review, none of the included studies used exercise as a comparator

intervention and only one study measured exercise capacity as an outcome measure ([Pryor 2010](#)).

Quality of the evidence

We have included seven RCTs, enrolling 208 participants. Six studies were published as full papers and one in abstract form only. A copy of the unpublished paper was obtained following correspondence with the authors ([Mcllwaine 1991](#)). Studies compared AD to a variety of airway clearance techniques and six studies used a cross-over design. A recent study examining cross-over studies in Cochrane Reviews found that the studies' analysis and presentation of results were often not appropriate or clear, with less than a third of studies presenting results that could be included in a meta-analysis ([Nolan 2016](#)). Validated QoL measures were not available for the earlier studies ([Gee 2000](#); [Quittner 2009](#)).

Overall, the quality of the evidence from the studies was judged to be mainly low or very low ([Summary of findings table 1](#); [Summary of findings table 2](#); [Summary of findings table 3](#); [Summary of findings table 4](#); [Summary of findings table 5](#); [Summary of findings table 6](#); [Summary of findings table 7](#)). We judged only one lung function outcome for one comparison (AD versus Cornet®) to have moderate quality of evidence ([Summary of findings table 5](#)). The main reasons for downgrading the levels of evidence were the small numbers of participants, the lack of clarity of the reporting in the studies and the inability to blind participants.

With regard to study design, while the blinding of participants or research staff is challenging for this intervention, blinded outcome assessors were used in all but two of the studies ([App 1998](#); [Miller 1995](#)), improving the quality of the evidence gathered and reducing the risk of detection bias. One study reported the use of a blinded statistician ([Pryor 2010](#)). Three studies describe appropriate methods of random sequence generation and carry a low risk of bias in this respect ([Mcllwaine 2010](#); [Osman 2010](#); [Pryor 2010](#)); but none of the included studies reported on the allocation concealment process. Half of the cross-over studies described using a washout period, raising the potential for carryover effects and may influence outcomes recorded in the second arm of a study.

Of note regarding reporting issues, one two-year cross-over study was judged to have a high risk of bias due to incomplete outcome data ([Figure 3](#)). The authors acknowledged that data from the second arm of the study was affected by high dropout rates (59%) and non-adherence (41%) in the PD&P arm ([Mcllwaine 2010](#)). In addition, this study was considered to have selective reporting bias, as FVC, chest x-ray scores and hospital admissions were measured, but not reported ([Mcllwaine 2010](#)).

Furthermore, the tools used to record personal preference in the included studies were generally not well-described or validated; and no study incorporated measures of adherence.

Potential biases in the review process

Adequate searches identified relevant studies with relatively limited participant numbers. Four studies were conducted more than 18 years ago and additional data requested from the authors were not available. In one study, AD was included with a number of other airway clearance techniques and compared to HFCWO, which limited the data available for this review ([Osman 2010](#)).

Two authors (PM, PB) use AD in their clinical practice, but are not sponsored by any institution and have not been paid to provide training on this technique.

Agreements and disagreements with other studies or reviews

Previous Cochrane Reviews of conventional physiotherapy ([Main 2005](#)), ACBT ([Mckoy 2016](#)), PEP therapy ([Mcllwaine 2015](#)) and oscillating devices ([Morrison 2017](#)) have not identified one technique to be significantly superior and this is consistent with the current review. There is no clear evidence to support the use of one airway clearance technique over another, but there is a reasonable base to support some form of airway clearance, particularly in productive people with CF ([Warnock 2015](#)).

A Canadian team have undertaken a systematic review of AD and arrived at similar conclusions to this review, albeit by a slightly different route ([Morgan 2015](#)). Their published paper outlines the appropriate methodology they have employed and the majority of studies they selected are the same as in this review. They did not include one study which is included in this review as they felt the approach to AD was distinct ([App 1998](#)). Whilst the intervention may not have been strictly to the guidance of Jean Chevallier's description, we felt it important to include this evidence ([App 1998](#)). They also included one study which assessed outcomes after a single treatment ([Giles 1995](#)). We decided not to select single treatment studies, for two reasons. Firstly, we did not feel these studies examined outcomes that were of relevance to people with CF and secondly, a single treatment does not enable the individual to establish confidence and expertise with the technique. A separate South African team have also examined AD and presented their conclusions in a conference abstract ([Corten 2015](#)). They undertook a systematic review evaluating the effect of AD and assisted AD compared to no physiotherapy, sham physiotherapy, or other methods of physiotherapy in children with CF ([Corten 2015](#)). Assisted AD is a passive technique used with babies and young children involving manual compression over the chest wall during expiration. We did not include this technique, as it is quite distinct from AD. Seven studies were identified in the Corten review, which concluded there was insufficient evidence to determine the efficacy and safety of AD and assisted AD in children.

Authors' conclusions

Implications for practice

Autogenic drainage (AD) is a challenging technique that requires commitment from the individual. As such, it is

important that this intervention is reviewed to ensure its effectiveness for people with cystic fibrosis (CF). It is comparable to other airway clearance techniques and may be considered as an alternative technique in a targeted patient group, e.g. those well-motivated, who want to explore techniques that support their independence. However, the authors of an early study reported that three children aged 11 years performed poorly with AD, finding it difficult to concentrate for the required period whilst learning the technique (Mcllwaine 1991). It is important to consider the age-appropriateness of the therapy techniques, particularly in younger people with CF who may find AD challenging. Furthermore, individual preference and acknowledgement of personal health beliefs are important factors in optimising adherence to airway clearance regimens suggested or offered (Flume 2009).

The included studies did not compare AD to exercise alone, although exercise is regularly used as an alternative to more formal airway clearance techniques (CFF 2015; New Zealand CF Association 2013; UK CF Trust 2015). More information is required to evaluate the effectiveness of exercise alone for airway clearance compared to all other techniques.

Implications for research

It is important to consider the changing clinical condition of our patient cohort, many of whom are now identified through newborn screening and consequently have improved clinical status.

In light of the many variables which influence the measurement of forced expiratory volume in one second (FEV₁) in the short term, some studies are focusing on frequency of exacerbation and time to next exacerbation as primary outcome measures (Konstan 2007; VanDevanter 2015). Despite these variables, FEV₁ remains the pulmonary function test parameter with the most validity when considering relatively short-term study outcomes, as it correlates well with other outcomes, such as quality of life (QoL) and survival, which are important to people with CF. Given that the proposed physiological impact of AD is to augment airway clearance, measures of ventilatory capacity such as lung clearance index (LCI) are attractive and potentially may provide more sensitive identification of early lung disease and response to interventions such as AD. Currently there is insufficient external validity of this measure to include it as a primary outcome, but it will represent an important secondary outcome in future reviews.

The majority of studies in this review were of cross-over design and several of these described changing from one technique to another with no washout period. The magnitude and duration of carry-over effects are unknown in the CF population, but can influence the second arm of a study (Nolan 2016; Southern 2003). It must be noted that, especially in cross-over studies, participant preference can also impact upon withdrawals and may limit the overall quality of a body of evidence (Pryor 2010). For this reason, future studies examining AD should avoid a cross-over design where possible, or should be designed to include an adequate washout period.

Incorporating a validated personal preference tool, measures of adherence and health-related QoL in future research would promote a patient-centred approach to clinical practice and would provide the clinical insight to respond to the needs of the individual. The acquisition of meaningful data from further long-term, randomised controlled studies utilising large cohorts to control for participant variability when comparing airway clearance modalities is required to rigorously evaluate AD and other airway clearance techniques.

Acknowledgements

The review authors would like to acknowledge the assistance of our managing editors Nikki Jahnke and Tracey Remington, and Sarah Nevitt for her help with the summary of findings table. The authors would also like to thank Maggie Mcllwaine and Leyla Osman for kindly providing an additional unpublished paper and additional raw data respectively and the previous review team for their work on the protocol.

This project was supported by the National Institute for Health Research, via Cochrane Infrastructure funding to the Cochrane Cystic Fibrosis and Genetic Disorders Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

Contributions of authors

At protocol stage: Narasimman Swaminathan prepared the protocol with feedback throughout the editorial process from Amita Ray, Karen Robinson and Nikki Jahnke.

At full review stage: Pamela McCormack, Paul Burnham and Kevin Southern revised the protocol, drafted and contributed to the review. Pamela McCormack and Paul Burnham independently selected the studies for inclusion in the review and extracted data. Paul Burnham contacted authors for additional information.

Pamela McCormack acts as guarantor of the review.

Declarations of interest

All authors: none known.

Differences between protocol and review

Post hoc changes for initial review version

Outcome measures

1. In the protocol, sputum weight was included as a primary outcome measure. For the review we downgraded sputum weight to a secondary measure and we promoted quality of life (QoL) assessment to a primary outcome. Reasons for this

change were:

- to better reflect the improving condition of people with cystic fibrosis (CF);
- to reflect concerns over the validity and reliability of sputum weight collection as a primary outcome; and
- to implement advice following discussion with other members of the Cochrane Review Group, including editors of physiotherapy reviews.

By making this change we feel the review better reflects outcomes that are meaningful to people with CF, although we appreciate that for more severely affected individuals sputum weight may be relevant and we keep this as an important secondary outcome.

2. We have included lung clearance index into the secondary outcomes as a post hoc change. It is an emerging outcome measure with increasing validity, which may provide a more sensitive assessment of change in respiratory function.
3. The secondary outcomes have also been re-ordered so that they are listed in order of importance in the view of the new author team.

Inclusion criteria

The new authors also did not accept that single intervention episodes were appropriate for this technique and therefore excluded any studies that lasted for only a single episode.

Reporting data

When reporting short-term studies (up to one month), the new authors reported outcomes of up to seven days, and from one to four weeks. Likewise, the outcome data for longer-term studies were reported as those measured at one month, three months, six months, 12 months and annually thereafter.

Summary of findings table

A summary of findings table for each comparison of the review was added as a post hoc change. Outcomes presented in these tables were presented based on clinical relevance rather than those which contributed the most data.

Published notes

A new author team took on this review after the protocol had been published.

Characteristics of studies

Characteristics of included studies

App 1998

Methods	<p>RCT.</p> <p>Cross-over design: AD or Flutter® therapy used for 4 weeks each with an additional one-week “washout period” prior to starting each arm, without any kind of physiotherapy administered.</p> <p>Multicentre.</p> <p>Location: Germany.</p>
Participants	<p>17 participants with CF diagnosed by clinical history and a positive sweat test.</p> <p>17 initially randomised, 3 dropouts reported (1 for time-related reasons and the other 2 for acute bronchopulmonary exacerbation), therefore 14 analysed (7 in each treatment group).</p> <p>Age: range 7 to 41 years; mean (SD) 19.6 (10.3) years.</p> <p>Gender split: 6 male, 8 female.</p>
Interventions	<p>Treatment 1: 2x daily AD for 30 minutes.</p> <p>Treatment 2: 2x daily Flutter® therapy for 30 minutes.</p>
Outcomes	<p>Respiratory function (FEV₁, FVC) measured at the beginning and end of each 4-week therapy cycle. Measurements were taken before and after 30 minutes physiotherapy.</p> <p>Sputum volume (wet) was collected, weighed and stored at the end of each physiotherapy session.</p> <p>Blood oxygen saturation levels measured by pulse oximetry technique.</p> <p>This paper also considered the implications of the Flutter® on sputum viscoelasticity but this was not an outcome measured in this review.</p>
Notes	<p>Only first-arm data used for analysis as it was felt a 1-week washout was insufficient to exclude a carry-over effect into the second arm.</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Paper only states that patients were "randomly assigned to one of the two treatment arms". Method of randomisation not described.
Allocation concealment (selection bias)	Unclear risk	Not stated. Insufficient information provided about the concealment of allocation process.
Blinding of participants and personnel (performance bias)	Low risk	Neither participants nor physiotherapy personnel were blinded to the self-administered physiotherapy techniques under study. As it is not possible to blind by design, the risk of bias is deemed to be low.
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated.
Incomplete outcome data (attrition bias)	Low risk	3 participants 'dropped out' with reasons stated: 1 for business-related time constraints after the first examination; and the other 2 for acute bronchopulmonary exacerbations during the course of the study (1 from each arm).
Selective reporting (reporting bias)	Unclear risk	Oxygen saturation levels were taken but only reported at baseline. It is unknown whether this parameter changed over the course of the study or as a result of any intervention received. FEV ₁ and FVC baseline characteristics given as % predicted values. However, the values recorded during the study are not presented as % predicted but as absolute figures (L).
Other bias	Low risk	None identified.

