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Active cycle of breathing technique for cystic fibrosis (Review)

Wilson LM, Saldanha IJ, Robinson KA

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TABLE OF CONTENTS

[Intervention Review]

Active cycle of breathing technique for cystic fibrosis

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ABSTRACT

Background

People with cystic fibrosis (CF) experience chronic airway infections as a result of mucus buildup within the lungs. Repeated infections often cause lung damage and disease. Airway clearance therapies aim to improve mucus clearance, increase sputum production, and improve airway function. The active cycle of breathing technique (ACBT) is an airway clearance method that uses a cycle of techniques to loosen airway secretions including breathing control, thoracic expansion exercises, and the forced expiration technique. This is an update of a previously published review.

Objectives

To compare the clinical effectiveness of ACBT with other airway clearance therapies in CF.

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 clinical trials registries and the reference lists of relevant articles and reviews.

Date of last search: 29 March 2021.

Selection criteria

We included randomised or quasi-randomised controlled clinical studies, including cross-over studies, comparing ACBT with other airway clearance therapies in CF.

Data collection and analysis

Two review authors independently screened each article, abstracted data and assessed the risk of bias of each study. We used GRADE to assess our confidence in the evidence assessing quality of life, participant preference, adverse events, forced expiratory volume in one second (FEV_1) % predicted, forced vital capacity (FVC) % predicted, sputum weight, and number of pulmonary exacerbations.

Main results

Our search identified 99 studies, of which 22 (559 participants) met the inclusion criteria. Eight randomised controlled studies (259 participants) were included in the analysis; five were of cross-over design. The 14 remaining studies were cross-over studies with inadequate reports for complete assessment. The study size ranged from seven to 65 participants. The age of the participants ranged from six to 63 years (mean age 18.7 years). In 13 studies follow up lasted a single day. However, there were two long-term randomised controlled studies with follow up of one to three years. Most of the studies did not report on key quality items, and therefore, have an unclear risk of bias in terms of random sequence generation, allocation concealment, and outcome assessor blinding. Due to the nature

of the intervention, none of the studies blinded participants or the personnel applying the interventions. However, most of the studies reported on all planned outcomes, had adequate follow up, assessed compliance, and used an intention-to-treat analysis.

Included studies compared ACBT with autogenic drainage, airway oscillating devices (AOD), high-frequency chest compression devices, conventional chest physiotherapy (CCPT), positive expiratory pressure (PEP), and exercise. We found no difference in quality of life between ACBT and PEP mask therapy, AOD, other breathing techniques, or exercise (very low-certainty evidence). There was no difference in individual preference between ACBT and other breathing techniques (very low-certainty evidence). One study comparing ACBT with ACBT plus postural exercise reported no deaths and no adverse events (very low-certainty evidence). We found no differences in lung function (forced expiratory volume in one second (FEV_1) % predicted and forced vital capacity (FVC) % predicted), oxygen saturation or expectorated sputum between ACBT and any other technique (very low-certainty evidence). There were no differences in the number of pulmonary exacerbations between people using ACBT and people using CCPT (low-certainty evidence) or ACBT with exercise (very low-certainty evidence), the only comparisons to report this outcome.

Authors' conclusions

There is little evidence to support or reject the use of the ACBT over any other airway clearance therapy and ACBT is comparable with other therapies in outcomes such as participant preference, quality of life, exercise tolerance, lung function, sputum weight, oxygen saturation, and number of pulmonary exacerbations. Longer-term studies are needed to more adequately assess the effects of ACBT on outcomes important for people with cystic fibrosis such as quality of life and preference.

PLAIN LANGUAGE SUMMARY

A comparison of active cycle of breathing technique (ACBT) with other methods of airway clearance therapies in people with cystic fibrosis

Review question

What are the effects of active cycle of breathing technique (ACBT) compared with other methods of airway clearance in people with cystic fibrosis?

Background

Chronic infections are common in cystic fibrosis, and repeated infections can cause lung damage and disease. People with cystic fibrosis use airway clearance therapies to clear mucus and improve lung function. The ACBT uses a combination of three breathing methods to loosen and clear mucus. This is an update of a previously published review.

Search date

The evidence is current to: 29 March 2021.

Study characteristics

While we included 22 studies comparing ACBT with other airway clearance therapies in the review, only eight studies (259 participants) reported data that we could include in the analysis. Each of the eight studies compared different techniques: ACBT was compared with autogenic drainage, airway oscillating devices, high-frequency chest compression devices, positive expiratory pressure, conventional chest physiotherapy, and ACBT together with exercise. Most studies lasted a single day, but there were two studies that lasted between one and three years. Participants ranged in age from six to 63 years and most (59%) were male.

