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Standard (head-down tilt) versus modified (without head-down tilt) postural drainage in infants and young children with cystic fibrosis (Review)

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[Intervention Review]

Standard (head-down tilt) versus modified (without head-down tilt) postural drainage in infants and young children with cystic fibrosis

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ABSTRACT

Background

Postural drainage is used primarily in infants with cystic fibrosis from diagnosis up to the moment when they are mature enough to actively participate in self-administered treatments. However, there is a risk of gastroesophageal reflux associated with this technique.

This is an update of a review published in 2015.

Objectives

To compare the effects of standard postural drainage (15° to 45° head-down tilt) with modified postural drainage (15° to 30° head-up tilt) with regard to gastroesophageal reflux in infants and young children up to six years old with cystic fibrosis in terms of safety and efficacy.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group's Cystic Fibrosis Trials Register. We also searched the reference lists of relevant articles and reviews. Additional searches were conducted on ClinicalTrials.gov and on the WHO International Clinical Trials Registry Platform for any planned, ongoing and unpublished studies.

The date of the most recent literature searches: 19 June 2017.

Selection criteria

We included randomised controlled studies that compared two postural drainage regimens (standard and modified postural drainage) with regard to gastroesophageal reflux in infants and young children (up to and including six years old) with cystic fibrosis.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. Two review authors independently identified studies for inclusion, extracted outcome data and assessed risk of bias. We resolved disagreements by consensus or by involving a third review author. We contacted study authors to obtain missing or additional information. The quality of the evidence was assessed using GRADE.

Main results

Two studies, involving a total of 40 participants, were eligible for inclusion in the review. We included no new studies in the 2018 update. The included studies were different in terms of the age of participants, the angle of tilt, the reported outcomes, the number of sessions and the study duration. The following outcomes were measured: appearance or exacerbation of gastroesophageal reflux episodes; percentage of peripheral oxygen saturation; number of exacerbations of upper respiratory tract symptoms; number of days on antibiotics for acute exacerbations; chest X-ray scores; and pulmonary function tests. One study reported that postural drainage with a 20° head-down position did not appear to exacerbate gastroesophageal reflux. However, the majority of the reflux episodes in this study reached the upper oesophagus (moderate-quality evidence). The second included study reported that modified postural drainage (30° head-up tilt) was associated with fewer number of gastroesophageal reflux episodes and fewer respiratory complications than standard postural drainage (30° head-down tilt) (moderate-quality evidence). The included studies had an overall low risk of bias. One included study was funded by the Sydney Children's Hospital Foundation and the other by the Royal Children's Hospital Research Foundation and Physiotherapy Research Foundation of Australia. Data were not able to be pooled by meta-analysis due to differences in the statistical presentation of the data.

Authors' conclusions

The limited evidence regarding the comparison between the two regimens of postural drainage is still weak due to the small number of included studies, the small number of participants assessed, the inability to perform any meta-analyses and some methodological issues with the studies. However, it may be inferred that the use of a postural regimen with a 30° head-up tilt is associated with a lower number of gastroesophageal reflux episodes and fewer respiratory complications in the long term. The 20° head-down postural drainage position was not found to be significantly different from the 20° head-up tilt modified position. Nevertheless, the fact that the majority of reflux episodes reached the upper oesophagus should make physiotherapists carefully consider their treatment strategy. We do not envisage that there will be any new trials undertaken that will affect the conclusions of this review; therefore, we do not plan to update this review.

PLAIN LANGUAGE SUMMARY

Postural drainage in infants and young children with cystic fibrosis

Review question

We reviewed the evidence about how different postural drainage positions affect gastroesophageal reflux in infants and young children up to six years old with cystic fibrosis. We compared standard postural drainage (includes head-down tilt) with modified postural drainage (includes horizontal positions and head-up tilt). This is an update of a previously published review.

Background

Although cystic fibrosis is a disorder that affects many organs, pulmonary disease is the most common cause of illness and death. Chest physiotherapy is recommended to clear the airways and improve lung function. Postural drainage is a type of chest physiotherapy used to treat children with cystic fibrosis. However, there is a risk of gastroesophageal reflux (the return of stomach contents back up into the oesophagus (throat area)) associated with this technique.

Search date

The evidence is current to: 19 June 2017.

Study characteristics

The review included two studies concerning 40 children with cystic fibrosis up to six years of age. One included study used a 20° head-down tilt and head-up tilt of 20 degrees and the other used modified postural drainage (30° head-up tilt) compared to standard postural drainage (using a 30° head-down tilt). Children were randomly selected for one treatment or the other. One study was carried out over a 24-hour period and the second over two days, but with a five-year follow-up period. The age range of the participants varied from three weeks to 34 months. One included study was funded by the Sydney Children's Hospital Foundation and the other by the Royal Children's Hospital Research Foundation and Physiotherapy Research Foundation of Australia.

Key results

One included study using a 20° head-down tilt and 20° head-up tilt did not find differences regarding the number of gastroesophageal reflux episodes between the two postural drainage regimens whereas the other study found that modified postural drainage (30° head-up tilt) was associated with fewer number of reflux episodes and fewer respiratory complications than standard postural drainage (using a 30° head-down tilt) in infants with cystic fibrosis. The age of participants, angle of tilt, reported outcomes, number of sessions and study duration differed between the two studies. However, the use of a 30° head-up tilt seems to result in fewer reflux episodes and respiratory complications than a 30° head-down tilt position. Even though one study did not find differences between two techniques, in most of the reflux episodes stomach contents reached the upper oesophagus with a potential for choking. This should make physiotherapists carefully

consider their choice of technique. We do not envisage that there will be any new trials undertaken that will affect the conclusions of this review; therefore, we do not plan to update this review.

Quality of the evidence

Both studies were of moderate (so we think further research could have an important impact on the results) quality and appeared to be well run and we do not think any factors will influence the results in a negative way.

SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings

Standard compared with modified postural drainage for cystic fibrosis

Patient or population: infants and young children with cystic fibrosis

Settings: hospital

Intervention: modified postural drainage

Comparison: standard postural drainage

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Standard postural drainage	Modified postural drainage				
Appearance or exacerbation of gastroesophageal reflux episode: clinical test Follow-up: did not report time period**	<p>In one study there was a significant increase in the number of episodes of gastroesophageal reflux compared with background in the SPD group whereas in the MPD group there was no significant difference from background.</p> <p>There were significantly more reflux episodes during SPD compared to MPD (P = 0.05).</p> <p>In the second study there was no significant difference in the total number of reflux episodes (P = 0.63) between treatments or between each treatment and background (MPD P = 0.31 and SPD P = 0.84, respectively).</p>		NA	40 participants (2 studies)	⊕⊕⊕⊖ moderate ^a	We were not able to pool data for this outcome due to differences in statistical presentation of data in these two included studies.
Appearance or exacerbation of gastroesophageal reflux episodes: pulmonary events Follow-up: did not report**	<p>When modified postural drainage was compared to gravity-assisted postural drainage, there was no significant difference in the number of proximal episodes (P = 0.75). When comparing modified postural drainage and standard postural drainage to background periods (median (IQR) of 0.53 (0.2 to 1.0)) there was also no significant difference in the number of proximal episodes (P = 0.33 and P = 0.73, respectively)</p>		NA	20 participants (1 study)	⊕⊕⊕⊖ moderate ^a	
Peripheral oxygen saturation (%)	<p>During SPD, the mean (SD) percentage of peripheral oxygen saturation was significantly lower during crying than in other states, 97.6% (3.17%) versus 98.9% (1.49%); P = 0.02. Also during SPD, the mean (SD) percentage of peripheral oxygen saturation was significantly higher when asleep,</p>		NA	20 participants (1 study)	⊕⊕⊕⊖ moderate ^b	