Mcllwaine 1991

Methods	<p>RCT.</p> <p>Cross-over design: participants randomised into 3 groups (PD&P, AD and PEP) and used this technique for the first "treatment period" of 2 months, they sequentially performed the other techniques. Each treatment technique was separated by an interval of 1 month "off period" when the pre-study regimen of PD was reinstated.</p> <p>Single centre.</p> <p>Location: Canada.</p>
Participants	<p>18 participants with CF diagnosed by sweat test > 60 mEq/L.</p> <p>Age: mean (range) 17.3 (11 to 27) years.</p> <p>FVC: range 38% predicted to 117% predicted.</p> <p>Shwachman score: range 50 - 94.</p>
Interventions	<p>Technique 1: 2x daily PEP mask treatment in sitting using cycles of 15 tidal volume breaths against a resistor creating a PEP of between 10 - 20 cms H₂O followed by FET and cough. Sequence repeated 6 times or for a minimum of 20 minutes (whichever was longer).</p> <p>Technique 2: 2x PD&P (PD&P, vibrations, deep breathing and FET) performed in 11 different PD positions, draining 6 positions in the morning and the other 5 in the afternoon. Treatment time of 30 minutes each session.</p> <p>Technique 3: 2x AD performed in sitting until all mucus was evacuated (maximum treatment session length no more than 45 minutes).</p>
Outcomes	<p>FEV₁, FVC, and FEF_{25-75%} clinical assessment and Shwachman score were measured at the start and end of each 2-month treatment period.</p> <p>Sputum expectorated during the weekly physiotherapist-supervised physiotherapy session was collected and weighed.</p> <p>Other measures included reported treatment duration, treatment comfort, requirement for assistance with treatment, flexibility of treatment times, control in performing own treatment, and how interruptive treatment was to daily living. Physical activity and compliance with treatment were monitored using a weekly questionnaire.</p>
Notes	<p>Unpublished paper obtained from authors.</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated. "In order to avoid seasonal variations which may have affected the outcome of the study, the patients were randomized into three groups. Each group was assigned by a different physiotherapy regiment for the first treatment period, then sequentially performed the other techniques".
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias)	Low risk	Neither participants nor physiotherapy personnel were blinded to the self-administered physiotherapy techniques under study. As it is not possible to blind by design, the risk of bias is deemed to be low overall. The extent to which the lack of blinding may have had an effect on the reporting of subjective outcomes such as patient preference and QoL measures is unclear.
Blinding of outcome assessment (detection bias)	Low risk	Physician was not told what type of physiotherapy was being performed by the participant at the time of assessment.
Incomplete outcome data (attrition bias)	Low risk	The results are reported from 14/18 participants who completed the study, 4 withdrawals discussed. 1 participant required hospitalisation during the first period of the study (treatment regimen was PD&P) due to exacerbation of her pulmonary disease and was found to have ABPA. She was then considered too unstable to continue in the study. A second participant was dropped at the end of the first period, after requiring Prednisone to control an allergic reaction to an antibiotic. 2 other participants (treatment regimen AD) refused to complete the cross-over study, instead they insisted on continuing AD. These participants were excluded from the analysis of sputum production.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	None identified.

Mcllwaine 2010

Methods	<p>RCT.</p> <p>Cross-over design.</p> <p>Single paediatric centre.</p> <p>Location: Canada.</p>
Participants	<p>36 participants with "proven diagnosis" of CF.</p> <p>Age: 12 - 18 years.</p> <p>Shwachman score 65 - 98.</p> <p>Compliant performing daily chest physiotherapy using PD&P technique for at least 1 year prior to the study.</p>
Interventions	<p>Treatment 1: 2 sessions of AD 30 min daily in sitting. The length of time to complete this technique varied with each participant but on average required 30 minutes.</p> <p>Treatment 2: 2 sessions of PD&P approximately 30 min daily, 6 positions drained in morning and 5 in evening using percussion, deep breathing exercises combined with vibrations on expiration. This was followed by huffs.</p> <p>Each treatment regimen was performed for 1 year before crossing over to the other treatment regimen for a further year.</p>
Outcomes	<p>FEV₁, FVC, FEF_{25-75%} sputum weight (partial and subjective), number of hospital admissions, participant preference, and need for extra treatment. A change in Shwachman and Huang scores were also measured.</p>
Notes	<p>The study was powered as a 2-year cross-over study. Only data from the first year were reported due to 10/17 participants from Group B (AD-PD&P) withdrawing from the study before starting PD&P arm; this completely biased the results. "No formal matched cross-over analysis of the data could be performed." Also, "...as the study was not powered to detect single group differences, these results may not truly reflect treatment differences."</p> <p>Sputum weight was not measured by the investigators, but it was the participants who "reported an increased expectoration with AD".</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were matched as pairs, using FEV ₁ (within 15%) as the primary match, Shwachman scores (within 15 points), age (within 3 years) and same sex as secondary matches. Members of each pair were randomly assigned by computer to 1 of the 2 groups (A or B).
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias)	Low risk	Neither participants nor physiotherapy personnel were blinded to the self-administered physiotherapy techniques under study. As it is not possible to blind by design, the risk of bias is deemed to be low.
Blinding of outcome assessment (detection bias)	Low risk	"...full clinical assessment, including Shwachman and Huang scores, performed at the CF clinic by physician blinded as to the method of physiotherapy the patient was performing in the study..." and "The pulmonary function technician was blinded as to the patient's physiotherapy technique." Not stated if statistician was blinded or not.
Incomplete outcome data (attrition bias)	High risk	36 participants entered the study. Data on 33 available at 12 months. 3 withdrew from the study in the first year: 2 in Group A (pregnancy, ABPA), 1 in Group B (non-compliant). In the first year of the study, 33 stayed in the group to which they were randomised. In the 2nd year, 10/17 participants from Group B (AD/PD) did not return for PD&P arm of study, due to preference to continue with AD (completely biased 2nd arm of study). Strong cross-over effect in 7 participants who continued with the study as they incorporated AD breathing technique into PD&P; therefore only year 1 data reported. The results from the 2nd year could not be analysed as single-group differences could not be studied. Secondary analysis of PFTs in Group A (PD&P, then AD) comparing years 1 and 2 was performed but no significant differences were found.
Selective reporting (reporting bias)	High risk	"Full clinical assessment" was undertaken and would include weight and height, but these are not reported. Adherence measured by monthly phone calls, but not reported in paper. Likewise, duration of hospitalisations and sputum bacteriology recorded but not reported. Antibiotic use was partially reported (none received home IV antibiotics). FEV ₁ , FEF _{25-75%} and Shwachman scores are fully reported though P values not given and only described as non-significant. Huang score was significantly improved (P = 0.04) in the AD group versus PD&P group. Baseline FVC and Huang score recorded but unreported.
Other bias	Low risk	None identified.

Miller 1995

Methods	<p>RCT.</p> <p>Cross-over design: each participant used 2 treatment regimens: AD alone or ACBT with PD in randomised order over 2 days 1 week apart.</p> <p>Single centre.</p> <p>Location: UK.</p>
Participants	<p>18 participants with CF, all clinically stable at the time of the study and were not receiving IV antibiotics.</p> <p>Age: 11 to 32 years.</p> <p>Gender split: 10 male, 8 female.</p> <p>Shwachman-Kulczycki scores modified with the Chrispin-Norman scores: range 34 - 87.</p>
Interventions	<p>Treatment 1: AD alone for 2 days, each day consisting of 2 identical treatment sessions (morning and afternoon) with each session lasting 30 minutes.</p> <p>Treatment 2: ACBT with PD for 2 days, each day consisting of 2 identical treatment sessions (morning and afternoon) with each session lasting 30 minutes.</p> <p>Treatment preceded either by nebulised salbutamol (2.5 mL salbutamol and 1.5 mL saline) or saline (4 mL), based on reversibility response to bronchodilator. Approximate nebulisation time of 8 minutes.</p> <p>Participants were asked to be regular with their home physiotherapy in the week leading up to the study and in the intervening period.</p>
Outcomes	<p>The same measurements were taken on day 1 and day 2.</p> <p>Lung function tests (FEV₁, FVC, FEF_{25-75%} and PEF) recorded at the beginning of the day and before and after each physiotherapy treatment.</p> <p>Oxygen saturation levels measured before, during and after each physiotherapy session.</p> <p>Sputum collected and weighed during treatment and for a further hour after it.</p> <p>Participant preference.</p> <p>Additional outcome: Xenon-133 gas ventilation study at the start and end of each day.</p>
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Eighteen patients with cystic fibrosis took part in a randomized two-day crossover trial". Method of randomisation not described.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias)	Low risk	Neither participants nor physiotherapy personnel were blinded to the self-administered physiotherapy techniques under study. As it is not possible to blind by design, the risk of bias is deemed to be low overall. The extent to which the lack of blinding may have had an effect on the reporting of subjective outcomes such as patient preference is unclear.
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated.
Incomplete outcome data (attrition bias)	Low risk	No exclusions, all participants analysed in the groups to which they were assigned.
Selective reporting (reporting bias)	Low risk	Taken overall, lung function tests were reported, but only FVC and FEF _{25-75%} in any detail. Xenon-133 gas ventilation study was reported, as were oxygen saturation levels, sputum weights and preference of technique. No baseline or raw data provided. Conclusions based on the statistical analysis were summarised.
Other bias	High risk	Those on their ACBT day were asked to breathe normally during their pre-treatment nebuliser. Those on AD, however, performed AD breathing exercises during inhalation, adding 8 minutes of "extra" treatment time. No statistically significant differences were found between the 2 treatment groups for any of the outcomes measured. Despite this, the risk of bias was deemed to be high as the stated treatment time for the 2 groups was unequal, favouring the AD group.

Osman 2010

Methods	<p>RCT.</p> <p>Cross-over design: 4 consecutive study days where participants received either HFCWO on days 1 and 3 and their "usual" ACT on days 2 and 4 or vice versa. Single centre.</p> <p>Location: UK.</p>
Participants	<p>30 participants with a diagnosis of CF based on genotype or sweat test who were admitted to hospital with an acute infective pulmonary exacerbation.</p> <p>Age: mean (SD) 29.4 (8.4) years.</p> <p>Gender split: 22 male, 8 female.</p> <p>FEV₁ % predicted: mean (SD) 38% (16.7).</p> <p>Inclusion criteria: FEV₁ ≥ 20% predicted, age ≥ 16 years and have an acute infective pulmonary exacerbation.</p>
Interventions	<p>4 consecutive study days where participants received either HFCWO on days 1 and 3 and their "usual" ACT on days 2 and 4 or vice versa.</p> <p>Treatment 1: 2x daily HFCWO sessions (am and pm) of 30 min each where participants remained in an upright position throughout the session; 8 minutes at each of the frequencies in sequence (10, 13 and 15 Hz), with each frequency followed by a 2-minute rest period. Pulse pressure set according to the individual's reported comfort. Participants advised to huff or cough as they felt necessary to expectorate secretions.</p> <p>Treatment 2: 2x daily "usual" ACT sessions (am and pm) of 30 min each. For those practicing an assisted ACT, the physiotherapist provided percussion (i.e. ACBT with PD&P), participants were allowed to perform combined ACTs where this was their usual practice.</p>
Outcomes	<p>Wet weight of expectorated sputum, FEV₁, oxygen saturation levels, perceived efficacy and comfort of each ACT as well as the incidence of urinary leakage during treatment was measured using a Visual Analogue Scale. ACT preference was documented for each participant.</p>
Notes	<p>"Usual" ACT incorporated: ACBT with PD&P (41%, n = 12), ACBT with modified PD alone (7%, n = 2), AD in sitting (28%, n = 8), AD with modified PD (7%, n = 2), PEP (7%, n = 2), Flutter® (10%, n = 3).</p> <p>ACTs in the published paper were analysed together and results were not separated out for the individual techniques.</p> <p>The study authors were contacted and provided us with the raw data for each participant, including what their usual therapies were and all first-arm data before the first cross-over on day 1. Only 10 out of the 30 participants in the study performed AD as their usual ACT. It was felt that analysing these AD participants in a subset would not add relevance due to the very small numbers.</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Allocation to HFCWO or usual ACT on day 1 was determined using a computer-generated randomisation table."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding of participants and personnel (performance bias)	Low risk	Neither participants nor physiotherapy personnel were blinded to the self-administered physiotherapy techniques under study. As it is not possible to blind by design, the risk of bias is deemed to be low overall. The extent to which the lack of blinding may have had an effect on the reporting of subjective outcomes such as QoL measures is unclear.
Blinding of outcome assessment (detection bias)	Low risk	Paper states that "An independent observer, blind to the daily method of airway clearance used, performed the spirometry, weighed the sputum samples and collected the 10 cm VAS throughout the study."
Incomplete outcome data (attrition bias)	Low risk	Single withdrawal discussed; participant excluded due to a hypoglycaemic episode. Results based on the remaining 29 participants.
Selective reporting (reporting bias)	Low risk	All outcomes reported; 2 out of 116 24-hour sputum samples were discarded as they were incomplete. Powered to detect a 4 g difference in expectorated sputum.
Other bias	Unclear risk	Supported by the Robert Luff Foundation and Hill Rom Inc. Although Hill Rom provided some equipment for the study, they did not participate in the design, collection, analysis, interpretation of data or in the writing of the manuscript.