Key results

We found that ACBT was comparable with other treatments in outcomes such as quality of life, personal preference, exercise tolerance, lung function, sputum weight, oxygen saturation, and the number of pulmonary exacerbations. We were not able to show that any single technique was better than another. Longer studies are needed to better assess the effects of ACBT on outcomes important for people with cystic fibrosis such as quality of life and personal preference.

Certainty of the evidence

We have little or no confidence in the evidence and think that further research is very likely to affect our conclusions of this review for any of the interventions analysed.

Many of the studies did not provide enough details of their methods to determine if there were any biases that might have affected the results. Many studies did not report how they decided who would get which treatment and how they made sure that the people who were putting people into the different treatment groups and those who were assessing the results did not know which group each individual was in. Most of the included studies had a cross-over design (where people have one treatment and then switch to the second), and many of these did not report the length of time in between different treatments. As it is possible that the first treatment might affect the results

of the next treatment, we only included results from the first treatment period. Many of the studies did not report separate results for just the first treatment period, so we did not include their results in our review.

All participants knew which treatment group they were in (it is not possible to disguise different physiotherapy techniques). This could have affected the results for some of the self-reported outcomes, such as quality of life, personal preference, or exercise tolerance, but is unlikely to have affected the more objective outcomes, such as lung function.

Most of the studies followed those taking part for less than one month and did this for most of the participants for the entire study period. In two out of the three longer studies more than 10% of the people taking part dropped out. The study results could be affected if the people who dropped out of the studies were not evenly spread across the different treatment groups.

Over half of the studies checked that participants were using the airway clearance therapy they were supposed to. Most of the studies reported on all their planned outcomes.

The findings of the review were limited as not many studies made the same comparisons; also, there were not many long-term studies and the studies we included did not report enough data.

SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings: ACBT compared with CCPT for people with cystic fibrosis

ACBT compared with CCPT for people with cystic fibrosis

Patient or population: people with cystic fibrosis

Settings: outpatients and hospital inpatients

Intervention: ACBT

Comparison: CCPT

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	CCPT	ACBT				
Quality of life Follow-up: NA	No studies reported on this outcome.					
Personal preference Follow-up: NA	No studies reported on this outcome.					
Adverse events Follow-up: NA	No studies reported on this outcome.					
FEV_1: % predicted (change from baseline) Follow-up: at least 6 months	No studies reported on the absolute change from baseline in % predicted, but 1 study reported the rate of change from baseline in % predicted, 1 study reported FEV_1 in L and 1 study reported the outcome narratively (see comments).					One 3-year study reported mean (SD) rates of decline in FEV_1 % predicted (regression slopes) for each group and then a P value for the difference between the groups. The mean (SD) rate of decline from baseline for participants in the ACBT alone group was statistically significant (-4.7 (7.1); P < 0.001); while there was no statistically significant mean (SD) difference from baseline in the CCPT group (-1.9 (5.8)). The difference in mean rate

						of decline between groups was also not significant P < 0.08 (Reisman 1988). 1 study reported no difference between groups in FEV_1 L at 12 months, MD 0.52 L (95% CI -0.25 to 1.29) (Hristara-Papadopoulou 2005). A further study reported similar results across both groups when FEV_1 was measured in % predicted and L (Osman 2010).
FVC: % predicted (change from baseline) Follow-up: at least 6 months	No studies reported on change in FVC % predicted but 1 study reported the rate of change from baseline, 1 reported in L and 1 reported narratively (see comments).					The original paper for the 3-year study reports the mean (SD) rate of decline in FVC % predicted in each group. The mean (SD) rate of decline from baseline for participants in the ACBT alone group as well as the CCPT group was not statistically significant (ACBT -1.6 (5.7) and CCPT 0.2 (4.9)). There was no difference between groups in mean rate of decline (Reisman 1988). 1 study reported no difference in FVC L between groups at 12 months, MD 0.70 L (95% CI -0.15 to 1.55) (Hristara-Papadopoulou 2005). A further study reported similar results across both groups when FVC was measured in % predicted and L (Osman 2010).
Sputum weight (change from baseline) Follow-up: at least 6 months	No studies reported on this outcome at this time point. See comments.					A cross-over study reported on sputum weight at 2 days. We are unable to analyse these data because there was only 1 participant in 1 of the arms (Osman 2010).
Number of pulmonary exacerbations Follow-up: at least 12 months	167 per 1000 participants experienced an exacerbation	274 per 1000 (104 to 725)	RR 1.64 (95% CI 0.62 to 4.34)	63 (1 study)	⊕⊕⊝⊝ low[a,b]	

*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% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
ACBT: active cycle of breathing technique; CCPT: conventional chest physiotherapy; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; NA: not applicable; RR: risk ratio.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Evidence downgraded due to high risk of bias. The study was considered to have a high risk of bias because of the lack of blinding participants or providers and the lack of reporting of other elements.
[b]Evidence downgraded due to imprecision. The sample sizes were small and the confidence intervals around the effect size were wide.