Follow-up: did not report**	even when crying was excluded; asleep, 99.2% (1.15%) versus awake 98.5% (1.66%); P = 0.01. During MPD, crying had no effect on oxygen saturation. Similarly, there was no difference in mean (SD) oxygen saturation during sleep and wakeful periods in MPD; awake 98.7% (1.44%) versus asleep 98.9% (1.44%); P = 0.389.				
Number of exacerbations of upper respiratory tract symptoms	The mean number of exacerbations of upper respiratory tract symptoms in the control group was 70 (SD 32.8)	The mean number of exacerbations of upper respiratory tract symptoms in the intervention group was 33 episodes lower (62 episodes lower to 4.5 episodes higher)	MD -33.00 (-61.54 to -4.46)	16 participants (1 study)	⊕⊕⊕⊖ moderate ^a
Follow-up: did not report**					
Number of days on antibiotics for acute exacerbations	The mean number of days on antibiotics was 116 (SD 88.6) days in the control group	The mean number of days on antibiotics in the intervention group was 49 days lower (122.6 days lower to 24.6 days higher)	MD -49.00 (-122.61 to 24.61)	16 participants (1 study)	⊕⊕⊕⊖ moderate ^a
Follow-up: did not report**					
Chest X-ray scores	At the 2½-year follow-up, radiological changes were significantly greater in infants receiving SPD (P = 0.03). Radiological changes at five years were worse in the SPD group, although the difference between groups did not reach statistical significance (P = 0.17)		NA	12 participants (1 study)	⊕⊕⊕⊖ moderate ^a
Follow-up: 2.5 - 5 years					
Pulmonary function test (FVC) % predicted	The mean number of FCV in the control group was 99.85 (SD 16.12)	The mean number of FCV in the intervention group was 16% of the predicted (0.16% lower to 32.16% higher)	MD 16.00 (-0.16, 32.16)	14 participants (1 study)	⊕⊕⊕⊖ moderate ^a
Follow-up: did not report**					

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**The studies did not clearly report the time of follow-up; however, they reported the duration of the studies ([Button 2003](#): 5-year study; [Doumit 2012](#): 2-year study).

CI: confidence interval; **MD**: mean difference; **FVC**: forced vital capacity; **MPD**: modified postural drainage; **SD**: standard deviation; **SPD**: standard postural drainage.

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.

^aDowngraded by one level for risk of bias. One trial was at unclear risk for blinding of outcome and one trial at unclear risk for selective reporting.
^bDowngraded by one level for risk of bias. Two trials were at unclear risk for blinding of outcome and one trial at unclear risk for selective reporting.

BACKGROUND

Description of the condition

Cystic fibrosis (CF) is a chronic autosomal recessive disease which affects 100,000 people worldwide (Brown 2017; Bhagirath 2016) with a frequency of one in 2000 to 3000 live births (Modaresi 2017). The incidence of CF varies across the globe. Although CF is

severely under-diagnosed in Asia, existing evidence indicates that its prevalence there is rare. In the European Union, one in 2000 to 3000 newborns are found to be affected by CF. In the USA, the incidence of CF is reported to be one in every 3500 births (WHO 2017). A further description of the worldwide incidence of CF can be seen below at the map poster which shows the molecular genetic epidemiology of CF worldwide (Figure 1).

Figure 1. The molecular genetic epidemiology of CF worldwide. Source: WHO 2017

CF arises from genetic defects in a single gene, which encodes the CF transmembrane conductance regulator (CFTR), a chloride channel that is widely distributed in epithelial surfaces. Epithelia in the airway, paranasal sinuses, pancreas, gut, biliary tree, vas deferens, and sweat ducts express CFTR and depend on it for normal function (Spoonhower 2016). Absence of normally functioning CFTR leads to decreased chloride secretion and increased sodium absorption across the epithelial surface. The result of this is depletion of the airway surface liquid (ASL) and impaired mucociliary clearance (MCC) (Davies 2014).

People with CF may suffer from: chronic sinusitis; nasal polyps; respiratory infections; infertility (especially in males); and gastrointestinal disorders (such as gastroesophageal reflux, exocrine pancreatic insufficiency, a higher risk of developing diabetes mellitus, poor absorption of nutrients and excessive absorption of fluid) (Ernst 2010; Michl 2016). Although CF is a multisystem disorder, pulmonary disease is the most common cause of morbidity and mortality (Modaresi 2017).

Children with CF are more likely than healthy children to suffer from pathological gastroesophageal reflux (GOR) (Cucchiara 1991; Baird 2015) which may be defined as an involuntary retrograde

and repeated passage of gastric contents into the esophagus (Norton 2000; Rybak 2017). The mechanism involved in this process is not completely described. However, the high incidence of gastroesophageal reflux in infants and children with CF may be secondary to lung disease (chronic coughing, hyperinflation) as well as being related to delayed gastric emptying and transient lower oesophageal sphincter relaxations which are increased during distension of the gastric fundus, and hyperalimentation of CF infants (Blondeau 2010; Heine 1998). Some children with CF do not grow out of their GOR or may develop it again later in life especially if they experience a worsening of their lung symptoms. GOR should also be considered as a potential reason for unexplained deterioration in lung function (RBHT 2017).

Chest physiotherapy alone, or in combination with exercise, has been widely used as an adjunct therapy in the treatment of CF in people of any age, contributing to improved survival (McIlwaine 2010). Physiotherapy can be classified as conventional, modern or instrumental techniques (Chaves 2013; Morrison 2017). Conventional chest physiotherapy techniques may include postural drainage, percussion and vibration, huffing and coughing (Main 2005; Yang 2013).

Description of the intervention

Currently, in many countries, CF is diagnosed at newborn screening (Lannefors 2004). Asymptomatic infants may be treated with postural drainage in the first weeks of life, when they are immature, have a greater propensity for GOR and are more vulnerable to relatively invasive treatments. Thus, postural drainage is primarily used in infants from diagnosis up to the moment when they are mature enough to actively participate in self-administered treatments (Lannefors 2004; RBHT 2017). Modified postural drainage is recommended for airway clearance in children with CF under two years of age (Button 2016; RBHT 2017).

Postural drainage involves the use of gravity to drain mucus from the lungs placing the patient in a position that employs gravity to move mucus centrally from the targeted lung unit whereas modified postural drainage involves positioning without the use of head-down tilt (Lannefors 2004; Michl 2016). There are 12 postural drainage positions, one for each pulmonary segment (Christian 2014). Postural drainage is usually associated with vibration, percussion, inhalation therapy, coughing, and breathing exercises. There are two regimens of postural drainage techniques (standard postural drainage and modified postural drainage) (Main 2016). Standard postural drainage includes greater (30° to 45°) head-down tilt and lesser (15° to 20°) head-down tilt. Greater modified postural drainage includes three horizontal positions and 30° head-up tilt for the supine position while lesser modified postural drainage includes three horizontal positions and 15° to 20° head-up tilt for the supine position.

How the intervention might work

Chest physiotherapy aims to maintain ventilation in all parts of the lungs in order to promote pulmonary clearance, postpone progression of pulmonary disease, stimulate establishment and maintain normal physical capacity (Brown 2017; Conway 2014).

Chest physiotherapy has been associated with an increase in gastroesophageal reflux episodes in people with CF. Previous studies have suggested that postural drainage techniques may exacerbate reflux, potentially resulting in aspiration or reflex bronchospasm and further impairment of pulmonary function. Such studies associated the higher incidence of gastroesophageal reflux with the head-down tilt position, especially when positioning the head and lungs lower than the lower oesophageal sphincter in infants with CF (Heine 1998; Orenstein 2003; Robinson 2014).

Why it is important to do this review

CF lung disease is characterized by depleted airway surface liquid (ASL) volume and thickened mucus, which results in impaired mucus clearance (Davies 2014; Dwyer 2011). The ionic and nutrient content, volume and pH of the ASL are all important in regulating mucociliary transport, ciliary function and antimicrobial activity. Antimicrobial factors found within the ASL are involved in innate and adaptive host defence mechanisms that protect the airway from inhaled pathogens (Haq 2016). The airway obstruction and colonization with a variety of bacteria generates a vicious cycle of infection resulting in airway damage (Robison 2002). Chest physiotherapy is a recommended intervention to promote airway clearance and improve lung ventilation and gas exchange. During physiotherapy sessions, techniques to facilitate airway clearance, such as postural drainage, are used. However, there is a risk of gastroesophageal reflux associated with this technique.