Pflegger 1992

Methods	<p>RCT.</p> <p>Cross-over design: in a random order, participants performed a different regimen of physiotherapy over 5 consecutive outpatient visits.</p> <p>Single centre.</p> <p>Location: Austria.</p>
Participants	<p>15 participants with CF, diagnosis confirmed by "repeatedly positive sweat tests". All participants in a "stable clinical situation". All participants trained to cooperate with pulmonary function testing (6 months prior to the study, each participant trained in 2 self-administered techniques (Hi-PEP mask (PEP) and AD) and encouraged to use these 2 techniques daily until the onset of the study), able to perform chest physiotherapy 1 to 3 times daily and produce > 20 mL sputum per day. One participant excluded due to an acute respiratory viral infection. The remaining 14 participants were analysed.</p> <p>Age: > 6 years. Mean (range) age 16.0 (9.8 - 22.4) years.</p> <p>Gender split: 5 male, 9 female.</p> <p>Shwachmann score mean (range): 62.2 (26 - 90).</p> <p>Chest X-ray score mean (range): 13.8 (6 - 20).</p>
Interventions	<p>Treatment time individualised and performed 1x daily. Each treatment session was equal to the time taken for the individual to clear the lungs using AD, as judged from pre-study experience.</p> <p>Regimen 1: Hi-PEP mask alone (PEP).</p> <p>Regimen 2: AD alone (AD).</p> <p>Regimen 3: Hi-PEP mask for the first half of the session, followed by AD (PEP-AD).</p> <p>Regimen 4: AD for the first half of the session, followed by Hi-PEP mask (AD-PEP).</p> <p>Regimen 5: control (spontaneous coughing only).</p>
Outcomes	<p>FEV₁ and FVC measured at all PFT measurement points. Total sputum weight (not stated whether wet or dry) during the complete treatment session also measured.</p>
Notes	<p>One participant excluded from the study due to an acute respiratory viral infection.</p>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants were "randomly selected from the patients of the local CF clinic". No further details.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias)	Low risk	Neither participants nor physiotherapy personnel were blinded to the self-administered physiotherapy techniques under study. As it is not possible to blind by design, the risk of bias is deemed to be low.
Blinding of outcome assessment (detection bias)	Low risk	Sputum was collected by the participants and weighed by an investigator blinded to the method of physiotherapy used. Does not state whether the statisticians or those carrying out the PFTs were blinded.
Incomplete outcome data (attrition bias)	Low risk	Single withdrawal discussed; participant excluded due to an acute respiratory viral infection. Results based on remaining 14 participants.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	High risk	Treatment time individualised and the authors state that each treatment session was equal to the time taken for the individual to clear the lungs using AD, as judged from pre-study experience. This would imply that duration of each of the 5 treatment sessions performed by an individual should be the same. Additionally, its duration would have been decided in advance and ought to remain unchanged over the course of the study. Nonetheless, the authors report that the "time needed to clear the lungs...for PEP, however, was shorter than for the other forms of physiotherapy and this difference reached statistical significance for AD ($P < 0.05$), PEP-AD ($P < 0.02$), and AD-PEP ($P < 0.05$)". In this case, the results reported are not consistent with the methods described.

Pryor 2010

Methods	<p>RCT.</p> <p>Parallel design.</p> <p>Single centre.</p> <p>Location: UK.</p>
Participants	<p>75 participants with "proven diagnosis" of CF (genotype and positive sweat test); 15 participants randomised to each of 5 intervention groups.</p> <p>Age: 16 years or older; range 17 - 63 years.</p> <p>Gender split: 47 males, 28 females.</p> <p>FEV₁: ≥ 25% predicted.</p> <p>Exclusion criteria: evidence of a current respiratory exacerbation, past history of pneumothorax, current severe haemoptysis, awaiting lung and heart or lung transplantation, pregnancy and recent (within 3 months) acquisition of <i>Burkholderia cepacia</i>.</p>
Interventions	<p>The number of sessions per day and the length of time for treatment was individualised in agreement with each participant, written instructions of the regimens agreed were given to each participant.</p> <p>Regimen 1: AD.</p> <p>Regimen 2: ACBT.</p> <p>Regimen 3: Cornet®.</p> <p>Regimen 4: Flutter®.</p> <p>Regimen 5: PEP.</p>
Outcomes	<p>Primary outcome: FEV₁.</p> <p>Secondary outcomes: FVC, BMI, the modified shuttle test, number of courses of IV antibiotics and the Short Form-36 and Chronic Respiratory Questionnaires.</p> <p>MEF₂₅ and residual volume as a percent of total lung capacity were reported in the study, but are not included in our analysis as they were not outcomes relevant to our review.</p> <p>Participants requested to attend monthly for 12 months, for a review of their ACT and to record the outcome measurements. The measurements of lung function and BMI were undertaken at 0, 6 and 12 months.</p>
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was computerised and used a random number sequence stratified by FEV ₁ % predicted (FEV ₁ < 50%; FEV ₁ ≥ 50%) and sputum expectorated (< 1 cupful per day; ≥ 1 cupful per day). Participants randomized to 1 of the 5 regimens of ACBT, AD, Cornet®, Flutter® or PEP.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias)	Low risk	Neither participants nor physiotherapy personnel were blinded to the self-administered physiotherapy techniques under study. As it is not possible to blind by design, the risk of bias is deemed to be low overall. The extent to which the lack of blinding may have had an effect on the reporting of subjective outcomes such as QoL measures is unclear.
Blinding of outcome assessment (detection bias)	Low risk	The measurements of lung function and BMI and the statistical analysis were undertaken by observers (physiologists and statistician) blind to the regimen to which the participants had been randomised.
Incomplete outcome data (attrition bias)	Low risk	75 entered the study, but only data on 65 available at 12 months (13.3 % excluded) - "Intention to treat was used for the primary outcome of FEV ₁ ". 53 stayed in the group to which they were randomised. 22 did not complete the study – reasons provided but not according to specific group allocation.
Selective reporting (reporting bias)	High risk	FEV ₁ is the only outcome reported in detail. However, there is no report of the 6-month data taken for lung function or BMI. FVC, BMI and exercise capacity report no significant difference and P values at 12 months. Some participants in each of the regimens required IV antibiotics, median number of courses per group 1.0 to 1.5, but these data were not analysed in the study due to small numbers and scattered nature of the data. QoL data reported.
Other bias	Unclear risk	Treatment used prior to baseline was not reported, which will have had an impact on the capacity of the individual to engage with a new technique.

Footnotes

ABPA: allergic bronchopulmonary aspergillosis

ACT: airway clearance technique

ACBT: active cycle of breathing technique

AD: autogenic drainage

BMI: body mass index

CF: cystic fibrosis

FEF_{25-75%}: forced mid-expiratory flow between 25% and 75% of forced vital capacity

FET: forced expiration technique

FEV₁: forced expiratory volume at one second

FVC: forced vital capacity

HFCWO: high frequency chest wall oscillation

IPV: intrapulmonary percussive ventilation

IV: intravenous

MEF_{25%}: maximal expiratory flow at 25% of forced vital capacity

PD: postural drainage

PD&P: postural drainage and percussion

PEP: positive expiratory pressure

PFT: pulmonary function test

QoL: quality of life

RCT: randomised controlled trial

VAS: visual analogue score

Characteristics of excluded studies***Giles 1995***

Reason for exclusion	Single treatment session with AD.
-----------------------------	-----------------------------------

Herrero 2016

Reason for exclusion	Single treatment session with AD.
-----------------------------	-----------------------------------

Lindemann 1992

Reason for exclusion	Single treatment session with AD.
-----------------------------	-----------------------------------

NCT01885650

Reason for exclusion	AD used in both treatment groups; study comparing NIV with no NIV.
-----------------------------	--

NCT02303808

Reason for exclusion	AD used in both treatment groups; study comparing inhalation with and without PEP.
-----------------------------	--

Reix 2012

Reason for exclusion	After careful appraisal of the methodology of the paper it was considered that exercise and expiratory manoeuvres were being compared to a modified ACBT, and not an AD technique.
-----------------------------	--

Roos 1987

Reason for exclusion	Study was not completed when abstract was published. Further information was unattainable from the authors after this length of time.
-----------------------------	---

Skopnik 1986

Reason for exclusion	No evidence of randomisation in this study. Ventilation scintigraphy was the only outcome measure and this is not an outcome under evaluation in this review.
-----------------------------	---

van Ginderdeuren 2001

Reason for exclusion	This study describes assisted AD in infants which is a different technique and not under review.
-----------------------------	--

van Ginderdeuren 2008

Reason for exclusion	The intervention under review in this study was not AD but a comparison of two different inhalation regimes prior to AD (i.e. saline alone or saline accompanied by IPV).
-----------------------------	---

van Ginderdeuren 2011

Reason for exclusion	AD is not compared to any other ACT. The variable is the time of administration of the hypertonic saline.
-----------------------------	---

Warwick 1990

Reason for exclusion	Intervention not appropriate for this review. Manual chest physiotherapy was compared to the Thairapy® bronchial drainage vest.
-----------------------------	---

Footnotes

ACBT; active cycle of breathing technique
 ACT: airway clearance technique
 AD: autogenic drainage
 IPV: intrapulmonary percussive ventilation
 NIV: non-invasive ventilation
 PEP: positive expiratory pressure

Characteristics of studies awaiting classification*Davies 2012*

Methods	RCT. Parallel design. Single centre. Location: UK.
Participants	Inclusion criteria: <ul style="list-style-type: none"> • diagnosis of CF; • hospitalised patients admitted with a pulmonary infection; • FEV₁ of 15% predicted or over; • 16 years of age or over. Exclusion criteria: <ul style="list-style-type: none"> • current severe haemoptysis; • rib fractures or history of spontaneous rib fractures; • pregnancy; • lung abscess; • end-stage disease; • requiring more than 2 assisted treatment sessions per day; • requiring treatment with positive pressure; • inability to give consent.
Interventions	Treatment 1: usual ACT - 2 self-administered treatment sessions a day and 2 treatments a day assisted by a physiotherapist (both using the participant's usual ACT (ACBT, AD, PEP, manual techniques or oscillating PEP)). Treatment 2: HFCWO - 2 self-administered treatments a day using HFCWO and 2 treatment sessions a day assisted by a physiotherapist using their usual ACT.
Outcomes	Primary outcome measures: mean % change in FEV ₁ . Secondary outcome measures: wet weight of sputum expectorated in 24 hours, length of time to next course of intravenous antibiotics, rate of change of C-reactive protein.
Notes	

Vendrusculo 2017

Methods	Prospective randomised controlled pilot study of cross-over design (two tests with one month washout in between).
Participants	Eligible participants: children with CF aged over 9 years and who were over 128 cm in height. Participants excluded if they were chronically infected with <i>Burkholderia cepacia</i> and non-tuberculous <i>Mycobacterium abscessus</i> . n = 12 Age, mean (SD): 12.83 (1.85) years. Gender split: 6 boys, 6 girls. FEV ₁ z score, mean (SD): -0.51 (0.76). FVC z score, mean (SD): -0.17 (0.97).
Interventions	Group 1: cardiopulmonary exercise testing with usual ACT (PEP and AD). Group 2: cardiopulmonary exercise testing alone.
Outcomes	Peak VO ₂ , V _E , V _E VO ₂ , V _E VCO ₂
Notes	

Footnotes

ACBT: active cycle of breathing techniques
 ACT: airway clearance technique
 AD: autogenic drainage
 CF: cystic fibrosis
 FEV₁: forced expiratory volume in one second
 FVC: forced vital capacity
 HFCWO: high frequency chest wall oscillation
 PEP: positive expiratory pressure
 RCT: randomised controlled trial
 V_E: minute ventilation
 V_EVCO₂: ventilation relative to carbon dioxide production
 V_EVO₂: ventilation relative to oxygen consumption
 VO₂: oxygen consumption

Characteristics of ongoing studies

Footnotes

AD: autogenic drainage
 CF: cystic fibrosis
 FEF_{25-75%}: forced mid-expiratory flow between 25% and 75% of forced vital capacity
 FEV₁: forced expiratory volume in one second