Summary of findings 2. Summary of findings: ACBT compared with PEP mask therapy for people with cystic fibrosis

ACBT compared with PEP mask therapy for people with cystic fibrosis

Patient or population: people with cystic fibrosis

Settings: outpatients and hospital inpatients

Intervention: ACBT

Comparison: PEP mask therapy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	PEP mask therapy	ACBT				
Quality of life (change from baseline) SF-36 score and CRQ score Follow-up: at least 6 months	There were no significant differences between groups for the physical domain of the SF-36 (P = 0.99) but both physical and mental domains decreased after 12 months (P = 0.05 and P = 0.002, respectively). There were no significant differences at the end of the study across the treatment groups for each of the 4 domains of the CRQ: dyspnoea (P = 0.7), fatigue (P = 0.85), emotion (P = 0.39), and mastery (P = 0.82).			30 (1 study)	⊕⊖⊖⊖ very low[a,b,c]	This was a 5-arm study which included 75 participants (15 in each arm). For this comparison, 30 participants were included (Pryor 2010).
Personal preference Follow-up: NA	No studies reported on this outcome.					

Adverse events Follow-up: NA	No studies reported on this outcome.	
FEV_1: % predicted (change from baseline) Follow-up: at least 6 months	No studies reported on this outcome.	None of the included studies that compared ACBT with PEP mask therapy reported on FEV_1 % predicted. However, 1 study with 26 participants reported that there was no difference between ACBT and PEP mask therapy in FEV_1 L (MD -0.08 L; 95% CI -0.85 to 0.69 L) (Pryor 2010).
FVC: % predicted (change from baseline) Follow-up: at least 6 months	No studies clearly reported on this outcome. See comments.	1 study reported that across the 5 treatment groups, there were no significant differences in terms of FVC (P = 0.54). It is unclear if the study is reporting FVC % predicted or L (Pryor 2010).
Sputum weight (change from baseline) Follow-up: NA	No studies reported analysable data for this outcome.	Osman 2010 reported participants may have produced more sputum with ACBT + CCPT than after PEP therapy, but there was only a single participant in the PEP group precluding formal analysis.
Number of pulmonary exacerbations Follow-up: NA	No studies reported on this outcome.	

*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% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
ACBT: active cycle of breathing technique; CI: confidence interval; CRQ: Chronic Respiratory Disease Questionnaire; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MD: mean difference; NA: not applicable; PEP: positive expiratory pressure; SF-36: Short Form-36.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Evidence downgraded due to high risk of bias. The study was considered to have a high risk of bias because of the lack of blinding participants or providers, incomplete follow-up, and it did not conduct an intention-to-treat analysis.
[b]Evidence downgraded due to imprecision. The sample size was small.
[c]Evidence downgraded due to suspected publication bias.

Summary of findings 3. Summary of findings: ACBT compared with OD for people with cystic fibrosis

ACBT compared with OD for people with cystic fibrosis

Patient or population: people with cystic fibrosis

Settings: outpatients and hospital inpatients

Intervention: ACBT

Comparison: OD

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	OD				
Quality of life (change from baseline) in SF-36 score and CRQ score Follow-up: at least 6 months	There were no significant differences between groups for the physical domain of the SF-36 (P = 0.99) but physical and mental domains decreased after 12 months (P = 0.05 and P = 0.002, respectively). There were no significant differences at the end of the study across the treatment groups for each of the 4 domains of the CRQ: dyspnoea (P = 0.7), fatigue (P = 0.85), emotion (P = 0.39), and mastery (P = 0.82).			30 (1 study)	⊕⊖⊖⊖ very low[a,b,c]	This was a 5-arm study which included 75 participants (15 in each arm). For this comparison, 30 participants were included (Pryor 2010).
Personal preference Follow-up: at least 6 months	No studies reported on this outcome at 6 months. See comments.					2 studies reported on preference after 2 days of using ACBT or OD. There were no consistent findings across these 2 studies regarding personal preference between the 2 treatments (Milne 2004; Phillips 2004).
Adverse events Follow-up: NA	No studies reported on this outcome.					

FEV_1: % predicted (change from baseline) Follow-up: at least 6 months	No studies reported on this outcome at 6 months. See comments.	A cross-over study reported on the FEV_1 % predicted after 2 non-consecutive days of treatment. The change in FEV_1 % predicted was similar for ACBT + CPPT and AOD (MD 5.41% predicted; 95% CI -15.62 to 26.44% predicted) and for ACBT + CCPT and HFCC (MD 0.30% predicted; 95% CI -15.63 to 16.23% predicted) (Osman 2010).
FVC: % predicted (change from baseline) Follow-up: at least 6 months	No studies reported on this outcome at 6 months. See comments.	A cross-over study reported on the FVC % predicted after 2 non-consecutive days of use. The change in FVC % predicted was similar for ACBT + CPPT and AOD (MD -6.49% predicted; 95% CI -22.81 to 9.84% predicted) and for ACBT + CCPT and HFCC (MD -5.08% predicted; 95% CI -20.62 to 10.47% predicted) (Osman 2010).
Sputum weight (change from baseline) Follow-up: at least 6 months	No studies reported on this outcome at 6 months. See comments.	3 studies reported on sputum weight after 1 or 2 days of treatment. The studies differed in terms of their comparisons and study designs and were limited in their reporting of the results.
Number of pulmonary exacerbations Follow-up: NA	No studies reported on this outcome.	