Gastroesophageal reflux is increased in people with CF and may contribute to the worsening of pulmonary function among other complications (Baird 2015; Mousa 2012). Thus, within this review, we aim to summarise and assess evidence from randomised controlled studies comparing two postural drainage regimens with regard to gastroesophageal reflux in infants and young children up to six years old with CF.

OBJECTIVES

To compare the safety and efficacy of standard postural drainage (greater (30° to 45° head-down tilt) and lesser (15° to 20° head-down tilt)) with modified postural drainage (greater (30° head-up tilt) or lesser (15° to 20° head-up tilt)) with regard to gastroesophageal reflux in infants and young children up to six years old with CF.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled studies, regardless of year or language of publication.

Types of participants

Children from birth up to and including, six years of age, diagnosed with CF on the basis of clinical criteria and sweat testing or genotype analysis.

We have chosen to focus the review on infants and young children (six years of age and under) as this population is more likely to suffer from pathological gastroesophageal reflux.

Types of interventions

Standard postural drainage (greater (30° to 45° head-down tilt) and lesser (15° to 20° head-down tilt)) compared with a modified postural drainage (greater (30° head-up tilt) or lesser (15° to 20° head-up tilt)).

Types of outcome measures

Primary outcomes

1. Appearance or exacerbation of gastroesophageal reflux episodes (number and duration of episodes) identified by:
 - a. clinical symptoms (e.g. vomiting, regurgitation, rumination)
 - b. clinical tests (e.g. oesophageal pH monitoring, oesophageal impedance-pH monitoring, ultrasonography, oesophagogastric scintigraphy)
 - c. pulmonary events (e.g. pulmonary aspiration episodes)

Secondary outcomes

1. Airway clearance measured by:
 - a. sputum weight
 - b. volume
2. Percentage of peripheral oxygen saturation
3. Number of exacerbations of upper respiratory tract symptoms
4. Number of days on antibiotics (oral, inhaled or intravenous) for acute exacerbations

5. Hospital stays for respiratory problems
 - a. number of stays
 - b. duration of stay (days)
6. Chest X-ray scores
7. High-resolution computed tomography (HRCT) scores
8. Pulmonary function tests (immediate and long-term differences)
 - a. spirometry
 - i. forced vital capacity (FVC)
 - ii. forced expiratory volume in one second (FEV₁)
 - iii. forced expiratory flow at 25% to 75% (FEF_{25%-75%})
 - b. lung clearance index (LCI) derived from multiple breath washout (MBW)
 - c. plethysmography
9. Adverse events (defined as any undesired outcome due to the intervention excluding events related to gastroesophageal reflux)

Search methods for identification of studies

Electronic searches

We searched the Cystic Fibrosis and Genetic Disorders Group's Cystic Fibrosis Trials Register using the terms: postural drainage AND gastroesophageal reflux.

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

Date of the most recent search of the Cystic Fibrosis and Genetic Disorders Group's Cystic Fibrosis Trials Register: 19 June 2017.

Trials registers such as ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictcp/en/) were consulted using the terms 'cystic fibrosis' AND 'postural drainage' in order to identify for planned, ongoing and unpublished studies. There were no restrictions on year or language of the studies. The most recent search was carried out on 02 August 2017.

Searching other resources

The reference lists of the relevant articles found by the above methods were consulted for additional studies.

Data collection and analysis

Selection of studies

Two review authors (DF and GC) independently screened titles and abstracts of all the potential studies identified from the search for inclusion. The authors (DF and GC) retrieved the full-text study reports, independently screened the full-texts and

identified studies for inclusion and recorded reasons for exclusion of ineligible studies. We resolved final decisions and disagreements by consulting a third review author (KM). We recorded the selection process in sufficient detail to complete a PRISMA flow diagram (Moher 2009), as well as the tables of characteristics of included and excluded studies.

Data extraction and management

We used a data collection form for study characteristics and outcome data which was piloted on one study in the review. According to methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a), we collected the following information:

- methods (trial design, total duration of the trial, trial setting, withdrawals, and date of trial);
- participants (total number, mean age, age range, gender, country, inclusion criteria, and exclusion criteria);
- interventions (total number of each group - standard and modified postural drainage, number of sessions, intervention details which allows its replication);
- outcomes (primary and secondary outcomes specified and collected, and time points reported);
- notes: funding for trial, and notable conflicts of interest of trial authors.

Two review authors (DF and GC) independently extracted outcome data from the included studies. The authors noted in the 'Characteristics of included studies' if outcome data were not reported in a usable way. One review author (DF) transferred data into the Review Manager software file (RevMan 2014) and any disagreements were resolved by discussion and consensus involving a third review author (KM). We double-checked that data were entered correctly by comparing the data presented in the systematic review with study reports. A second review author (KM) spot-checked study characteristics for accuracy against the trial report.

For future updates of this review, if we are able to include sufficient data, we will analyse studies of up to seven days treatment separately from studies of longer duration. We will group outcome data from longer-term studies (more than seven days) into those measured at one, three, six, 12 months, and annually thereafter.

Assessment of risk of bias in included studies

Two review authors (DF and GC) independently assessed the risk of bias using the Cochrane's tool for assessing risk of bias which includes the following items:

1. random sequence generation;
2. allocation concealment;
3. blinding of participants and personnel;
4. blinding of outcome data;
5. incomplete outcome data;
6. selective outcome reporting;
7. other sources of bias.

Since it is not possible to blind therapists and participants in studies of this kind of intervention, the authors restricted evaluation of blinding to outcome assessors. We classified the risk of bias as

either high, low or unclear, and provided quotes from the study report with a justification for the judgment in the 'Risk of bias' table, according to the methods described in chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b). We resolved any disagreements by discussion or by involving another review author (KM).

Measures of treatment effect

We entered outcome data for each study in the data tables in the Review Manager software to calculate treatment effects (RevMan 2014). We have reported continuous outcomes as a mean difference (MD) with 95% confidence intervals (CI). For future updates of this review, if different units of measurement are used in newly-included studies, we will combine the results using the standardised mean difference (SMD) and 95% CI. If data for dichotomous outcomes are included in future updates, we will report the relative risk (RR) with the corresponding 95% CI.

Unit of analysis issues

In future updates of this review, where possible, in cases of events that can occur several times per person, we will calculate the rate ratio (RR), which compares the rate of events in two groups by dividing one by the other (Higgins 2011c).

Cross-over studies

For future updates of this review, when including sufficient data from parallel and cross-over studies (with an adequate washout period), we plan to use the inverse variance method, as recommended by Elbourne (Elbourne 2002). For the cross-over studies, in this method, we will use the results from paired analyses (including an estimate of treatment effect and its standard error).

Cluster-randomised studies

We will include data from cluster-randomised studies if the information is available. For cluster-randomised studies, we will adjust results when the unit of analysis in the study is presented as the total number of individual participants instead of number of clusters. We will adjust the results using the mean cluster size and intra-cluster correlation co-efficient (ICC) (Higgins 2011c). For meta-analysis, we will combine data from individually randomised studies using the generic inverse-variance method as described in chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011c).

Dealing with missing data

We contacted the corresponding authors of the included studies for further data and these have been included in the review (Button 2003; Doumit 2012).

Assessment of heterogeneity

If, for future updates, we are able to include a sufficient number of studies, we will assess heterogeneity in the study results by inspecting the forest plots to detect non-overlapping CIs and by applying the Chi² test (with a P value of 0.10 indicating statistical significance). In addition to this we will use the I² statistic with a categorisation of heterogeneity as follows: up to 50% as a moderate level; and above 50% as a substantial level (Higgins 2011c).