Summary of findings tables

1 Autogenic drainage versus conventional physiotherapy

AD compared with conventional physiotherapy for CF						
Patient or population: adults and children with CF						
Settings: outpatients						
Intervention: AD						
Comparison: conventional physiotherapy						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Conventional physiotherapy	AD				
FEV₁ % predicted (change from baseline) Follow-up: up to 12 months	The mean change in FEV ₁ (% predicted) was 2.09% in the conventional physiotherapy group (also see comment).	The mean change in FEV ₁ (% predicted) was 1.12% lower (2.64% lower to 0.40% higher) in the AD group (also see comment).	NA	54 participants (2 studies)	⊕⊕⊕⊕ very low ^{1,2}	Data available for analysis for 31 participants from the first treatment period of one study. No significant difference in FEV ₁ between groups in the second study.
QoL (Likert scale 0 - 10) Follow-up: up to 12 months	See comment.		NA	54 participants (2 studies)	⊕⊕⊕⊕ very low ^{1,2,3}	Participants subjectively reported AD to be superior to conventional physiotherapy in terms of comfort, level of control and degree of interruption in their daily life.
Participant preference Follow-up: 12 months	See comment.	See comment.	NA	36 participants (1 study)	⊕⊕⊕⊕ very low ^{1,2,3}	All participants reported a preference for autogenic drainage and many refused to go back to conventional physiotherapy.
Exercise tolerance	Not reported.		NA	NA	NA	
Adverse events	Not reported.		NA	NA	NA	
Number of admissions to hospital Follow-up: 12 months	There were 16 hospitalisations in the conventional physiotherapy group.	There were 13 hospitalisations in the AD group.	NA	36 participants (1 study)	⊕⊕⊕⊕ very low ^{1,2}	Unclear which treatment period of the cross-over study these hospitalisations occurred in, so data not analysed.
Need for extra treatment	See comment.		NA	36 participants (1 study)	⊕⊕⊕⊕ very low ^{1,2}	No participants received home intravenous antibiotic treatment.
*The basis for the assumed risk (e.g. the median control group risk across studies) is the event rate or mean risk in the control group unless otherwise stated.						
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).						
AD: autogenic drainage; CF: cystic fibrosis; CI: confidence interval; FEV ₁ : forced expiratory volume in one second; NA: not applicable; QoL: quality of life.						
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.						

Footnotes

1. Downgraded once due to imprecision; small numbers of participants included in the comparison.
2. Downgraded twice due to serious risk of bias; incomplete outcome data and selectively reported results.
3. Downgraded once due to applicability; outcomes are recorded subjectively.

2 Autogenic drainage versus spontaneous cough

AD compared with spontaneous cough for CF						
Patient or population: adults and children with CF						
Settings: outpatients						
Intervention: AD						
Comparison: spontaneous cough						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Spontaneous cough	AD				
FEV ₁ % predicted Follow-up: each treatment performed on 1 day	See comment.		NA	14 participants (1 study)	⊕⊕⊕⊕ very low ^{1,2,3}	There was no significant difference between groups in terms of FEV ₁ (% predicted).
QoL	Not reported.		NA	NA	NA	
Participant preference	Not reported.		NA	NA	NA	
Exercise tolerance	Not reported.		NA	NA	NA	
Adverse events Follow-up: each treatment performed on 1 day	See comment.		NA	14 participants (1 study)	⊕⊕⊕⊕ very low ^{1,2,3}	No adverse events were reported during the study.
Number of admissions to hospital	Not reported.		NA	NA	NA	
Need for extra treatment	Not reported.		NA	NA	NA	
<p>*The basis for the assumed risk (e.g. the median control group risk across studies) is the event rate or mean risk in the control group unless otherwise stated.</p> <p>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).</p> <p>AD: autogenic drainage; CF: cystic fibrosis; CI: confidence interval; FEV₁: forced expiratory volume in 1 second; NA: not applicable; QoL: quality of life.</p> <p>GRADE Working Group grades of evidence</p> <p>High quality: further research is very unlikely to change our confidence in the estimate of effect.</p> <p>Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</p> <p>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.</p> <p>Very low quality: we are very uncertain about the estimate.</p>						

Footnotes

1. Downgraded once due to imprecision; small numbers of participants included in the comparison. As results were not presented from paired analyses for one study, we treated the cross-over studies as if they were parallel studies which is a conservative approach as it does not take into account within-patient correlation.
2. Downgraded once due to risk of bias; inconsistency between methods described and results reported regarding time for individuals to clear lungs.
3. Downgraded once due to applicability; each treatment performed only once and very limited follow up (less than 1 week).

3 Autogenic drainage versus active cycle of breathing technique

AD compared with ACBT for CF						
Patient or population: adults and children with CF						
Settings: outpatients						
Intervention: AD						
Comparison: ACBT						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	ACBT	AD				
FEV₁ (L) Follow-up: up to 12 months	The mean FEV ₁ was 1.94 L in the ACBT group (also see comment).	The mean FEV ₁ was 0.70 L higher (0.09 L lower to 1.49 L higher) in the autogenic drainage group (also see comment).	NA	44 participants (2 studies)	⊕⊕⊕⊖ low ^{1,2}	Data were available for analysis for 26 participants from 1 study. A significant deterioration in FEV ₁ (% predicted) was also observed for the cohort of this study. No significant differences in pulmonary function tests in the other study.
QoL (SF-36 and CRQ) Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊖ low ^{1,3}	There were no significant differences between groups in the mental and physical domains of the SF-36. There were no significant differences between the dyspnoea, fatigue, emotion and mastery domains of the CRQ.
Participant preference Follow-up: up to 12 months	See comment.		NA	44 participants (2 studies)	⊕⊕⊕⊖ very low ^{1,2,3}	1 study reported that 9 participants preferred AD, 8 participants preferred ACBT and 1 participant had no preference. In the other study 13 out of the total of 75 participants (all treatments in the study) withdrew as they did not like the treatment they were randomised to (not specified by intervention).
Exercise tolerance (modified shuttle test) Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊖ low ^{1,3}	No significant difference between groups.
Adverse events Follow-up: 2 days	See comment.		NA	18 participants (1 study)	⊕⊕⊕⊖ very low ^{1,2,4}	1 study reported a decrease in oxygen saturation levels in 4 participants in the ACBT group but no participants experienced this during any AD sessions.
Number of admissions to hospital	Not reported.		NA	NA	NA	
Need for extra treatment Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊖ low ^{1,3}	The median number of antibiotics courses per treatment group ranged from 1.0 to 1.5 (no further information given).

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is the event rate or mean risk in the control group unless otherwise stated.

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).

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is the event rate or mean risk in the control group unless otherwise stated.

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).

AD: autogenic drainage; **ACBT**: active cycle of breathing technique; **CRQ**: Chronic Respiratory Questionnaire; **CF**: cystic fibrosis; **CI**: confidence interval; **FEV₁**: forced expiratory volume in 1 second; **NA**: not applicable; **QoL**: quality of life; **SF-36**: short form 36.

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.

Footnotes

1. Downgraded once due to imprecision; small numbers of participants included in the comparison.
2. Downgraded once due to unclear risk of bias; many elements of study designs not clearly described.
3. Downgraded once due to risk of bias; by design, study cannot be blinded and lack of masking may have influenced subjective outcomes. Further no details of treatment used prior to baseline reported, which may also have influenced subjective outcomes.
4. Downgraded once due to applicability; each treatment performed only once and very limited follow up (less than one week).

4 Autogenic drainage versus positive expiratory pressure

AD compared with PEP for CF						
Patient or population: adults and children with cystic fibrosis						
Settings: outpatients						
Intervention: AD						
Comparison: PEP						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	PEP	AD				
FEV₁ (L) Follow-up: up to 12 months	The mean FEV ₁ was 2.02 L in the PEP group (also see comment).	The mean FEV ₁ was 0.62 L higher (0.30 L lower to 1.54 L higher) in the AD group (also see comment).	NA	62 participants (3 studies)	⊕⊕⊕⊖ low ^{1,2}	Data were available for analysis for 26 participants from 1 study. A significant deterioration in FEV ₁ (% predicted) was also observed for the cohort of this study. In the other 2 studies, there was no significant difference between groups in terms of FEV ₁ .
QoL (SF-36 and CRQ) Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊖ low ^{1,3}	There were no significant differences between groups in the mental and physical domains of the SF-36. There were no significant differences between the dyspnoea, fatigue, emotion and mastery domains of the CRQ.

Participant preference Follow-up: up to 12 months	See comment.	NA	30 participants (1 study)	⊕⊕⊖⊖ low ^{1,3}	13 out of the total of 75 participants (all treatments in the study) withdrew as they did not like the treatment they were randomised to (not specified by intervention).
Exercise tolerance: modified shuttle test Follow-up: up to 12 months	See comment.	NA	NA	NA	No significant difference between groups.
Adverse events	Not reported.	NA	NA	NA	
Number of admissions to hospital	Not reported.	NA	NA	NA	
Need for extra treatment Follow-up: up to 12 months	See comment.	NA	30 participants (1 study)	⊕⊕⊖⊖ low ^{1,3}	The median number of antibiotics courses per treatment group ranged from 1.0 to 1.5 (no further information given).

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is the event rate or mean risk in the control group unless otherwise stated.

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).

AD: autogenic drainage; **CRQ**: Chronic Respiratory Questionnaire; **CF**: cystic fibrosis; **CI**: confidence interval; **FEV₁**: forced expiratory volume in 1 second; **NA**: not applicable; **PEP**: positive expiratory pressure; **QoL**: quality of life; **SF-36**: short form 36.

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.

Footnotes

1. Downgraded once due to imprecision; small numbers of participants included in the comparison. As results were not presented from paired analyses for one study, we treated the cross-over studies as if they were parallel studies which is a conservative approach as it does not take into account within-patient correlation.
2. Downgraded once due to risk of bias; inconsistency between methods described and results reported regarding time for individuals to clear lungs and many elements of study designs not clearly described.
3. Downgraded once due to risk of bias; by design, study cannot be blinded and lack of masking may have influenced subjective outcomes. Further no details of treatment used prior to baseline reported, which may also have influenced subjective outcomes.

5 Autogenic drainage versus Cornet®

AD compared with Cornet® for CF						
Patient or population: adults with cystic fibrosis						
Settings: outpatients						
Intervention: AD						
Comparison: Cornet®						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Cornet®	AD				
FEV₁ (L) Follow-up: up to 12 months	The mean FEV ₁ was 1.9 L in the Cornet® group (also see comment).	The mean FEV ₁ was 0.74 L higher (0.07 L lower to 1.55 L higher) in the AD group (also see comment).	NA	27 participants (1 study)	⊕⊕⊕⊖ moderate ¹	Data for 27 participants were available for analysis. A significant deterioration in FEV ₁ (% predicted) was also observed for the cohort of this study.
QoL (SF-36 and CRQ) Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊖ low ^{1,2}	There were no significant differences between groups in the mental and physical domains of the SF-36. There were no significant differences between the dyspnoea, fatigue, emotion and mastery domains of the CRQ.
Participant preference Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊖ low ^{1,2}	13 out of the total of 75 participants (all treatments in the study) withdrew as they did not like the treatment they were randomised to (not specified by intervention).
Exercise tolerance: modified shuttle test Follow-up: up to 12 months	See comment.		NA	NA	NA	No significant difference between groups.
Adverse events	Not reported.		NA	NA	NA	
Number of admissions to hospital	Not reported.		NA	NA	NA	
Need for extra treatment Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊖ low ^{1,2}	The median number of antibiotics courses per treatment group ranged from 1.0 to 1.5 (no further information given).
*The basis for the assumed risk (e.g. the median control group risk across studies) is the event rate or mean risk in the control group unless otherwise stated.						
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).						
AD: autogenic drainage; CRQ: Chronic Respiratory Questionnaire; CF: cystic fibrosis; CI: confidence interval; FEV ₁ : forced expiratory volume in 1 second; NA: not applicable; QoL: quality of life; SF-36: short form 36.						
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.						

Footnotes

1. Downgraded once due to imprecision; small numbers of participants included in the comparison.
2. Downgraded once due to risk of bias; by design, study cannot be blinded and lack of masking may have influenced subjective outcomes. Further no details of treatment used prior to baseline reported, which may also have influenced subjective outcomes.