*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% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
ACBT: active cycle of breathing technique; AOD: airway oscillating device (Flutter); CCPT: conventional chest physiotherapy; CI: confidence interval; CRQ: Chronic Respiratory Questionnaire; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; HFCC: high-frequency chest compression devices (Vest); MD: mean difference; NA: not applicable; OD: oscillating devices.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Evidence downgraded due to high risk of bias. The study was considered to have a high risk of bias because of the lack of blinding participants or providers, incomplete follow-up, and it did not conduct an intention-to-treat analysis.

[b]Evidence downgraded due to imprecision. The sample size was small.
[c]Evidence downgraded due to suspected publication bias.

Summary of findings 4. Summary of findings: ACBT compared with other breathing techniques for people with cystic fibrosis

ACBT compared with other breathing techniques for people with cystic fibrosis

Patient or population: people with cystic fibrosis

Settings: outpatients and hospital inpatients

Intervention: ACBT

Comparison: other breathing techniques

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Other breathing techniques	ACBT				
Quality of life (change from baseline) Follow-up: at least 6 months	There were no significant differences between groups for the physical domain of the SF-36 (P = 0.99) but physical and mental domains decreased after 12 months (P = 0.05 and P = 0.002, respectively). There were no significant differences at the end of the study across the treatment groups for each of the 4 domains of the CRQ: dyspnoea (P = 0.7), fatigue (P = 0.85), emotion (P = 0.39), and mastery (P = 0.82).			30 (1 study)	⊕⊝⊝⊝ very low[a,b,c]	This was a five arm study which included 75 participants (15 in each arm). For this comparison 30 participants were included (Pryor 2010).
Personal preference Follow-up: at least 6 months	No studies reported on this outcome at 6 months. See comments.					One 2-day cross-over study reported similar rates of preference between ACBT and AD (Miller 1995).
Adverse events Follow-up: NA	No studies reported on this outcome.					
FEV_1: % predicted (change from baseline)	No studies reported on this outcome at 6 months. See comments.					1 study reported on FEV_1 % predicted after 2 non-consecutive days of treatment. The change

Follow-up: at least 6 months		in FEV_1 % predicted was similar for ACBT + CCPT and AD (MD -8.30% predicted; 95% CI -35.22 to 18.62) (Osman 2010).
FVC: % predicted (change from baseline) Follow-up: at least 6 months	No studies reported on this outcome at 6 months. See comments.	1 study reported on FVC % predicted after 2 non-consecutive days of treatment. The change in FVC % predicted was similar for ACBT + CCPT and AD (MD -11.02; 95% CI -32.84 to 10.80) (Osman 2010).
Sputum weight (change from baseline) Follow-up: at least 6 months	No studies reported on this outcome at 6 months. See comments.	2 studies compared ACBT with AD after 1 or 2 days of use. There were no statistically significant differences between treatments in terms of sputum weight (Miller 1995; Osman 2010).
Number of pulmonary exacerbations Follow-up: NA	No studies reported on this outcome.	

*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% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
ACBT: active cycle of breathing technique; AD: autogenic drainage; CCPT: conventional chest physiotherapy; CI: confidence interval; CRQ: Chronic Respiratory Questionnaire; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MD: mean difference; NA: not applicable.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a] Evidence downgraded due to high risk of bias. The trial was considered to have a high risk of bias because of the lack of blinding participants or providers, incomplete follow-up, and did not conduct an intention-to-treat analysis.
[b]Evidence downgraded due to imprecision. The sample size was small.
[c]Evidence downgraded due to suspected publication bias.