Assessment of reporting biases

If we are able to include sufficient data (10 studies or more), we will assess reporting bias among the studies using the funnel plot as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011d). If asymmetry is present, we will explore possible causes including publication bias, risk of bias, outcome reporting bias and true heterogeneity.

Data synthesis

If we are able to include sufficient data, we will use Review Manager 5 to combine outcomes when possible (RevMan 2014). We will use a fixed-effect model unless substantial heterogeneity (a value of I² over 50%) is observed, in which case they will use a random-effects model.

Subgroup analysis and investigation of heterogeneity

If we are able to include sufficient data (10 studies or more) and identify substantial heterogeneity (a value of I² over 50%) we plan to conduct the following subgroup analyses:

1. treatment length (studies of up to seven days treatment and studies of longer duration);
2. age (newborn, infants and pre-school children);
3. treatment setting (inpatient and outpatient)
4. angle of the head-down tilt (30° to 45° head-down tilt and 15° to 20° head-down tilt);
5. association with other chest physiotherapy techniques (vibration, percussion, inhalation therapy, breathing exercises and instrumental techniques).

Sensitivity analysis

If we are able to include sufficient data (at least four studies), sensitivity analysis will be performed in order to explore the influence on the results of the following factors:

1. study quality (RCTs with poor methodology);
2. study size (stratify by sample size);
3. allocation concealment (high risk of bias versus low risk of bias);
4. assessor blinding (high risk of bias versus low risk of bias).

Summary of findings and quality of the evidence (GRADE)

In a post hoc change from protocol, we have presented a summary of findings tables for the comparison of standard versus modified postural drainage (Summary of findings 1).

The following outcomes were reported in the tables (chosen based on relevance to clinicians and consumers): appearance or exacerbation of gastroesophageal reflux episode (clinical test and pulmonary events), peripheral oxygen saturation, number of exacerbations of upper respiratory tract symptoms, number of days on antibiotics for acute exacerbations, chest x-ray scores and pulmonary function test (FVC).

Outcomes were presented in the summary of findings table at the end of follow-up or latest reported follow-up time. We determined the quality of the evidence using the GRADE approach and GRADEproGDT software (GRADEpro GDT 2014); and downgraded evidence in the presence of a high risk of bias in at least one study, indirectness of the evidence, unexplained heterogeneity

or inconsistency, imprecision of results, high probability of publication bias. We downgraded evidence by one level if we considered the limitation to be serious and by two levels if very serious. We justified all decisions to downgrade the quality of studies in footnotes, and we made comments to aid readers' understanding of the review where necessary.

RESULTS

Description of studies

Results of the search

The search of the Cystic Fibrosis and Genetic Disorders Group's Cystic Fibrosis Trials Register identified 12 references. The

additional searches identified two potentially relevant studies. In total, 14 references (relating to four studies) were identified. After duplicates were removed a total of four studies remained. Of these, three were identified as potentially relevant and the full text articles were retrieved for closer inspection; two of these are included in the review. See figure below for full details on the results of the search ([Figure 2](#)).

Figure 2. Study flow diagram.

The most recent search of the Cystic Fibrosis and Genetic Disorders Group's Cystic Fibrosis Trials Register and the search carried out on clinical trials registers (ClinicalTrials.gov and the WHO ICTP) did not identify any potentially eligible trials. Thus, we included no new studies in this 2018 update.

Included studies

In total two studies, with a total of 40 participants are included in this review ([Button 2003](#); [Doumit 2012](#)). The Button study was a long-term randomised controlled study, which has multiple publications under one study ID ([Button 2003](#)).

Both included studies were funded. The Button study was funded by Royal Children's Hospital Research Foundation and by Physiotherapy Research Foundation of Australia ([Button 2003](#)). The Doumit study was funded by Sydney Children's Hospital Foundation ([Doumit 2012](#)).

See '[Characteristics of included studies](#)' for full details of each study.

Study design

The Doumit study had a cross-over design ([Doumit 2012](#)). The Button study had two main parts: cross-over study and then a parallel designed-study period ([Button 2003](#)).

Participants

Both included studies were conducted in Australia ([Button 2003](#); [Doumit 2012](#)). Each study had a total sample of 20 participants ([Button 2003](#); [Doumit 2012](#)). The age range of the participants from the included studies varied from three weeks to 34 months. Both studies were performed in a hospital setting.

Interventions

The Button study had two main parts. Firstly, infants were randomised to standard postural drainage (SPD) or modified postural drainage (MPD) then they undertook a two day cross-over study (the order of positions in SPD and MPD was computer generated). In order to provide adequate statistical power SPD and MPD were evaluated twice. Secondly, infants carried out the treatment they were randomised to for a further five years. During SPD, infants were positioned supine horizontal, prone with a 30°

head-down tilt, left side down with a 30° head-down tilt, and right side down with a 30° head-down tilt. For MPD, these four positions were modified by adding a 30° head-up tilt: supine 30° head-up, prone horizontal, left side down horizontal, and right side down horizontal. Manual techniques were applied in cycles of percussion for two minutes, followed by six vibratory "squeezes" (each timed with every third or fourth expiration), for a total of 30 minutes. In the second part of the study each session commenced with inhalation of 2 mL of nebulized normal saline for five to 10 minutes via a jet nebulizer and infant facemask ([Button 2003](#)).

In the Doumit study, each child received two 20-minute sessions of chest physiotherapy ([Doumit 2012](#)). One session involved percussion with expiratory vibrations for five minutes in four modified postural drainage positions. These positions were supine with a 20° head-up tilt, left side lying with no tilt, right side lying with no tilt and prone with no tilt. The alternate session involved percussion with expiratory vibrations for five minutes in four "gravity-assisted" postural drainage positions. These positions were supine with no tilt, left side lying with a 20° head-down tilt, right side lying with a 20° head-down tilt and prone with a 20° head-down tilt.

Outcomes

The outcomes in the Button study were oesophageal pH recordings, peripheral oxygen saturation, pulmonary function tests, radiological assessment, number of exacerbations of upper respiratory tract symptoms, and number of days on antibiotics for acute exacerbations ([Button 2003](#)). The main outcome in the Doumit study was the pH-multichannel intraluminal impedance (pH-MII) measurement, which is able to detect both acid and non-acid gastroesophageal reflux ([Doumit 2012](#)).

Excluded studies

After retrieving the full-text of potentially eligible studies, in total one study was excluded from the review ([Phillips 1998](#)). The reason for exclusion is described in the relevant table ([Characteristics of excluded studies](#)).

Risk of bias in included studies

Full details of the risk of bias judgments can be found in the relevant table ([Characteristics of included studies](#)) and below ([Figure 3](#)).

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias): Appearance or exacerbation of gastroesophageal reflux episodes	Blinding of outcome assessment (detection bias): Number of exacerbations of upper respiratory tract symptoms	Blinding of outcome assessment (detection bias): Number of days on antibiotics	Blinding of outcome assessment (detection bias): Chest X-ray scores	Blinding of outcome assessment (detection bias): Pulmonary function test	Blinding of outcome assessment (detection bias): Percentage of peripheral oxygen saturation	Incomplete outcome data (attrition bias): All outcomes	Selective reporting (reporting bias)	Other bias
Button 2003	+	+	+	+	+	+	+	?	+	?	+
Doumit 2012	+	+	+	?	?	?	?	?	+	+	+

Allocation

Sequence generation

Sequence generation was adequate in the two included studies and was judged to be of low risk of bias (Button 2003; Doumit 2012). These studies randomised the order of sessions using block randomisation.

Allocation concealment

In both included studies allocation concealment was undertaken by opaque sealed envelope, and as therefore judged to have a low risk of bias (Button 2003; Doumit 2012).

Blinding

A study is classed as double-blinded if neither the investigator nor the participant involved knows the identity of the intervention. Blinding reduces bias in a study. Double-blinding is not possible or practical in these studies due to the interventions assessed (standard and modified postural drainage). However, it is possible to blind the outcome assessors of the studies.