6 Autogenic drainage versus Flutter®

AD compared with Flutter® for CF						
Patient or population: adults and children with cystic fibrosis						
Settings: outpatients						
Intervention: AD						
Comparison: Flutter®						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Flutter®	AD				
FEV ₁ (L) Follow-up: up to 12 months.	The mean FEV ₁ was 0.21 L higher (0.64 L lower to 1.21 L higher) in the AD group in the parallel study The mean FEV ₁ was 0.10 L higher (0.95 L lower to 1.15 L higher) in the AD group in the cross-over study		NA	39 participants (2 studies including one cross-over study) ⁴	⊕⊕⊕⊕ low ^{1,2}	A significant deterioration in FEV ₁ (% predicted) was also observed for the cohort of the parallel study.
QoL (SF-36 and CRQ) Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊕ low ^{1,3}	There were no significant differences between groups in the mental and physical domains of the SF-36. There were no significant differences between the dyspnoea, fatigue, emotion and mastery domains of the CRQ.
Participant preference Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊕ low ^{1,3}	13 out of the total of 75 participants (all treatments in the study) withdrew as they did not like the treatment they were randomised to (not specified by intervention).
Exercise tolerance: modified shuttle test Follow-up: up to 12 months	See comment.		NA	NA	NA	No significant difference between groups.
Adverse events	Not reported.		NA	NA	NA	
Number of admissions to hospital	Not reported.		NA	NA	NA	
Need for extra treatment Follow-up: up to 12 months	See comment.		NA	30 participants (1 study)	⊕⊕⊕⊕ low ^{1,3}	The median number of antibiotics courses per treatment group ranged from 1.0 to 1.5 (no further information given).

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is the event rate or mean risk in the control group unless otherwise stated.

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).

AD: autogenic drainage; **CRQ**: Chronic Respiratory Questionnaire; **CF**: cystic fibrosis; **CI**: confidence interval; **FEV₁**: forced expiratory volume in 1 second; **NA**: not applicable; **QoL**: quality of life; **SF-36**: short form 36.

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.

Footnotes

1. Downgraded once due to imprecision; small numbers of participants included in the comparison.
2. Downgraded once due to unclear risk of bias; many elements of study designs not clearly described.
3. Downgraded once due to risk of bias; by design, study cannot be blinded and lack of masking may have influenced subjective outcomes. Further no details of treatment used prior to baseline reported, which may also have influenced subjective outcomes.
4. Data from the cross-over study were analysed at the end of the first treatment period, before cross-over occurred.

7 Autogenic drainage versus high frequency chest wall oscillation

AD compared with HFCWO for CF						
Patient or population: adults with cystic fibrosis						
Settings: hospital admission						
Intervention: AD						
Comparison: HFCWO						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	HFCWO	AD				
FEV ₁	Not reported ¹ .		NA	NA	NA	
QoL	Not reported ¹ .		NA	NA	NA	
Participant preference	Not reported ¹ .		NA	NA	NA	
Exercise tolerance (modified shuttle test)	Not reported ¹ .		NA	NA	NA	
Adverse events	Not reported ¹ .		NA	NA	NA	
Number of admissions to hospital	Not reported ¹ .		NA	NA	NA	
Need for extra treatment	Not reported ¹ .		NA	NA	NA	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is the event rate or mean risk in the control group unless otherwise stated.

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).

AD: autogenic drainage; **CF:** cystic fibrosis; **CI:** confidence interval; **FEV₁:** forced expiratory volume in 1 second; **HFCWO:** high frequency chest wall oscillation; **NA:** not applicable; **QoL:** quality of life.

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.

Footnotes

1. No outcome data presented as several interventions (AD, Flutter®, positive expiratory pressure and conventional physiotherapy) were grouped together as "usual airway clearance techniques" and compared to HFCWO. Insufficient data comparing AD and HFCWO.

Additional tables

References to studies

Included studies

App 1998

[CRSSTD: 6836841]

App EM, Danzl G, Schweiger K, Kieselmann R, Reinhardt D, Lindemann H, et al. Sputum rheology changes in cystic fibrosis lung disease following two different types of physiotherapy - VRP1 (flutter) versus autogenic drainage. *American Journal of Respiratory and Critical Care Medicine* 1995;151(4 Suppl):A737. [CFGD Register: PE29a; CRSREF: 6836842]

* App EM, Kieselmann R, Reinhardt D, Lindemann H, Dasgupta B, King M, et al. Sputum rheology changes in cystic fibrosis lung disease following two different types of physiotherapy: flutter vs autogenic drainage. *Chest* 1998;114(1):171-7. [CFGD Register: PE29b; CRSREF: 6836843]

Mcllwaine 1991

Published and unpublished data [CRSSTD: 6836844]

Davidson AGF, Mcllwaine PM, Wong TK, Nakielna EM, Pirie GE. Physiotherapy in cystic fibrosis: A comparative trial of positive expiratory pressure, autogenic drainage and conventional percussion and drainage techniques. *Pediatric Pulmonology* 1988;5(Suppl 2):137. [CFGD Register: PE44a; CRSREF: 6836845]

Mcllwaine PM, Davidson AGF, Wong LTK, Pirie GE, Nakielna EM. Comparison of positive expiratory pressure and autogenic drainage with conventional percussion and drainage therapy in the treatment of CF. *Excerpta Medica, Asia Pacific Congress Series* 1988;74:R(d)3. [CFGD Register: PE44b; CRSREF: 6836846]

Mcllwaine PM, Davidson AGF. Comparison of positive expiratory pressure and autogenic drainage with conventional percussion and drainage therapy in the treatment of CF. In: 17th European Cystic Fibrosis Conference; 1991 Jun 18-21; Copenhagen, Denmark. 1991:S8.4. [CFGD Register: PE44c; CRSREF: 6836847]

Mcllwaine PM, Wong LTK, Pirie GE, Davidson AGF. Comparison of positive expiratory pressure and autogenic drainage therapy in the treatment of cystic fibrosis. Unpublished Article 2014. [CENTRAL: 999917; CRS: 5500125000000738; CRSREF: 6836848]

Mcllwaine 2010

[CRSSTD: 6836849]

Davidson AGF, Wong LTK, Pirie GE, Mcllwaine PM. Long-term comparative trial of conventional percussion and drainage physiotherapy versus autogenic drainage in cystic fibrosis. *Pediatric Pulmonology* 1992;14(Suppl 8):235. [CFGD Register: PE47a; CRSREF: 6836850]

* Mcllwaine M, Wong LT, Chilvers M, Davidson GF. Long-term comparative trial of two different physiotherapy techniques; postural drainage with percussion and autogenic drainage, in the treatment of cystic fibrosis. *Pediatric Pulmonology* 2010; 45(11):1064-9. [CRSREF: 6836851; MEDLINE: PE47c]

Mcllwaine PM, Wong LTK, Pirie GE, Davidson AGF. Long-term comparative trial of conventional percussion and drainage physiotherapy versus autogenic drainage in cystic fibrosis. In: 11th International Cystic Fibrosis Congress; 1992; Dublin, Ireland. 1992:AHP32. [CFGD Register: PE47b; CRS-ID: 5500100000004465; CRSREF: 6836852]

Miller 1995

[CRSSTD: 6836853]

Hall DO, Miller S, Clayton CB, Nelson R. Chest physiotherapy in cystic fibrosis: A comparative study of autogenic drainage and the active cycle of breathing technique. In: 19th European Cystic Fibrosis Conference; 1994 May 29- Jun 3; Paris, France. 1994:O64. [CFGD Register: PE28a; CRSREF: 6836854]

Miller S, Hall DO, Clayton CB, Nelson R. Chest physiotherapy in cystic fibrosis (CF) a comparative study of autogenic drainage (AD) and active cycle of breathing technique (ACBT) (formerly FET). *Pediatric Pulmonology* 1993;16(Suppl 9):267. [CFGD Register: PE28b; CRSREF: 6836855]

* Miller S, Hall DO, Clayton CB, Nelson R. Chest physiotherapy in cystic fibrosis: A comparative study of autogenic drainage and the active cycle of breathing techniques with postural drainage. *Thorax* 1995;50(2):165-9. [CFGD Register: PE28c; CRSREF: 6836856]

Osman 2010

[CRSSTD: 6836857]

Osman LP, Roughton M, Hodson ME, Pryor JA. High frequency chest wall oscillation in cystic fibrosis. *Journal of Cystic Fibrosis* 2008;7(Suppl 2):S73. [CFGD Register: PE171a; CRSREF: 6836858]

Osman LP, Roughton M, Hodson ME, Pryor JA. Short-term comparative study of high frequency chest wall oscillation and European airway clearance techniques in patients with cystic fibrosis. *Thorax* 2010;65(3):196-200. [CFGD Register: PE171b; CRSREF: 6836859]

Pflegler 1992

[CRSSTD: 6836860]

* Pflegler A, Theißl B, Oberwaldner B, Zach MS. Self-administered chest physiotherapy in cystic fibrosis: a comparative study of high-pressure PEP and autogenic drainage. *Lung* 1992;170(6):323-30. [CFGD Register: PE16a; CRSREF: 6836861]

Theißl B, Pflegler A, Oberwaldner B, Zach M. Chest physiotherapy (PT) in cystic fibrosis (CF) - a comparative study of high-pressure PEP and autogenic drainage. *Pediatric Pulmonology* 1990;9(Suppl 5):259. [CFGD Register: PE16b; CRSREF: 6836862]

Pryor 2010

[CRSSTD: 6836863]

Pryor JA, Tannenbaum E, Cramer D, Scott SF, Burgess J, Gyi K, et al. A comparison of five airway clearance techniques in the treatment of people with Cystic Fibrosis. *Journal of Cystic Fibrosis* 2006;5(Suppl):S76. [CFGD Register: PE164a; CRSREF: 6836864]

* Pryor JA, Tannenbaum E, Scott SF, Burgess J, Cramer D, Gyi K, et al. Beyond postural drainage and percussion: Airway clearance in people with cystic fibrosis. *Journal of Cystic Fibrosis* 2010;9(3):187-92. [CENTRAL: 759356; CFGD Register: PE164b; CRS: 5500050000000050; CRSREF: 6836865; [PubMed: 20153269](#)]

Excluded studies**Giles 1995**

[CRSSTD: 6836866]

Giles DR, Wagener JS, Accurso FJ, Butler Simon N. Short-term effects of postural drainage with clapping vs autogenic drainage on oxygen saturation and sputum recovery in patients with cystic fibrosis. *Chest* 1995;108(4):952-4. [CFGD Register: PE66; CRSREF: 6836867; MEDLINE: 96010150]

Herrero 2016

[CRSSTD: 6836868]

Cortina BH, Pagola MSM, Cadenas AF, Cortes ATR, Del Corral T, Del Mar Sanchez Palenzuela M, et al. Resistive inspiratory manoeuvre as airway clearance technique in stable patients with cystic fibrosis: a randomised crossover trial. *European Respiratory Journal* 2016;48 Suppl 60:PA1364. [CFGD Register: PE249b; CRSREF: 6836869]

Herrero Cortina B, San Miguel Pagola M, Fernandez Cadenas A, Rios Cortes AT, Del Corral T, Sanchez Palenzuela MDM, et al. Resistive inspiratory manoeuvre as airway clearance technique in patients with cystic fibrosis: a randomised crossover trial. *Journal of Cystic Fibrosis* 2016;15 Suppl:S33-S34. [Abstract no.: WS21.4; CFGD Register: PE249a; CRSREF: 6836870]

NCT02261987. Resistive Inspiratory Manoeuvre as Airway Clearance Technique in Cystic Fibrosis. clinicaltrials.gov/ct2/show/NCT02261987?term=autogenic+drainage+AND+cystic+fibrosis&rank=1 (accessed prior to 21 August 2017). [CRSREF: 6836871]

Lindemann 1992

[CRSSTD: 6836872]

Lindemann H. The value of physical therapy with VRP 1-Desitin ("Flutter") [Zum Stellenwert der Physiotherapie mit dem VRP 1-Desitin ("Flutter")]. *Pneumologie* 1992;46(12):626-30. [CFGD Register: PE17; CRSREF: 6836873]

NCT01885650

[CRSSTD: 6836874]

NCT01885650. The addition of non-invasive ventilation to airway clearance techniques in adults with cystic fibrosis (NIV) [Non-invasive ventilation (NIV) for positive pressure support. A randomised cross-over trial to evaluate the short-term effects of NIV as an adjunct to airway clearance techniques in adults with cystic fibrosis.]. clinicaltrials.gov/ct2/show/NCT01885650 Date first received: 17 June 2013. [CRSREF: 6836875]

NCT02303808

[CRSSTD: 6836876]

NCT02303808. Positive expiratory pressure during inhalation of hypertonic saline in patients with cystic fibrosis [Effect of introducing a positive expiratory pressure device during inhalation of hypertonic saline in patients with cystic fibrosis: a randomized crossover trial.]. clinicaltrials.gov/ct2/show/NCT02303808 Date first received: 25 November 2014. [CRSREF: 6836877]