Summary of findings 5. Summary of findings: ACBT compared with exercise for people with cystic fibrosis

ACBT compared with exercise for people with cystic fibrosis
Patient or population: people with cystic fibrosis

Settings: outpatients and hospital inpatients

Intervention: ACBT

Comparison: ACBT + exercise

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 + Exercise	ACBT				
Quality of life (change from baseline) CFQ-R score Follow-up: at least 6 months	There was no difference between groups in the median CFQ-R scores for the subdomains of emotional function (P = 0.431) and treatment difficulties (P = 0.579) at 6 months.		N/A	19 (1 study)	⊕⊖⊖⊖ very low[a,b,c]	
Personal preference Follow-up: NA	No studies reported on this outcome.					
Adverse events Follow-up: at 6 months	There were no adverse events reported during the study.		NA	19 (1 study)	⊕⊖⊖⊖ very low[a,d]	
FEV_1: % predicted (change from baseline) Follow-up: at least 6 months	There was no difference between groups in the median FEV_1 % predicted at 6 months (P = 0.873).		NA	19 (1 study)	⊕⊖⊖⊖ very low[a,b]	
FVC: % predicted (change from baseline) Follow-up: at least 6 months	There was no difference between groups in the median FVC % predicted at 6 months (P = 0.749).		NA	19 (1 study)	⊕⊖⊖⊖ very low[a,b]	
Sputum weight (change from baseline) Follow-up: NA	No studies reported on this outcome.					
Number of pulmonary exacerbations Follow-up: NA	0 out of 11 people.	1 out of 11 people	NA	22 (1 study)	⊕⊖⊖⊖ very low[a,d]	

*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% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
ACBT: active cycle of breathing technique; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MD: mean difference; NA: not applicable.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Evidence downgraded due to unclear risk of bias. Information in clinical trials registry entry was insufficient to determine risk of bias.
[b]Evidence downgraded twice due to imprecision. The sample size was small.
[c]Evidence downgraded due to suspected publication bias. Results used for the analysis were published only in the clinical trials registry. The journal article reported on only 2 of the 8 subdomains of the Cystic Fibrosis Questionnaire-Revised Child Version.
[d]Evidence downgraded twice due to imprecision. Few or no events occurred during the study.

BACKGROUND

Description of the condition

Cystic fibrosis (CF) is a hereditary multisystem disorder. It is a relatively common autosomal recessive disease. The incidence is estimated to be between 1 in 3000 to 1 in 6000 in Australia, Canada, the USA and Europe, but is less common in other parts of the world (Scotet 2020). It predominately affects the lungs, liver, and exocrine glands of the pancreas and intestines. Individuals with CF have a defect in the gene responsible for the chloride channel that co-ordinates salt transport across cells (Rowe 2005). Abnormal sodium transport results in the production of viscous mucus and an environment susceptible to chronic airway obstruction. This leads to pulmonary colonisation by pathogenic bacteria. Pulmonary disease is the leading cause of morbidity and mortality in people with CF, accounting for over 60% of deaths (Cystic Fibrosis Foundation Patient Registry 2020; Cystic Fibrosis Trust 2020a).

Currently, there is no cure for CF, but treatment has been developed to increase the life span and quality of life of individuals with CF. In the USA, the predicted mean age of survival increased from 34.1 years in 2004 to 46.2 years in 2019 (Cystic Fibrosis Foundation Patient Registry 2020). The predicted mean age of survival in the UK and Canada in 2019 was 49.1 and 54.3 years, respectively (Cystic Fibrosis Canada 2020; Cystic Fibrosis Trust 2020a), Importance has been placed on early diagnosis as well as effective disease management. Advances in treatment have greatly decreased disease-related morbidity and mortality over the past 20 years (Giron 2021).

Description of the intervention

There are a number of methods used to remove airway secretions in individuals with CF. These include a variety of medications and inhalation therapies, as well as breathing exercises and devices. The goals of chest physiotherapy (usually initiated soon after diagnosis) are to improve mucus clearance, increase sputum production, and improve airway function. A Cochrane Review concluded that chest physiotherapy was beneficial for mucus transport in people with CF (Warnock 2015). There is a significant increase in the volume of sputum produced when performing chest physiotherapy compared with cough alone (Lorin 1971).

Conventional chest physiotherapy (CCPT) has been the standard treatment used to treat excessive mucus secretions in CF in North America since the 1950s (McIlwaine 1997). Other airway clearance therapies became popular in the 1990s (McIlwaine 2007). These include the active cycle of breathing technique (ACBT), positive expiratory pressure (PEP) mask therapy, high-pressure PEP (HiPEP) mask therapy, airway oscillating devices (AOD), autogenic drainage (AD), high-frequency chest compression devices (HFCC), and the resistive inspiratory manoeuvre (RIM). In the early 1990s, concern about oxygen desaturation during chest physiotherapy was addressed with the use of sufficient pauses for relaxation and breathing control during ACBT (Pryor 1990b). In the late 1990s, the use of AOD was shown to enhance mucus expectoration during exacerbations of CF lung disease (Gondor 1999). A number of these therapies can be self-administered by the individual, while others require the assistance of a trained physiotherapist, parent, or caregiver. The self-administered techniques can be performed anywhere once the individual is properly trained. The self-administered techniques included in this review are ACBT, AD, and exercise. The techniques in this review which can be self-administered but require the use of a device include PEP, HiPEP, AOD, and HFCC. The techniques in this review which require assistance include CCPT and RIM. Descriptions of all interventions can be found in the Types of interventions section.