Blinding of outcome assessors was fully described in one included study in which the pH-multichannel intraluminal impedance monitoring was manually analysed by an assessor blinded to the order of chest physiotherapy sessions (Doumit 2012). The method used was considered adequate and the study was then judged to be of low risk of bias. In the Button study blinding of outcome assessors was described for radiological and pulmonary function assessments (Button 2003). The Brasfield scores from the radiological assessment were calculated by a consultant radiologist blinded to treatment allocation and the pulmonary function test was performed by a respiratory technician who was also blinded to treatment allocation. These two outcomes were judged to have a low risk of bias. The authors provided further information regarding the methods of the other outcomes assessed by this study and they were also judged to have a low risk of bias.

Incomplete outcome data

The included studies described withdrawals and dropouts and they were judged to have a low risk of bias because the missing outcome data were balanced in numbers across intervention groups (Button 2003) and because the reasons for missing outcome data were unlikely to be related to true outcome (Doumit 2012).

In the Button study, from the 20 infants who were randomised, four were excluded in the end of the first 12 months of the study because their parents had not complied with the physiotherapy regimen (Button 2003). Thus, the outcomes measured at the end of the first 12 months of the study (number of exacerbations of upper respiratory tract symptoms and number of days on antibiotics for acute exacerbations) were available for these 16 infants (eight in each group). Two more children were excluded because they moved to a different state and were unavailable for reassessment. Thus, seven infants in each group were available at 2½-year follow-up for radiological assessments. At five-year follow-up, the parents of two children (one in each group) did not consent to a chest X-ray, as the children appeared well, so this outcome was available for 12 children. At five-year follow-up, pulmonary function tests were available from seven infants in each group of postural drainage.

In the Doumit study, from the 24 children recruited, 20 completed the 24-hour pH-multichannel intraluminal impedance monitoring because four probes were inadvertently dislodged prior to the second physiotherapy session, and these results were not included in the analysis (Doumit 2012).

Selective reporting

One included study adequately reported outcome data for its outcome as listed in the methods, although the protocol for this study is not available in trial registers (Doumit 2012). This study was then judged to have a low risk of bias.

The second included study does not have its protocol available in trial registers (Button 2003). Thus, it was then judged to have an unclear risk of bias. However, it is important to emphasize that at the time this study commenced trial registers were widely used.

Other potential sources of bias

We were unable to identify any other potential biases in the two included studies, so they were judged to have a low risk of bias (Button 2003; Doumit 2012).

Effects of interventions

See: [Summary of findings 1 Summary of findings](#)

The quality of the evidence has been graded for those outcomes included in the summary of findings table. For the definitions of these gradings, please refer to the summary of findings tables ([Summary of findings 1](#)).

Primary outcomes

1. Appearance or exacerbation of gastroesophageal reflux episodes (number and duration of episodes)

a. clinical symptoms

Clinical symptoms (e.g. vomiting, regurgitation, rumination) were not reported in the included studies (Button 2003; Doumit 2012).

b. clinical tests

Both included studies assessed clinical tests (e.g. oesophageal pH monitoring, oesophageal impedance-pH monitoring, ultrasonography, oesophagogastric scintigraphy) (Button 2003; Doumit 2012). In the first part of the Button study, after the diagnosis of CF and parental counselling, 20 infants underwent prolonged oesophageal pH recordings (30 hours) using an ambulatory system with antimony pH electrodes (Button 2003). Results for oesophageal pH recordings were analysed for the 30-hour period of the study and then expressed as 'per hour'. Physiotherapy periods were compared with 'background'. 'Background' excluded meals and the first two postprandial hours, and physiotherapy sessions. It was found that SPD was associated with a significant increase in the number of episodes of gastroesophageal reflux compared with background ($P = 0.0005$). The number of reflux episodes during modified postural drainage was not significantly different from background ($P = 0.1$). Overall, there were significantly more reflux episodes during SPD compared to modified postural drainage ($P = 0.05$) (moderate-quality evidence).

The Doumit study measured pH-multichannel intraluminal impedance (pH-MII) monitoring (Doumit 2012). This study involved

20 children who received sessions of MPD and SPD in a random order. While the authors provided additional data, we were still unable to use these within the meta-analyses as these data were not normally distributed and, therefore, could not be entered into Review Manager 5 (RevMan 2014). A median (interquartile range) (IQR) of 1 (0 to 2.5) reflux episodes occurred during modified postural drainage whereas a median (IQR) of 1 (0.8 to 3) occurred during SPD. When MPD was compared to gravity-assisted postural drainage, there was no significant difference in the total number of reflux episodes ($P = 0.63$). When comparing MPD and SPD to background periods (median (IQR) of 0.9 (0.5 to 1.3)) there was also no significant difference in the total number of reflux episodes ($P = 0.31$ and $P = 0.84$, respectively) (moderate-quality evidence).

We were not able to pool data for this outcome due to differences in statistical presentation of data in these two included studies.

c. pulmonary events

The Doumit study assessed and characterised reflux episodes by pH-multichannel intraluminal impedance (pH-MII) monitoring (Doumit 2012). By this, it was possible to analyse that proximal migration (a surrogate marker of the potential for aspiration) was evident in 72% (total median (IQR) of 47 (26 to 77)) of all the gastroesophageal reflux episodes observed.

A median (IQR) of 1 (0 to 2) proximal episodes occurred during modified postural drainage whereas a median (IQR) of 0 (0 to 2) occurred during standard postural drainage. When modified postural drainage was compared to gravity-assisted postural drainage, there was no significant difference in the number of proximal episodes ($P = 0.75$). When comparing modified postural drainage and standard postural drainage to background periods (median (IQR) of 0.53 (0.2 to 1.0)) there was also no significant difference in the number of proximal episodes ($P = 0.33$ and $P = 0.73$, respectively) (moderate-quality evidence).

Secondary outcomes

1. Airway clearance measured by:

a. sputum weight

This outcome was not reported by the included studies (Button 2003; Doumit 2012).

b. volume

This outcome was not reported by the included studies (Button 2003; Doumit 2012).

2. Percentage of peripheral oxygen saturation

This outcome was assessed in the first part of the Button study involving 20 infants (Button 2003). Peripheral oxygen saturation was recorded using a pulse oximeter. The oximetry probe was placed over the end of the hallux. Measurements were recorded prior to each physiotherapy session and during a two minute rest period following physiotherapy. This outcome was assessed according to the postural drainage regimen and also the arousal state of the included infants which was divided into five different categories: quiet sleep; sleep while sucking on a pacifier; quiet wakefulness; wakefulness while sucking on a pacifier; and crying. During SPD, the mean (SD) percentage of peripheral oxygen saturation was significantly lower during crying than in other states, 97.6% (3.17%) versus 98.9% (1.49%); $P = 0.02$. Also during

SPD, the mean (SD) percentage of peripheral oxygen saturation was significantly higher when asleep, even when crying was excluded; asleep, 99.2% (1.15%) versus awake 98.5% (1.66%); $P = 0.01$. During MPD, crying had no effect on oxygen saturation. Similarly, there was no difference in mean (SD) oxygen saturation during sleep and wakeful periods in MPD; awake 98.7% (1.44%) versus asleep 98.9% (1.44%); $P = 0.389$ (moderate-quality evidence).

3. Number of exacerbations of upper respiratory tract symptoms

One study measured this outcome (Button 2003). In this study, 20 infants were randomised but the parents of four infants did not comply with the physiotherapy regimen. Thus, this outcome involved 16 children (eight children receiving SPD and eight receiving MPD). Infants receiving SPD had significantly more days with upper respiratory tract symptoms than infants in the MPD group during the first 12 months of the study, MD -33.00 (95% CI -61.54 to -4.46); $P = 0.04$ (moderate-quality evidence) (Analysis 1.1).

4. Number of days on antibiotics (oral, inhaled or intravenous) for acute exacerbations

The Button study assessed this outcome in 16 children (eight in each group of postural drainage) during the first 12 months of the study (Button 2003). The number of days on antibiotic treatment was higher in the SPD group than for infants receiving MPD, although this difference did not reach statistical significance, MD -49.00 (95% CI -122.61 to 24.61); $P = 0.17$ (moderate-quality evidence) (Analysis 1.2).