Reix 2012

[CRSSTD: 6836878]

Reix P, Aubert F, Kassai B, Bige V, Bellon G. Better satisfaction of cystic fibrosis paediatric patients with autogenic drainage associated to exercise compared to conventional chest physiotherapy. *Journal of Cystic Fibrosis* 2009;8(Suppl 2):S73. [Abstract no: 293; CFGD Register: PE183a; CRSREF: 6836879]

* Reix P, Aubert F, Werck-Gallois MC, Toutain A, Mazzocchi C, Moreux N, et al. Exercise with incorporated expiratory manoeuvres was as effective as breathing techniques for airway clearance in children with cystic fibrosis: a randomised crossover trial. *Journal of Physiotherapy* 2012;58(4):241-7. [CENTRAL: 841658; CFGD Register: PE183b; CRS: 5500125000000095; CRSREF: 6836880; [PubMed: 23177226](https://pubmed.ncbi.nlm.nih.gov/23177226/)]

Roos 1987

[CRSSTD: 6836881]

Roos S, Birrer P, Rudeberg A, Kraemer R. First experience with intrapulmonary percussive ventilation (IPV) in the treatment of patients with cystic fibrosis. In: 15th Annual Meeting of the European Working Group for Cystic Fibrosis; 1987; Oslo, Norway. 1987. [CFGD Register: PE34; CRSREF: 6836882]

Skopnik 1986

[CRSSTD: 6836883]

Skopnik H, Waters W, Horwitz AE, Roth B, Genz-Bohm G. Evaluation of knock and vibration therapy and autogenic drainage in cystic fibrosis using a ventilation zintigraphical method [Beurteilung der Klopf- und Vibrations-Therapie und autogene Drainage bei cystischer Fibrose mittels eines ventilationsszintigraphischen Verfahrens]. *Monatsschrift für Kinderheilkunde* 1986;134:583. [CFGD Register: PE131; CRSREF: 6836884]

van Ginderdeuren 2001

[CRSSTD: 6836885]

van Ginderdeuren F, Malfroot A, Dab I. Influence of "assisted autogenic drainage (AAD)" "bouncing", and "AAD combined with bouncing" on gastro-oesophageal reflux (GOR) in infants. In: 24th European Cystic Fibrosis Conference; 2001 Jun 6-9; Vienna, Austria. 2001:P112. [CFGD Register: PE124; CRSREF: 6836886]

van Ginderdeuren 2008

[CRSSTD: 6836887]

van Ginderdeuren F, Verbanck S, Van Cauwelaert K, Vanlaethem S, Schuermans D, Vincken W, et al. Chest physiotherapy in cystic fibrosis: short-term effects of autogenic drainage preceded by wet inhalation of saline versus autogenic drainage preceded by intrapulmonary percussive ventilation with saline. *Respiration; International Review of Thoracic Diseases* 2008; 76(2):175-80. [CFGD Register: BD178; CRS-ID: 550010000004752; CRSREF: 6836888]

van Ginderdeuren 2011

[CRSSTD: 6836889]

van Ginderdeuren F, Vanlaethem S, Eyns H, De Schutter I, Dewachter E, Malfroot A. Influence of inhaled hypertonic saline (NaCl 6%) before or during autogenic drainage on sputum weight, oxygen saturation, heart frequency and dyspnoea in cystic fibrosis. *Journal of Cystic Fibrosis* 2011;10 Suppl 1:S62. [CFGD Register: BD164; CRS-ID: 5500100000010552; CRSREF: 6836890]

Warwick 1990

[CRSSTD: 6836891]

Warwick WJ, Wielnski CI. Matched pair comparison of manual chest physical therapy (CPT) and the thairapy bronchial drainage vest (ThBVD) system. *Pediatric Pulmonology* 1990;9(Suppl 5):177. [CFGD Register: PE43; CRSREF: 6836892]

Studies awaiting classification

Davies 2012

[CRSSTD: 6836893; *ClinicalTrials.gov*: NCT01057524]

Davies GA, Banks AE, Agent P, Osman LP, Bilton D, Hodson ME. The use of high frequency chest wall oscillation during an infective pulmonary exacerbation of cystic fibrosis. *Paediatric Pulmonology* 2012;47 (S35):366,abstract no :396. [CFGD register: PE197; CRSREF: 6836894]

Vendrusculo 2017

[CRSSTD: 6836895]

Vendrusculo FM, Johnstone Z, Dhouieb E, Donadio MVF, Cunningham S, Urquhart DS. Airway clearance physiotherapy can reduce dead space and lead to improvements in ventilatory inhomogeneity during exercise in patients with cystic fibrosis: a pilot study. *Journal of Cystic fibrosis* 2017;16 Suppl 1:S8. [Abstract no.: WS04.6; CFGD Register: PE250; CRSREF: 6836896]

Ongoing studies

Other references

Additional references

Agostini 2007

Agostini P, Knowles N. Autogenic drainage: the technique, physiological basis and evidence. *Physiotherapy* 2007; 93(2):157-63.

Andersen 1979

Andersen JB, Qvist H, Kann T. Recruiting collapsed lung through collateral channels with positive end-expiratory pressure. *Scandinavian Journal of Respiratory Disease* 1979;60(5):260-6.

Boucher 2004

Boucher RC. New concepts of the pathogenesis of cystic fibrosis lung disease. *European Respiratory Journal* 2004; 23:146-58.

Button 2016

Button BM, Wilson C, Dentice R, Cox N, Middleton A, Tannenbaum E, et al. Physiotherapy for Cystic Fibrosis in Australia and New Zealand: A Clinical Practice Guideline. *Respirology* 2016;21(4):656-7.

Cantin 2015

Cantin AM, Hartl D, Konstan MW, Chmiel JF. Inflammation in cystic fibrosis lung disease: Pathogenesis and therapy. *Journal of Cystic Fibrosis* 2015;14(4):419-30.

CFF 2015

Cystic Fibrosis Foundation. Cystic Fibrosis Foundation Patient Registry 2014 Annual Data Report. www.cff.org/2014-Annual-

Data-Report.pdf (accessed 18 August 2016).

Chevallier 1984

Chevallier J. Autogenic drainage. In: Lawson D, editors(s). *CysticFibrosis: Horizons*. London: Churchill Livingstone, 1984:65–78.

Corten 2015

Corten L, Jelsma J, Morrow BM. Autogenic Drainage and Assisted Autogenic Drainage in children with CF: A systematic review. *Journal of Cystic Fibrosis* 2015;14 Suppl 1:S100.

Curtin 2002

Curtin F, Elbourne D, Altman DG. Meta-analysis combining parallel and cross-over clinical trials. III: The issue of carryover. *Statistics in Medicine* 2002;21(15):2161-73.

David 1991

David A. Autogenic Drainage; The German approach. In: Pryor J, editors(s). *Respiratory Care*. Edinburgh: Churchill Livingstone, 1991:143.

Dwyer 2011

Dwyer TJ, Alison JA, McKeough ZJ, Daviskas E, Bye PT. Effects of exercise on respiratory flow and sputum properties in patients with cystic fibrosis. *Chest* 2011;139:870–7.

Elbourne 2002

Elbourne DR, Altman DG, Higgins JPT, Curtin F, Worthington HV, Vail A. Meta-analyses involving cross-over trials: methodological issues. *International Journal of Epidemiology* 2002;31(1):140-9.

Farrell 2008

Farrell PM. The prevalence of cystic fibrosis in the European Union. *Journal of Cystic Fibrosis* 2008;7(5):450–3.

Flume 2009

Flume PA, Robinson KA, O’Sullivan BP, Finder JD, Vender RL, Willey-Courand DB, et al. Cystic fibrosis pulmonary guidelines: airway clearance therapies. *Respiratory Care* 2009;54(4):522-37.

Gee 2000

Gee L, Abbott J, Conway SP, Etherington C, Webb AK. Development of a disease specific health related quality of life measure for adults and adolescents with cystic fibrosis. *Thorax* 2000;55(11):946-54.

Groth 1985

Groth S, Stafanger G, Dirksen H, Andersen JB, Falk M, Kelstrup M. Positive expiratory pressure (PEP-Mask) physiotherapy improves ventilation and reduces volume of trapped gas in cystic fibrosis. *Bulletin Europeen de Physiopathologie Respiratoire* 1985;21(4):339-43.

Guyatt 1987

Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 1987;42(10):773-8.

Higgins 2003

Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327(7414):557-60.

Higgins 2011

Higgins JPT, Altman DG, editor(s). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). The Cochrane Collaboration. Available from www.handbook.cochrane.org.

Homnick 1995

Homnick DN, White F, de Castro C. Comparison of effects of an intrapulmonary percussive ventilator to standard aerosol and chest physiotherapy in treatment of cystic fibrosis. *Pediatric Pulmonology* 1995;20(1):50-5.

Huang 1981

Huang NN, Keith HH, Palmer J, Hsuan F. A scoring system for short-term evaluation of patients with cystic fibrosis: a possible means for assessment of antibiotic efficacy. In: Warwick WJ, editors(s). *1,000 years of cystic fibrosis collected papers*. Minnesota: University Dept of Pediatrics Medical School in cooperation with International Cystic Fibrosis Association, National Heart, Lung and Blood Institute and Fogarty International Center, 1981:207-16.

IPG/CF 2009

International Physiotherapy Group for CF (IPG/CF). Blue booklet on physiotherapy techniques. *Physiotherapy for people with cystic fibrosis: from infant to adult*. www.ecfs.eu/ipg_cf/booklet (accessed 21 August 2017).

Kirkham 2010

Kirkham JJ, Altman DG, Williamson PR. Bias due to changes in specified outcomes during the systematic review process. *PLoS ONE* 2010;5(2):e9810.

Konstan 1994

Konstan MW, Stern RC, Doershuk CF. Efficacy of the Flutter device for airway mucus clearance in patients with cystic fibrosis. *Journal of Pediatrics* 1994;124(5 Pt 1):689-93.

Konstan 1997

Konstan MW, Berger M. Current understanding of the inflammatory process in cystic fibrosis: Onset and etiology. *Pediatric Pulmonology* 1997;24:137-42.

Konstan 2007

Konstan MW, Morgan WJ, Butler SM, Pasta DJ, Craib ML, Silva SJ, et al. Risk factors for rate of decline in forced expiratory volume in one second in children and adolescents with cystic fibrosis. *Journal of Pediatrics* 2007;151(2):134-9. [DOI: 10.1016/j.jpeds.2007.03.006]

Main 2005

Main E, Prasad A, van der Schans CP. Conventional chest physiotherapy compared to other airway clearance technique for cystic fibrosis. *Cochrane Database of Systematic Reviews* 2005, Issue 1. Art. No.: CD002011 DOI: 10.1002/14651858.CD002011.pub2.

McIlwaine 2014

McIlwaine MP, Lee Son MN, Richmond ML. Physiotherapy and cystic fibrosis: what is the evidence base? *Current Opinion in Pulmonary Medicine* 2014;20(6):613-7.

McIlwaine 2015

McIlwaine M, Button B, Dwan K. Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis. *Cochrane Database of Systematic Reviews* 2015, Issue 6. Art. No.: CD003147 DOI: 10.1002/14651858.CD003147.pub4.

Mckoy 2016

Mckoy NA, Wilson LM, Saldanha IJ, Odelola OA, Robinson KA. Active cycle of breathing technique for cystic fibrosis. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD007862 DOI: 10.1002/14651858.CD007862.pub4.

Morgan 2015

Morgan K, Osterling K, Gilbert R, Dechman G. Effects of autogenic drainage on sputum recovery and pulmonary function in people with cystic fibrosis: A systematic review. *Physiotherapy Canada* 2015;67(4):319-26.

Morrison 2017

Morrison L, Milroy S. Oscillating devices for airway clearance in people with cystic fibrosis. *Cochrane Database of Systematic Reviews* 2017, Issue 5. Art. No.: CD006842 DOI: 10.1002/14651858.CD006842.pub4.

New Zealand CF Association 2013

Cystic Fibrosis Association of NZ. Cystic Fibrosis Association of NZ Annual Data Report 2012. cfnz.org.nz/wp-content/uploads/2015/12/CFANZ-Annual-Report-2012.pdf (accessed 18 August 2016).

Nolan 2016

Nolan SJ, Hambleton I, Dwan K. The use and reporting of the cross-over study design in clinical trials and systematic reviews: a systematic assessment. *PLoS One* 2016;11(7):e0159014. [DOI: 10.1371/journal.pone.0159014]

Oberwaldner 1986

Oberwaldner B, Evans JC, Zach MS. Forced expirations against a variable resistance: a new chest physiotherapy method in cystic fibrosis. *Pediatric Pulmonology* 1986;2(6):358-67.