How the intervention might work

In ACBT, a cycle of techniques is used to loosen airway secretions. The techniques include breathing control, thoracic expansion exercises, and the forced expiration technique (FET). In breathing control, the individual performs tidal breathing (gentle relaxed breathing) using the lower chest, at his or her own rate and depth (International Physiotherapy Group for CF 2009). Individuals are encouraged to relax their shoulders and upper chest. Breathing control is the resting period between the active parts of ACBT. Thoracic expansion exercises consist of deep breathing with inspiration and passive relaxed expiration. In FET, huffing and breathing control are combined so that one or two forced expirations (huffs) are interspersed with periods of breathing control (International Physiotherapy Group for CF 2009). Huffing is a type of cough which includes inhaling and active exhaling (Cystic Fibrosis Foundation 2023). The length of the huff is altered to optimise clearance. Huffing helps mobilise and clear peripherally-situated secretions (Pryor 1999). One of the benefits of this technique is that it can be self-administered by the person with CF.

Why it is important to do this review

People with CF experience chronic airway infections as a result of mucus buildup within the lungs. Repeated infections cause lung damage and disease which are the main causes of death in individuals with CF. For this reason, airway clearance therapies play an important role in the treatment of CF. Scientists have not agreed upon a definitive method of treatment, thus both conventional and alternative treatments are in widespread use. Many treatment centres apply those methods that are most familiar to them and neglect others. Globally, it has been observed that CCPT is widely used in the USA; ACBT is most commonly used in the UK; PEP, flutter (AOD) and AD are commonly used in the rest of Europe; and exercise is the favoured treatment in the Scandinavian countries (Prasad 1998b). Other Cochrane Reviews have explored the effectiveness of airway clearance therapies in CF including CCPT (Main 2005; Warnock 2015), PEP (McIlwaine 2019), AOD (Morrison 2020) and autogenic drainage (Burnham 2021). Three of the reviews included results on comparisons involving ACBT versus other therapies. One review compared ACBT with CCPT (Main 2005), one compared ACBT with AOD (including flutter, acapella, cornet, intrapulmonary percussive ventilation (IPV), and extra-thoracic oscillations) (Morrison 2020), and one compared ACBT with autogenic drainage (Burnham 2021). A review comparing ACBT with all therapies is needed.

This is an updated version of a previously published review (McKoy 2012; McKoy 2016; Robinson 2010).

OBJECTIVES

To compare the clinical effectiveness of ACBT with other airway clearance therapies in CF.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised or quasi-randomised controlled clinical studies, including cross-over studies, were eligible.

Types of participants

We included individuals with CF diagnosed based on clinical criteria, sweat testing or genotype analysis.

Types of interventions

We compared ACBT with other airway clearance therapies. This includes comparisons as a single technique (e.g. ACBT versus AD or ACBT versus AD and AOD) or in conjunction with other techniques (e.g. ACBT versus ACBT and CCPT).

Airway clearance therapies include the following techniques.

Intervention

ACBT

This self-administered technique combines breathing control with thoracic expansion and the FET. It may also include postural drainage and chest clapping.

The ACBT methods were initially described as FET. In 1990, the term ACBT was developed to emphasise the importance of breathing control and thoracic expansion, in addition to FET, within the technique (Webber 1998). As a result of this reclassification, we included all studies which described FET interventions that contained all of the components of ACBT outlined above. We used the definitions of the ACBT components as described by the Cystic Fibrosis Foundation and the Cystic Fibrosis Trust in the process (Cystic Fibrosis Foundation 2023; Cystic Fibrosis Trust 2020b).

Comparators

CCPT

CCPT combines a collection of techniques which include postural drainage, percussion, chest shaking, huffing, and coughing. It excludes the use of exercise, PEP, or other mechanical devices. This technique requires assistance.

PEP

PEP therapy

Breathing with a PEP of 10 cm to 25 cm of water; this technique can be self-administered but requires a device. In adults and adolescents PEP valves or mouthpieces are more commonly used than masks, which are more commonly used by children with CF.

HiPEP therapy

A modification of PEP that includes a full forced expiration against a fixed mechanical resistance, which usually generates pressures ranging from 40 cm to 100 cm of water (McIlwaine 2019). This technique can be self-administered but requires a device.

Oscillatory devices

AOD

Includes flutter, cornet, acapella, and intrapulmonary percussive ventilation (IPV). This technique can be self-administered but requires a device.

HFCC

The Vest™ (formerly known as ThAIRapy Vest and manufactured by Hill-Rom) and the Hayek Oscillator (manufactured by Breasy Medical Equipment Ltd) provide external chest wall compression. This also includes high-frequency chest wall oscillations (HFCWO) which utilizes The Vest™ with interim periods of huffs or coughs. This technique can be self-administered but requires a device.