5. Hospital stays for respiratory problems

a. number of stays

This outcome was not reported by either of the included studies (Button 2003; Doumit 2012).

b. duration of stay (days)

This outcome was not reported by either of the included studies (Button 2003; Doumit 2012).

6. Chest X-ray scores

This outcome was assessed in the Button study (Button 2003). Brasfield scores were calculated at diagnosis, at the end of the 12-month study, after 2½ years and after 5 years. However, only 12 children provided data for the final assessment, while 14 children provided data for previous assessments. At the 2½-year follow-up, radiological changes were significantly greater in infants receiving SPD ($P = 0.03$). Radiological changes at five years were worse in the SPD group, although the difference between groups did not reach statistical significance ($P = 0.17$) (moderate-quality evidence).

7. High-resolution computed tomography (HRCT) scores

This outcome was not reported by the included studies (Button 2003; Doumit 2012).

8. Pulmonary function tests (immediate and long-term differences)

a. spirometry

iii. forced expiratory flow at 25% to 75% (FEF_{25%-75%})

In the Button study pulmonary function test was performed at the five-year follow-up with children at five and six years old (Button

2003). This assessment was available for 14 children (seven for each group - SPD and MPD).

In the original study report, the mean FVC was significantly higher in the MPD group compared to SPD ($P = 0.036$). However, there was a discrepancy when data were analysed using Review Manager 5, MD 16.00 (95% CI -0.16 to 32.16) (moderate-quality evidence) (Analysis 1.3) (RevMan 2014). Mean FEV₁ was also significantly higher in the MPD group compared to SPD, MD 18.85 (95% CI 4.55 to 33.15); $P = 0.012$ (Analysis 1.4). The difference for FEF_{25%-75%} did not reach significance, MD 19.70 (95% CI -10.71 to 50.11); $P = 0.12$ (Analysis 1.5).

The mean (SD) post-intervention values for this outcome were provided by the study author (Button 2003).

b. lung clearance index (LCI) derived from multiple breath washout (MBW)

This outcome was not reported by the included studies (Button 2003; Doumit 2012).

c. plethysmography

This outcome was not reported by the included studies (Button 2003; Doumit 2012).

9. Adverse events

This outcome was not reported by the included studies (Button 2003; Doumit 2012).

DISCUSSION

Summary of main results

This systematic review compared the safety and efficacy of SPD with regard to gastroesophageal reflux in infants and young children up to six years old with CF. A total of two studies involving 40 infants and young children satisfied the inclusion criteria, but differed in some characteristics, such as: age of participants; angle of tilt; reported outcomes; number of sessions; and study duration.

Both included studies assessed the primary outcome of this review (appearance or exacerbation of gastroesophageal reflux episodes) (Button 2003; Doumit 2012). However, only one included study assessed some of the secondary outcomes: percentage of peripheral oxygen saturation; number of exacerbations of upper respiratory tract symptoms; number of days on antibiotics for acute exacerbations; chest X-ray scores; and pulmonary function tests (Button 2003). As there were differences in statistical presentation of data in the included studies, they were not able to be pooled in meta-analyses.

Both included studies confirmed that gastroesophageal reflux is a common co-morbidity diagnosed in infants and young children with CF (Button 2003; Doumit 2012). One study that used a 20° head-down tilt and a 20° head-up tilt affirmed that there was no significant difference between total number and proximal number of reflux episodes in the modified or gravity-assisted positions (Doumit 2012) while the other included study that used a 30° head-down tilt and a 30° head-up tilt found that SPD, but not MPD, was associated with a significant increase in gastro-oesophageal reflux in infants with CF (Button 2003). Moreover, MPD was associated

with fewer respiratory complications than SPD in infants with CF (Button 2003).

Overall completeness and applicability of evidence

The studies identified and included in this review were not sufficient to address all of the outcomes proposed by the review. Both included studies assessed the primary outcome of this review (Button 2003; Doumit 2012), while some of the secondary outcomes were addressed by only one included study (Button 2003). The outcomes which were not addressed by the included studies were: airway clearance; hospital stays for respiratory problems; high-resolution computed tomography scores; and occurrence of adverse events (excluding events related to gastroesophageal reflux).

Moreover, the angle of the head-down used by the included studies did not address all the range proposed by the review (15° to 20° and 30° to 45°). The angle of the head-down was 20° in the Doumit study and 30° in the Button study (Button 2003; Doumit 2012). According to Button, by reducing the angle of head-down tilt, the likelihood of increasing episodes of reflux is reduced (Button 1999). This may explain the lack of difference found between the two postural drainage regimens regarding the occurrence of gastroesophageal reflux and the number of proximal episodes in the Doumit study (Doumit 2012) and the higher occurrence of respiratory complications associated with the standard postural drainage in the Button study (Button 2003) and also the differences between the two postural drainage regimens regarding the occurrence of gastroesophageal reflux (Button 2003). Furthermore, the angles of MPD regimen of both included studies were also different. There are two different forms of MPD: greater (30° head-up tilt) and lesser (15° to 20° head-up tilt). In the Doumit study a 20° head-up tilt was used, whilst in the Button study a 30° head-up tilt was employed (Button 2003). Even though the Doumit study did not find differences between the two postural drainage regimens regarding the number of reflux episodes and the number of proximal episodes, proximal migration (a marker of the potential for aspiration) was evident in 72% of the reflux episodes which challenges the safety of this technique (Doumit 2012).

The types of participants proposed by the review were children from birth up to six years old diagnosed with CF. In the Doumit study, the median age of participants was 12 months (range 8 to 34 months), and in the Button study, the mean age was 2.1 months (range 3 weeks to 4 months) (Button 2003; Doumit 2012). The Button study followed those children for up to five years (Button 2003). It is important to emphasise that there is a decline in gastroesophageal reflux episodes over the first 12 months of life (Hegar 2009; Nelson 1998). Thus, the different age ranges from these studies may have affected the results. As data from these studies were not possible to be pooled such a difference could not be analysed.

Quality of the evidence

We assessed the review outcomes as being of moderate quality according to the GRADE criteria. We downgraded the quality of the evidence in relation to the risk of bias assessments (selective reporting and blinding).

This systematic review was limited by the quality of existing data. Some points must be taken into consideration when analysing

the results of this review: small number of included studies; small sample size; and some methodological aspects that may lead to risk of bias.

Currently, there are only two studies included in this systematic review. Each study included 20 participants, but there were some dropouts in one study. It should be noted, that a study by Moher reviewed 383 randomised controlled trials and concluded that most trials with negative results did not have sample sizes large enough to detect a relative difference (Moher 1994). Furthermore, the CONSORT statement provides a recommendation on how to determine a sample size (CONSORT 2010). Doumit affirmed that the absence of a difference between the two postural drainage regimens was not due to the small sample size once the power calculation showed that 16 participants was necessary to show a two-fold increase in number of reflux episodes and the total number of included participants exceeded that (Doumit 2012). The Button study affirmed that its results need to be interpreted cautiously in the context of a relatively small sample size and that this fact was due to difficulties in the follow-up towards the end of the study (Button 2003).

A methodological difference between the included studies which also needs to be taken into consideration is the number of outcome assessments. The primary outcome of this review was assessed during a 24-hour pH-MII monitoring in one study (Doumit 2012) and during a 30-hour pH recording using an ambulatory system with antimony pH electrodes in the other study (Button 2003). Moreover, the secondary outcomes (provided by one included study) - with the exception of percentage of peripheral oxygen saturation - were assessed during a five-year follow-up (Button 2003).