Okeson 2007

Okeson C, McGowen P. The percussive characteristics of the acapella, flutter and quake during low-volume tidal breathing. *Chest* 2007;132(4 Meeting abstracts):608a. [DOI: 10.1378/chest.132.4_MeetingAbstracts.608a]

Prevotat 2017

Prevotat A, Wallaert E, Halm AM, Perez T, Reychler G, Wallaert B. Immediate effects of autogenic drainage on ventilatory mechanics in CF adult patients. *Journal of Cystic Fibrosis* 2017;16(Suppl 1):S7.

Pryor 1999

Pryor JA. Physiotherapy for airway clearance in adults. *European Respiratory Journal* 1999;14(6):1418-24.

Quittner 2009

Quittner AL, Modi AC, Wainwright C, Otto K, Kirihaara J, Montgomery AB. Determination of the minimal clinically important difference scores for the Cystic Fibrosis Questionnaire-Revised respiratory symptom scale in two populations of patients with cystic fibrosis and chronic *Pseudomonas aeruginosa* airway infection. *Chest* 2009;135(6):1610-8.

Radtke 2015

Radtke T, Nolan SJ, Hebestreit H, Kriemler S. Physical exercise training for cystic fibrosis. *Cochrane Database of Systematic Reviews* 2015, Issue 6. Art. No.: CD002768 DOI: 10.1002/14651858.CD002768.pub3.

Rand 2013

Rand S, Hill L, Prasad A. Physiotherapy in cystic fibrosis: optimising techniques to improve outcomes. *Paediatric Respiratory Reviews* 2013;14(4):263-9.

Schünemann 2011

Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Guyatt GH. Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JPT, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration. Available from www.handbook.cochrane.org.

Southern 2003

Southern KW, Smyth RL. Design of clinical trials in cystic fibrosis. *Lancet* 2003;361(9354):349-50.

Tiddens 2010

Tiddens HA, Donaldson SH, Rosenfeld M, Paré PD. Cystic fibrosis lung disease starts in the small airways: Can we treat it more effectively? *Pediatric Pulmonology* 2010;45(2):107-17. [DOI: 10.1002/ppul.21154]

UK CF Trust 2015

UK CF Trust. UK Cystic Fibrosis Registry 2014 Annual Data Report. www.cysticfibrosis.org.uk/the-work-we-do/uk-cf-registry/reporting-and-resources (accessed 18 August 2016).

VanDevanter 2015

VanDevanter DR, Pasta DJ, Konstan MW. Treatment and demographic factors affecting time to next pulmonary exacerbation in cystic fibrosis. *Journal of Cystic Fibrosis* 2015;14(6):763-769. [DOI: 10.1016/j.jcf.2015.02.007]

Volsko 2003

Volsko TA, DiFiore JM, Chatburn RL. Performance comparison of two oscillatory positive pressure devices: Acapella versus Flutter. *Respiratory Care* 2003;48(2):124-30.

Warnock 2015

Warnock L, Gates A. Chest physiotherapy compared to no chest physiotherapy for cystic fibrosis. *Cochrane Database of Systematic Reviews* 2015, Issue 12. Art. No.: CD001401 DOI: 10.1002/14651858.CD001401.pub3.

Warwick 1991

Warwick WJ, Hansen LG. The long-term effect of high frequency chest compression therapy on pulmonary complications of cystic fibrosis. *Pediatric Pulmonology* 1991;11(3):265-71.

Other published versions of this review

Swaminathan 2012

Swaminathan N, Robinson KA, Ray A. Autogenic drainage for airway clearance in cystic fibrosis. *Cochrane Database of Systematic Reviews* 2012, Issue 1. Art. No.: CD009595 DOI: 10.1002/14651858.CD009595.

Classification pending references

Data and analyses

1 AD versus PD&P

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 FEV ₁ (change in % predicted)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
1.1.1 at 12 months	1		Mean Difference(IV, Fixed, 95% CI)	No totals
1.2 Hospital admissions	1		Mean Difference(IV, Fixed, 95% CI)	No totals
1.2.1 at 12 months	1		Mean Difference(IV, Fixed, 95% CI)	No totals
1.3 FVC (change in % predicted)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
1.3.1 at 12 months	1		Mean Difference(IV, Fixed, 95% CI)	No totals
1.4 FEF _{25-75%} (change in % predicted)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
1.4.1 at 12 months	1		Mean Difference(IV, Fixed, 95% CI)	No totals

2 AD versus spontaneous cough

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 FEV ₁ (% predicted)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
2.1.1 30 minutes following physiotherapy	1		Mean Difference(IV, Fixed, 95% CI)	No totals
2.2 FVC (% predicted)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
2.2.1 30 minutes following physiotherapy	1		Mean Difference(IV, Fixed, 95% CI)	No totals
2.3 Sputum weight (g)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
2.3.1 30 minutes following physiotherapy	1		Mean Difference(IV, Fixed, 95% CI)	No totals

3 AD versus ACBT

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 FEV ₁ (L)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
3.1.1 At 12 months	1		Mean Difference(IV, Fixed, 95% CI)	No totals

4 AD versus PEP

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.1 FEV ₁ (L)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
4.1.1 At 12 months	1		Mean Difference(IV, Fixed, 95% CI)	No totals
4.2 FEV ₁ (% predicted)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
4.2.1 30 minutes following physiotherapy	1		Mean Difference(IV, Fixed, 95% CI)	No totals
4.3 FVC (% predicted)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
4.3.1 30 minutes following physiotherapy	1		Mean Difference(IV, Fixed, 95% CI)	No totals
4.4 Sputum weight (g)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
4.4.1 Following physiotherapy	1		Mean Difference(IV, Fixed, 95% CI)	No totals

5 AD versus Cornet®

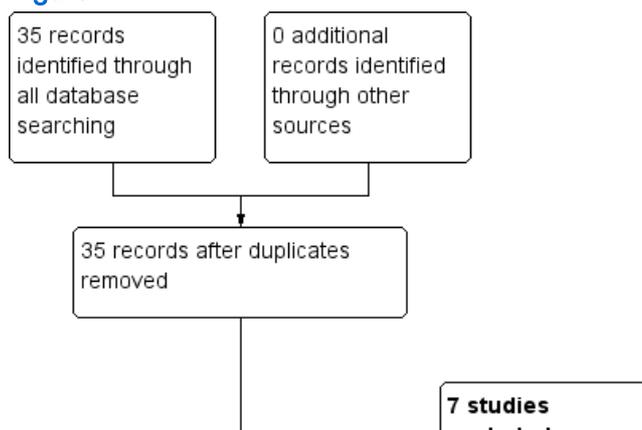
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 FEV ₁ (L)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
5.1.1 At 12 months	1		Mean Difference(IV, Fixed, 95% CI)	No totals

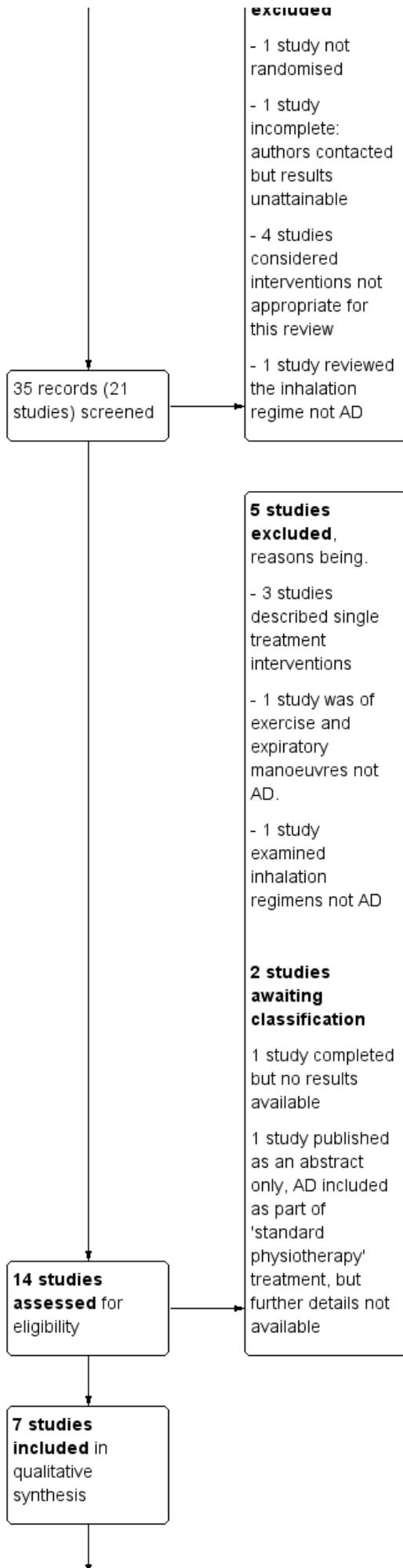
6 AD versus Flutter®

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
6.1 FEV ₁ (L)	2		Mean Difference(IV, Fixed, 95% CI)	No totals
6.1.1 At 1 month	1		Mean Difference(IV, Fixed, 95% CI)	No totals
6.1.2 At 12 months	1		Mean Difference(IV, Fixed, 95% CI)	No totals
6.2 FVC (L)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
6.2.1 At 1 month	1		Mean Difference(IV, Fixed, 95% CI)	No totals
6.3 Sputum volume wet (g)	1		Mean Difference(IV, Fixed, 95% CI)	No totals
6.3.1 At 1 month	1		Mean Difference(IV, Fixed, 95% CI)	No totals

Figures

Figure 1



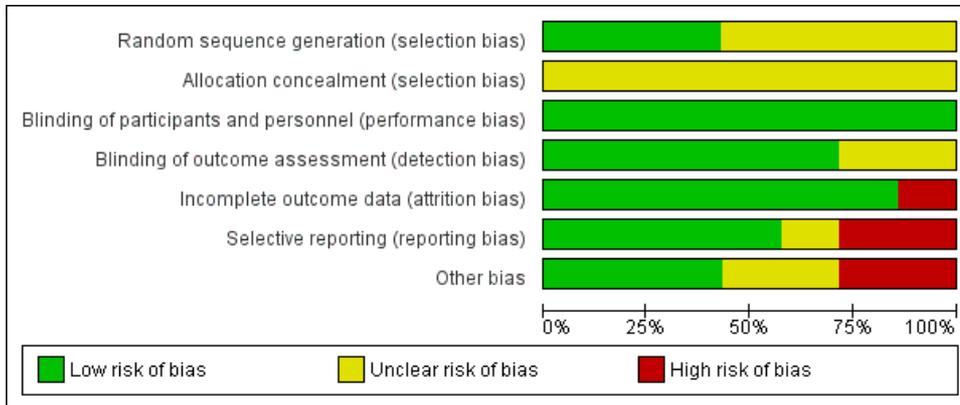


4 studies
included in
quantitative
synthesis
(meta-analysis)

Caption

Study flow diagram.

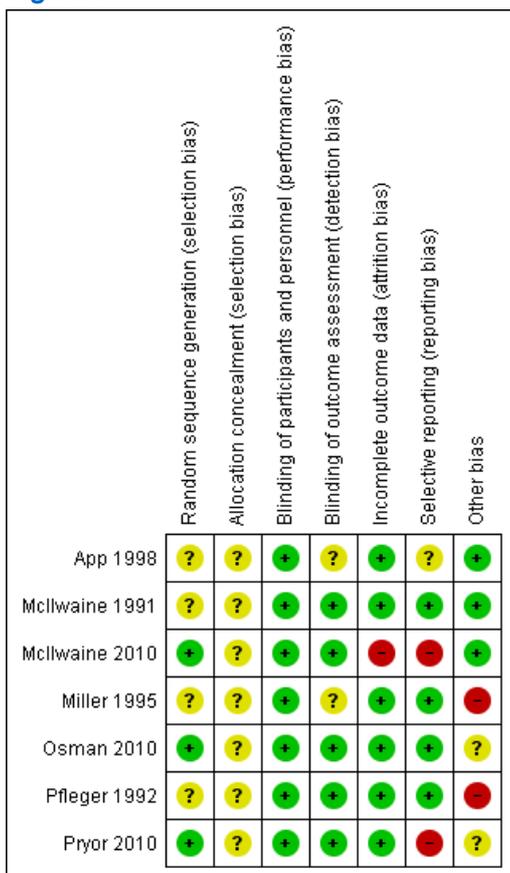
Figure 2



Caption

Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3



Caption

Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Sources of support

Internal sources

- No sources of support provided

External sources

- National Institute for Health Research, UK
This systematic review was supported by the National Institute for Health Research, via Cochrane Infrastructure funding to the Cochrane Cystic Fibrosis and Genetic Disorders Group.