Breathing techniques (excluding ACBT)

AD

A self-administered breathing technique that uses optimal expiratory flow rates at varying lung volumes to mobilise mucus while avoiding airway closure.

Exercise

A combination of endurance and strength training for the upper and lower body. This technique is self-administered.

Other therapy

RIM

Includes inspiration against resistance after forced expiration. Repeated inspirations at 80% of the maximum sustained inspiratory pressure are completed in groups of six efforts with rest intervals in between (Chatham 2004). This technique requires assistance and the use of a device.

Types of outcome measures

We assessed the following outcome measures.

Primary outcomes

1. Quality of life - all instruments that measure the ability of participants to perform activities of daily living (including but not limited to the Cystic Fibrosis Questionnaire (CFQ), Health Assessment Questionnaire (HAQ), Quality of Well Being (QWB) scale, and Nottingham Health Profile (NHP))
2. Personal preference - the nominated technique of choice by the participant at the conclusion of the study, or by comparison of technique acceptability
3. Mortality

Secondary outcomes

1. Adverse events
2. Exercise tolerance - subjective exercise tolerance or objective measures such as the six-minute walk test or treadmill test
3. Lung function
   a. forced expiratory volume in one second (FEV_1) in L or per cent (%) predicted
   b. forced vital capacity (FVC) in L or % predicted
4. Sputum
   a. dry weight (g)
   b. wet weight (g)

   c. volume (mL)
5. Oxygen saturation
   a. arterial blood gas
   b. pulse oximetry
   c. transcutaneous oximetry
6. Number of pulmonary exacerbations

Search methods for identification of studies

Studies were eligible for inclusion irrespective of publication status (e.g. abstract or online trial report) or language.

Electronic searches

We identified relevant studies from the Cystic Fibrosis and Genetic Disorders (CFGD) Group's Cystic Fibrosis Trials Register using the terms: active cycle breathing technique (ACBT) OR forced expiration technique (FET or Huff).

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 most recent search: 4 November 2022.

We searched the ClinicalTrials.gov trials registry (clinicaltrials.gov/) and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP); please see the appendices for the search strategies (Appendix 1). The date of the most recent search of the registries was 3 April 2021.

Searching other resources

We searched the reference lists of relevant articles and reviews for additional studies.

Data collection and analysis

Selection of studies

We used a two-tier screening process to identify relevant articles. Initially, we screened the titles and abstracts of articles identified through searching and obtained the full text versions of those considered potentially relevant. We then screened the full text articles to identify those studies which were eligible for data abstraction and should be included in the review. Two review authors independently screened each article. We resolved any disagreements by consensus or by consulting a third review author.

Data extraction and management

We imported the search results into reference management software (ProCite 1999). We used this software to track the results of the two-tier screening process. We then abstracted information from eligible review articles and entered data into RevMan 5 (RevMan 2020). The Managing Editor of the CFGD Group translated one paper from German (Hristara-Papadopoulou 2005).

We grouped studies together based on the time of assessment of outcomes. We considered outcomes as immediate if less than one day in duration; short term if up to one week in duration; medium term if up to one month in duration; and long term if beyond one month in duration.

Assessment of risk of bias in included studies

We assessed the risk of bias in included studies through assessment of sequence generation; allocation concealment; blinding of the study participants, personnel, and outcome assessors; compliance assessment; washout reporting; intention-to-treat analysis; adequate follow up; and selective reporting. Two review authors independently applied the methods for evaluating the risk of bias as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). A third author resolved any disagreements.

Measures of treatment effect

We analysed continuous outcomes by mean difference (MD) (or we calculated standardised mean difference (SMD) if study reports used different scales of measurement). We analysed dichotomous outcomes using risk ratios (RR). We have presented all outcomes with the associated 95% confidence intervals (CIs).

Unit of analysis issues

When conducting analyses, we took into consideration the level at which randomisation occurred (Deeks 2011). Randomised controlled studies with parallel group designs are studies where individuals are independently randomised to intervention groups. In randomised cross-over studies, individuals receive each intervention sequentially in a random order. Cross-over studies usually contain a washout period, which is a stage after the first treatment but before the second treatment, where time is given for the active effects of the first treatment to wear off before the new treatment begins (i.e. to reduce the carry-over effect). A concern with the cross-over design is the risk of a carry-over effect when the first treatment affects the second. If the carry-over effect exceeds the washout period, the washout is inadequate. For this review, we considered an adequate washout period for cross-over studies to be a minimum of one day.

When including both parallel and cross-over studies with an adequate washout period, we used the inverse variance method, as recommended by Elbourne 2002. In this method, we used the results from paired analyses (including an estimate of treatment effect and its standard error) of the cross-over studies. In the meta-analysis, the weight of each study is inversely proportional to the variance (one over the square of the standard error) (Deeks 2011). When including cross-over studies with an inadequate washout period, we used only the first-arm data. Even though all information is not considered in this method, this avoids inappropriate consideration of multiple arms.