Both included studies had an overall low risk of bias as assessed by Cochrane's tool for assessing risk of bias (Button 2003; Doumit 2012). Additional data regarding some methodological aspects were sent by the corresponding author of one included study which allowed the complete assessment of risk of bias (Button 2003). According to Savović, inadequate reporting of study methods can severely impede the assessment of study quality and the risk of bias in study results (Savović 2012). Also according to this study, this is a particular problem for the assessment of sequence generation and allocation concealment, which are often not described in study publications (Savović 2012). In addition, inadequately reported randomisation procedures have been associated with bias in estimating the effectiveness of interventions (Moher 2001). The CONSORT statement also contains advice on these methodological items (CONSORT 2010).

One item of Cochrane's tool for assessing risk of bias was not assessed as it is not possible to blind participants and physiotherapists in a study of this kind of intervention (postural drainage with and without a head-down tilt). According to Savović, the lack of or unclear double blinding can be associated with marked exaggeration of intervention effect estimates (Savović 2012).

Another important methodological aspect in a randomised controlled study is the registration of a study's protocol. The protocols of the included studies were not found in trials registers. This aspect is included in the CONSORT statement checklist (CONSORT 2010). A study's protocol registration provides information such as: main objective of the study; inclusion and exclusion criteria; primary and secondary outcomes; among other

methodological aspects. Clinical trial registers minimises or avoids the consequences of non-publication of entire studies and selective reporting of outcomes within studies (CONSORT 2010).

Potential biases in the review process

Although there was an attempt to apply a systematic process for including and excluding studies in this review besides following the criteria pre-specified in the protocol with robust methods for data collection and risk of bias assessment, the final decisions are open to interpretation or criticism.

Since the included studies differed in the statistical presentation of data, they were not able to be pooled in any meta-analysis, which may be considered a potential source of bias in this review. Meta-analyses may have showed if there are differences in results regarding treatment length, age, angle of the head-down tilt, and association with other chest physiotherapy techniques. Also, the inclusion of sufficient data could have explored the influence of some methodological aspects on the results.

Agreements and disagreements with other studies or reviews

The current version of this review has two included studies. These studies assessed appearance of gastroesophageal reflux episodes, percentage of peripheral oxygen saturation, number of exacerbations of upper respiratory tract symptoms, number of days on antibiotics, and spirometry. One included study did not find differences regarding the number of gastroesophageal reflux episodes and the number of proximal episodes between the two postural drainage regimens while the other study found that MPD was associated with a significantly lower number of gastroesophageal reflux episodes and also fewer respiratory complications (number of exacerbations of upper respiratory tract symptoms, FVC and FEV₁) than SPD in infants with CF.

Many studies use postural drainage as a 'gold standard' of airway clearance techniques. Thereby, postural drainage is normally used in the comparison of 'new' techniques (Hoo 2015; TSANZ 2016). However, the efficacy and safety of the traditional head-down postural drainage position in infants has been investigated (TSANZ 2016). A previous review of the literature on airway clearance therapies in people with CF affirmed that MPD without the head-down position should be only used in young children (Pisi 2009).

MPD has been currently used and recommended in infants and young children with CF (and also in people with extremely severe lung disease once they are unable to perform airway clearance techniques independently), as a way to reduce gastroesophageal reflux episodes (Pisi 2009; TSANZ 2016). Furthermore, the use of postural drainage with the head-down tilt has been considered as inappropriate in people with gastroesophageal reflux (Main 2016; TSANZ 2016).

In 2015, a systematic review was performed to evaluate the influence of chest physiotherapy on gastroesophageal reflux in infants. However, groups of different ages and pathologies, the use of more than one airway clearance technique with different degrees of head-down and head-up tilt and different postprandial moments made it impossible to draw general conclusions about the influence of chest physiotherapy on gastroesophageal reflux in infants and small children (Van Ginderdeuren 2015).

To our knowledge, this is the first systematic review to compare two postural drainage regimens regarding gastroesophageal reflux in infants and young children with CF. The available evidence regarding the comparison between the two regimens of postural drainage with regards to appearance or exacerbation of gastroesophageal reflux in infants and young children with CF is still weak due to the small number of included studies (two), the small number of participants assessed ($n = 40$), the impossibility to perform meta-analysis and some methodological aspects. Nevertheless, by the analysis of the individual data, it may be inferred that the use of a postural regimen with a 30° head-up tilt is associated with a lower number of gastroesophageal reflux episodes and fewer respiratory complications on a long-term basis. The age of the participant may also interfere with the occurrence of reflux episodes once there is a decline in gastroesophageal reflux episodes over the first 12 months of life. Physiotherapy for newly diagnosed infants with CF should first of all do no harm. Thus, the use of a MPD with a 30° head-up tilt seems to be safer than a postural drainage regimen with a use of a 30° head-down tilt. On the other hand, the lesser head-down tilt (15° to 20°) did not differ from the lesser (15° to 20°) head-up tilt MPD. However, the majority of GOR episodes reached the upper oesophagus which may be a marker of potential for aspiration.

AUTHORS' CONCLUSIONS

Implications for practice

The available evidence regarding the comparison between the two regimens of postural drainage is weak due to the small number of included studies, the small number of participants assessed, the inability to perform any meta-analyses and some methodological issues with the studies.

By the analysis of the individual data, it may be inferred that the use of a postural regimen with a 30° head-up tilt is associated with a lower number of gastroesophageal reflux episodes and fewer respiratory complications on a long-term basis. Conversely, the lesser (15° to 20°) head-down postural drainage was not found to be significantly different from the lesser (15° to 20°) head-up tilt modified postural drainage, the fact that the majority of episodes reached the upper oesophagus and the potential for

aspiration should make physiotherapists carefully consider their treatment strategy. The age of the participant may also interfere with the occurrence of reflux episodes once there is a decline in gastroesophageal reflux episodes over the first 12 months of life. There were not enough data published to carry out meta-analyses.

Implications for research

There is a need for well-conducted randomised controlled studies to compare the effects of standard postural drainage with modified postural drainage with regard to gastroesophageal reflux in infants and young children up to six years old with cystic fibrosis. Such studies must take into consideration some methodological aspects, such as the age of patients, allowing a further analysis on the effect of the two postural drainage regimens in different age ranges (infants and young children); the angle of the head-down tilt used; measurement of the repercussions of gastroesophageal reflux episodes on pulmonary system rather than this outcome alone. Furthermore, any randomised studies undertaken should be reported following the CONSORT statement ([CONSORT 2010](#)). We do not envisage that there will be any new trials undertaken that will affect the conclusions of this review; therefore, we do not plan to update this review.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Button 2003

Study characteristics

Methods	<p>Design: randomised controlled study</p> <p>Method of randomisation: computer generated</p> <p>Method of allocation concealment: opaque sealed envelopes</p> <p>Outcome assessor blinding: assessors were blinded to treatment allocation</p> <p>Withdrawals or dropouts: during the 5-year follow-up there were 4 withdrawals (2 in each group) and 2 dropouts during the follow-up (1 in each group)</p>
Participants	<p>Setting: hospital</p> <p>Mean age: 2.1 months (range 3 weeks – 4 months)</p> <p>Gender: 10 boys and 10 girls</p> <p>Total sample: 20 participants (10 in each group)</p> <p>Country: Australia</p>
Interventions	<p>This study had two main parts. First, infants were randomised to SPD or MPD then they undertook a two-day cross-over study (the order of positions in SPD and MPD was computer generated). Second, infants carried out the treatment they were randomised to for 5 years.</p> <p>During SPD participants were positioned supine horizontal, prone, left side down and right side down with a 30° head-down tilt. For modified postural drainage these 4 positions were modified by adding a 30° head-up tilt: supine 30° head-up, prone horizontal, left side down horizontal, and right side down horizontal</p> <p>Manual techniques were applied in cycles of percussion for 2 min, followed by 6 vibratory "squeezes" (each timed with every 3rd or 4th expiration), for a total of 30 min</p> <p>Each session commenced with inhalation of 2 mL of nebulized normal saline for 5 to 10 min via a jet nebulizer and infant facemask</p>
Outcomes	<p>pH monitoring (first part of the study)</p> <p>Percentage of peripheral oxygen saturation (first part of the study)</p> <p>Number of exacerbations of upper respiratory tract symptoms (during the first 12 months of the study)</p> <p>Number of days on antibiotics for acute exacerbations (during the first 12 months of the study)</p> <p>Radiological assessment (Brasfield scores were calculated at diagnosis, 1 year, 2½ years, and 5 years)</p> <p>Pulmonary function testing (at 5-year follow-up of children from 5 years old)</p>
Notes	<p>Funding support: Royal Children's Hospital Research Foundation and Physiotherapy Research Foundation of Australia.</p> <p>We have written to the author for further clarification and received further information</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation undertaken using block randomisation