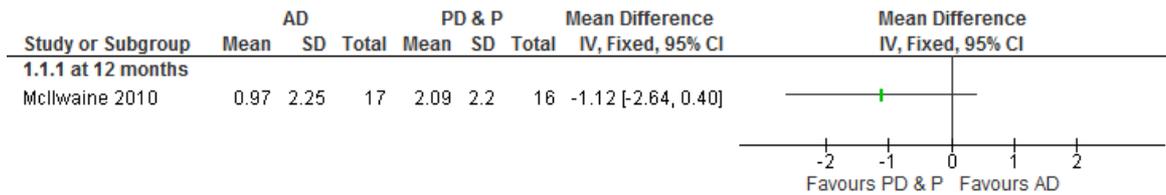
Feedback

Appendices

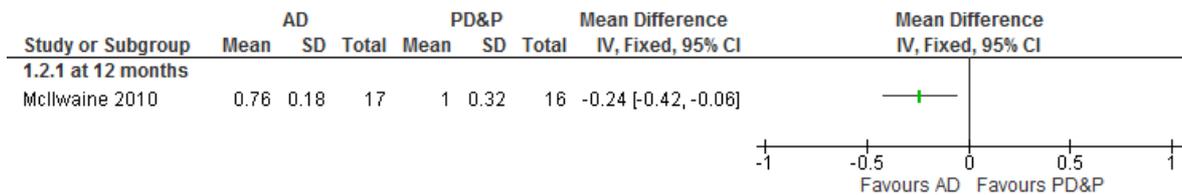
Graphs

1 - AD versus PD&P

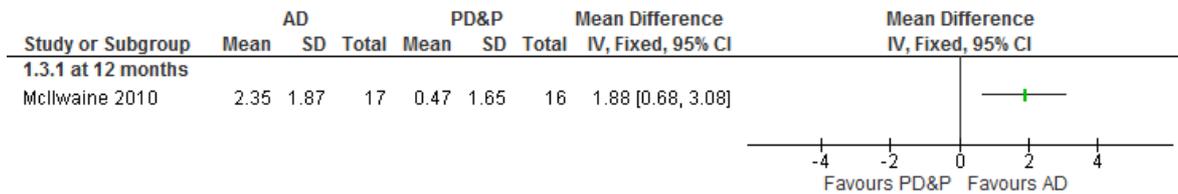
1.1 FEV₁ (change in % predicted)



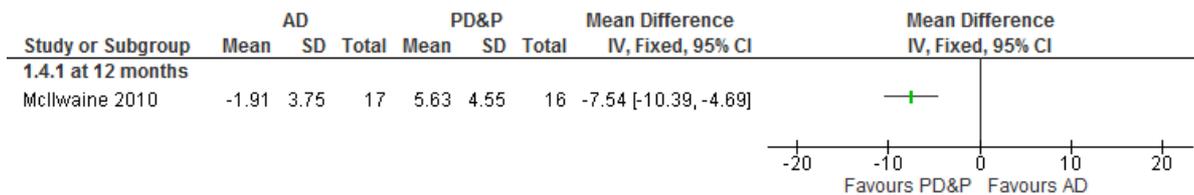
1.2 Hospital admissions



1.3 FVC (change in % predicted)

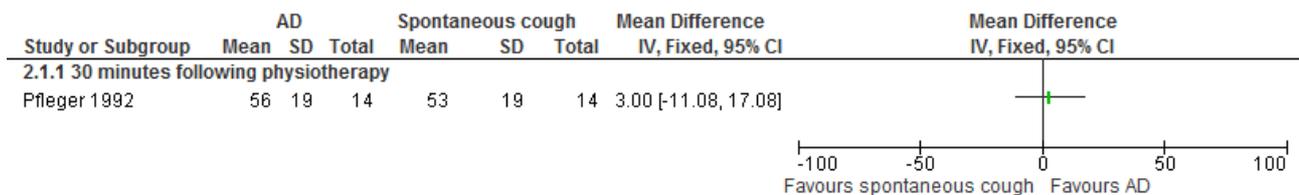


1.4 FEF_{25-75%} (change in % predicted)

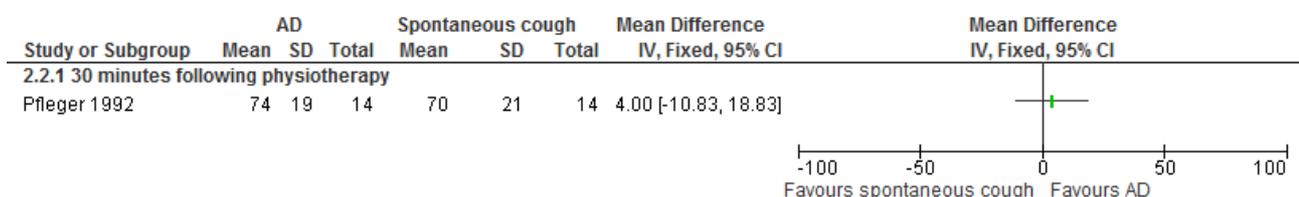


2 - AD versus spontaneous cough

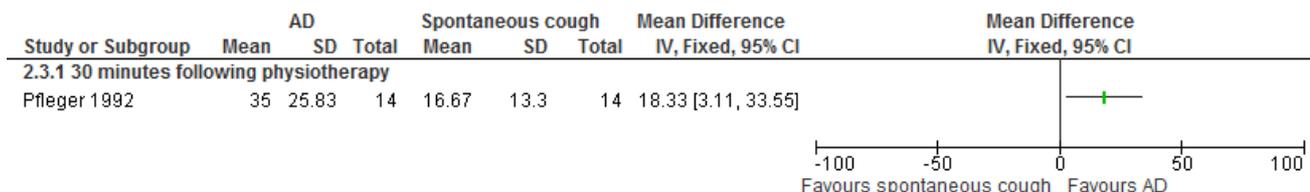
2.1 FEV₁ (% predicted)



2.2 FVC (% predicted)

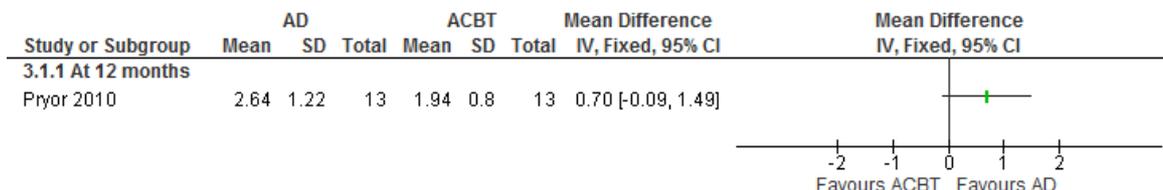


2.3 Sputum weight (g)



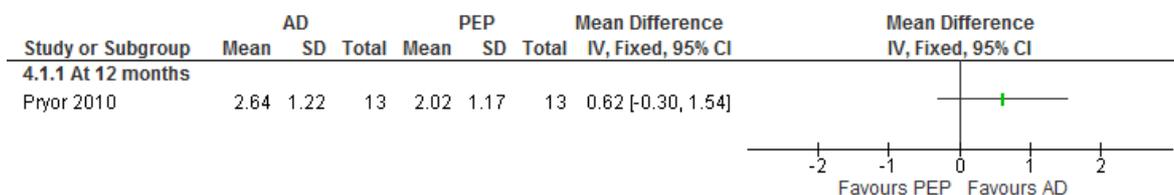
3 - AD versus ACBT

3.1 FEV₁ (L)

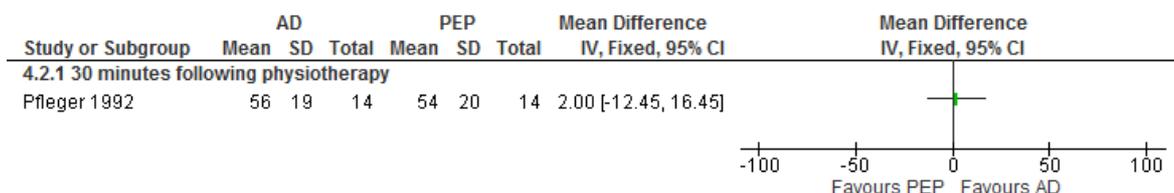


4 - AD versus PEP

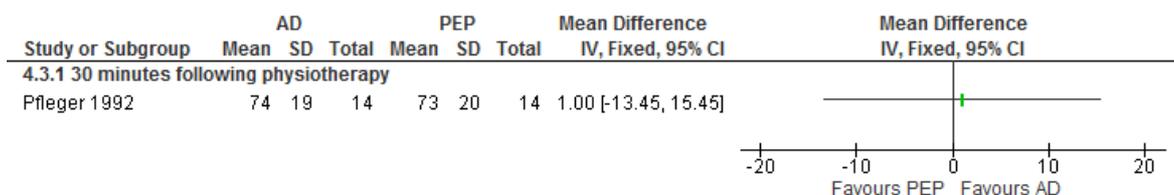
4.1 FEV₁ (L)



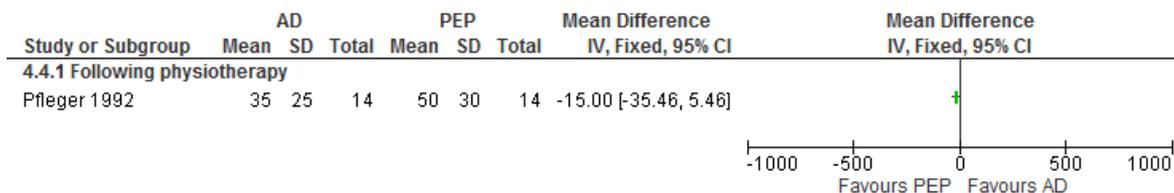
4.2 FEV₁ (% predicted)



4.3 FVC (% predicted)

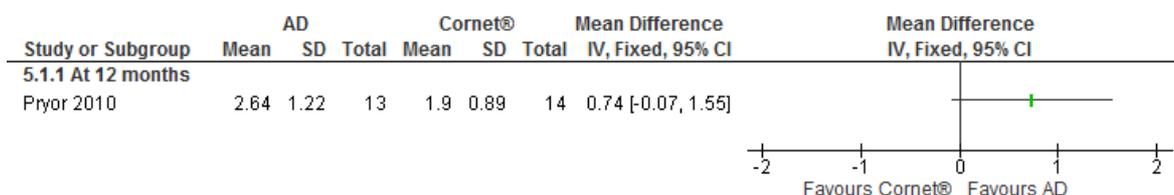


4.4 Sputum weight (g)



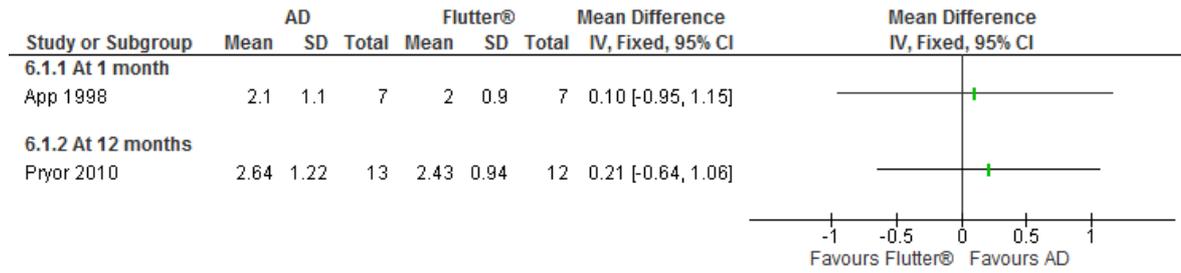
5 - AD versus Cornet®

5.1 FEV₁ (L)

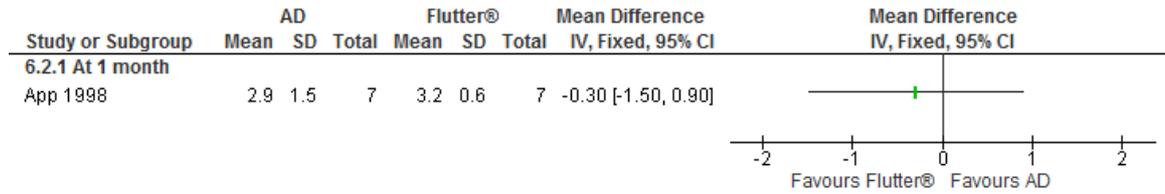


6 - AD versus Flutter®

6.1 FEV₁ (L)



6.2 FVC (L)



6.3 Sputum volume wet (g)