Button 2003 (Continued)

Allocation concealment (selection bias)	Low risk	Undertaken by sealed opaque envelope
Blinding of outcome assessment (detection bias) Appearance or exacerbation of gastroesophageal reflux episodes	Low risk	Blinding of outcome assessment ensured
Blinding of outcome assessment (detection bias) Number of exacerbations of upper respiratory tract symptoms	Low risk	Blinding of outcome assessment ensured
Blinding of outcome assessment (detection bias) Number of days on antibiotics	Low risk	Blinding of outcome assessment ensured
Blinding of outcome assessment (detection bias) Chest X-ray scores	Low risk	Blinding of outcome assessment ensured
Blinding of outcome assessment (detection bias) Pulmonary function test	Low risk	Blinding of outcome assessment ensured
Blinding of outcome assessment (detection bias) Percentage of peripheral oxygen saturation	Unclear risk	Blinding of outcome assessment ensured
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement of 'low risk' or 'high risk'
Other bias	Low risk	The study appears to be free of other sources of bias

Doumit 2012

Study characteristics

Methods	Design: cross-over study
	Method of randomisation: randomisation undertaken using block randomisation
	Method of allocation concealment: undertaken by sealed opaque envelope
	Outcome assessor blinding: the pH-multichannel intraluminal impedance (pH-MII) was manually analysed by an assessor blinded to the order of CPT sessions
	Withdrawal or dropouts: 4 dropouts

Doumit 2012 (Continued)

Participants	<p>Setting: hospital</p> <p>Mean age: 12 months (range 8 to 34 months)</p> <p>Gender: 8 males and 12 females</p> <p>Total sample: 20 children</p> <p>Country: Australia</p>
Interventions	<p>Each child received two 20-min sessions of CPT performed by a single, experienced physiotherapist</p> <p>One session involved percussion with expiratory vibrations for 5 min in 4 “modified” postural drainage positions. These positions were supine with 20° head-up tilt, left side lying with no tilt, right side lying with no tilt and prone with no tilt</p> <p>The alternate session involved percussion with expiratory vibrations for 5 min in 4 "gravity-assisted" postural drainage positions. These positions were supine with no tilt, left side lying with 20° head-down tilt, right side lying with 20° head-down tilt and prone with 20° head-down tilt</p>
Outcomes	pH-multichannel intraluminal impedance (pH-MII) monitoring
Notes	<p>Funding support: Sydney Children’s Hospital Foundation</p> <p>We have written to the author for further clarification. The author has responded with further information</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation undertaken using block randomisation
Allocation concealment (selection bias)	Low risk	Undertaken by sealed opaque envelope
Blinding of outcome assessment (detection bias) Appearance or exacerbation of gastroesophageal reflux episodes	Low risk	Blinding of outcome assessment ensured
Blinding of outcome assessment (detection bias) Number of exacerbations of upper respiratory tract symptoms	Unclear risk	Outcome not assessed
Blinding of outcome assessment (detection bias) Number of days on antibiotics	Unclear risk	Outcome not assessed
Blinding of outcome assessment (detection bias) Chest X-ray scores	Unclear risk	Outcome not assessed
Blinding of outcome assessment (detection bias)	Unclear risk	Outcome not assessed

Standard (head-down tilt) versus modified (without head-down tilt) postural drainage in infants and young children with cystic fibrosis (Review)

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Doumit 2012 (Continued)
Pulmonary function test

Blinding of outcome assessment (detection bias) Percentage of peripheral oxygen saturation	Unclear risk	Outcome not assessed
Incomplete outcome data (attrition bias) All outcomes	Low risk	Reasons for missing outcome data unlikely to be related to true outcome
Selective reporting (reporting bias)	Low risk	The study protocol is not available but the published reports include all expected outcomes
Other bias	Low risk	The study appears to be free of other sources of bias

CPT: chest physiotherapy
min: minute
MPD: modified postural drainage
SPD: standard postural drainage

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Phillips 1998	Participants received only one postural drainage regimen

DATA AND ANALYSES
Comparison 1. Standard versus modified postural drainage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Number of exacerbations of upper respiratory tract symptoms	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.2 Number of days on antibiotics (oral, inhaled or intravenous) for acute exacerbations	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.3 Pulmonary function tests (FVC)	1	14	Mean Difference (IV, Fixed, 95% CI)	16.00 [-0.16, 32.16]
1.4 Pulmonary function tests (FEV ₁)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.5 Pulmonary function tests (FEF _{25%-75%})	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Analysis 1.1. Comparison 1: Standard versus modified postural drainage, Outcome 1: Number of exacerbations of upper respiratory tract symptoms

Analysis 1.2. Comparison 1: Standard versus modified postural drainage, Outcome 2: Number of days on antibiotics (oral, inhaled or intravenous) for acute exacerbations

Analysis 1.3. Comparison 1: Standard versus modified postural drainage, Outcome 3: Pulmonary function tests (FVC)

Analysis 1.4. Comparison 1: Standard versus modified postural drainage, Outcome 4: Pulmonary function tests (FEV₁)

Analysis 1.5. Comparison 1: Standard versus modified postural drainage, Outcome 5: Pulmonary function tests (FEF_{25%-75%}) **WHAT'S NEW**

Date	Event	Description
8 April 2021	Review declared as stable	A search for relevant studies was undertaken on 19 Jun, 2017; no potentially-eligible trials were identified. No new studies are expected in this area.

HISTORY

Protocol first published: Issue 1, 2013

Review first published: Issue 3, 2015

Date	Event	Description
8 March 2018	New search has been performed	<p>A search of the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register did not identify any potentially eligible trials for inclusion in the review. Further searches were conducted on ClinicalTrials.gov and on the WHO International Clinical Trials Registry Platform no eligible trials were identified.</p> <p>A summary of findings table has been added and the relevant GRADE assessments relating to the quality of the evidence have been added across all sections of the review.</p>
8 March 2018	New citation required but conclusions have not changed	<p>Authorship of this review has changed. Thayla A Santino is new co-author on this update.</p> <p>We do not envisage that there will be any new trials undertaken that will affect the conclusions of this review; therefore, we do not plan to update this review.</p>
29 June 2017	Amended	Contact details updated.

CONTRIBUTIONS OF AUTHORS

Diana Freitas: drafted the final review.

Fernando Dias: drafted the final review.

Gabriela Chaves: contributed with methodological expertise and drafted the final review.

Thayla Santino: drafted the final review.

Standard (head-down tilt) versus modified (without head-down tilt) postural drainage in infants and young children with cystic fibrosis (Review)

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Cibele Ribeiro: drafted the final review.

Ricardo Guerra: contributed with methodological expertise.

Karla Mendonça: coordinated the review, made an intellectual contribution and drafted the final review.

DECLARATIONS OF INTEREST

All authors: none known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- National Institute for Health Research, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have included one new author in the current version of this review.

We included a 'Summary of findings' table and incorporated the relevant GRADE assessments relating to the quality of the evidence across all sections of the review.

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Bacterial Agents [therapeutic use]; Cystic Fibrosis [*complications]; Disease Progression; Drainage, Postural [*methods]; Gastroesophageal Reflux [*etiology]; Head-Down Tilt [adverse effects] [*physiology]; Lung [*metabolism]; Mucus [metabolism]; Randomized Controlled Trials as Topic; Time Factors

MeSH check words

Child, Preschool; Humans; Infant