A total of 19 of the 22 studies were randomised cross-over studies; for those studies with adequate washout periods, we have included all data (Hristara-Papadopoulou 2005; Miller 1995; Milne 2004; Phillips 2004). For studies with inadequate washout periods, we planned to include only first-arm data collected before the first

cross-over. In one study that had no washout period, we contacted the authors and were able to obtain first-arm data, which we have included (Osman 2010). We have contacted the corresponding authors of the remaining studies with inadequate or not reported washout periods, and are awaiting their responses (Bilton 1992; Chatham 2004; Fauroux 1999; Hofmeyr 1986; Holland 2003; Howard 2000; Hristara-Papadopoulou 2007; Kofler 1994; Mortensen 1991; Pike 1999; Pryor 1979; Pryor 1994; Steven 1992; Webber 1985). These studies are included in the qualitative synthesis of the review, but excluded from the quantitative synthesis.

Dealing with missing data

We contacted the original investigators of studies when we encountered missing, incomplete, or unclear data. If we could not locate the investigators or they did not send the requested data, we categorised these studies as 'Studies awaiting classification', to be included in future updates of the review, if data are made available.

Assessment of heterogeneity

If we are able to include sufficient data in future updates, we will assess heterogeneity within each outcome between the comparisons using the Chi^2 test and I^2 statistic (Deeks 2011).

Under the null hypothesis of homogeneity, we will consider a P value less than 0.10 to indicate the presence of heterogeneity in the Chi^2 test (Deeks 2011). We will interpret the results with care since the test could have low or high power. Low power is common when studies have a small sample size or there are a small number of studies, which may result in the lack of detection of heterogeneity when it is present. High power is common when there are many studies being analysed, resulting in the detection of heterogeneity that might be insignificant.

The I^2statistic measures the proportion of inconsistency in individual studies that cannot be explained by sampling error. In this test the degree of heterogeneity is quantified. The values of I^2 lie between 0% and 100%. We will consider results for I^2 which are less than 40% to indicate that heterogeneity might not be important, between 30% and 60% to indicate that heterogeneity may be moderate, between 50% and 90% to indicate that heterogeneity may be substantial, and between 75% and 100% to indicate considerable heterogeneity (Deeks 2011).

Assessment of reporting biases

We assessed outcome reporting bias. Study authors may record more outcome measures than they choose to publish, which can lead to misleading results (Sterne 2011). We compared the 'Methods' section of each included paper to the 'Results' section to ensure all outcomes were reported.

If we are able to include sufficient data in future updates, we will assess reporting bias among the studies using the funnel plot method discussed in the *Cochrane Handbook for Systematic Reviews of Interventions* (Sterne 2011). If asymmetry is present, we will explore possible causes including publication bias, poor methodological quality, and true heterogeneity.

Data synthesis

We entered data abstracted from included studies into RevMan 5 (RevMan 2020). We analysed each comparison separately.

If we are able to include sufficient data in future updates, we will assess heterogeneity. If we determine that heterogeneity may be moderate, substantial, or considerable, as indicated by an I^2 result greater than 30%, we will use the random-effects model to synthesise the results. Otherwise, we will synthesise the results using a fixed-effect model.

Subgroup analysis and investigation of heterogeneity

If we are able to include sufficient data in future updates, we will investigate heterogeneity by performing the following subgroup analyses:

1. treatment setting (home versus hospital);
2. treatment length (one day on and one day off, once daily, twice daily, three times daily, three times per week);
3. age (paediatric, adolescent, adult);
4. gender;
5. disease severity (FEV_1 % predicted above 90%, 70% to 89%, 40% to 69%, under 40%).

Sensitivity analysis

If we are able to include sufficient data in future updates, we will perform sensitivity analyses to identify the effects on the results of study size (stratify by sample size), study design (cross-over versus parallel studies), allocation concealment (high risk of bias versus low risk of bias), assessor blinding (high risk of bias versus low risk of bias), and loss to follow up (high risk of bias versus low risk of bias).

Summary of findings and assessment of the certainty of the evidence

In a post hoc change and in line with current Cochrane guidance, we have prepared a summary of findings table for the following comparisons: ACBT versus CCPT (Summary of findings 1), ACBT versus PEP mask therapy (Summary of findings 2), ACBT versus OD (Summary of findings 3), ACBT versus other breathing technique (Summary of findings 4), and ACBT compared with exercise (Summary of findings 5). We have listed the population, setting, intervention and comparison and have reported an illustrative risk for the experimental and control intervention (Schünemann 2011). We graded the overall certainty of the body of evidence as high, moderate, low or very low using GRADE (Schünemann 2006). We based our judgements on the risk of bias within the trials, their relevance to our population of interest (indirectness), unexplained heterogeneity or inconsistency, imprecision of the results or high risk of publication bias. We downgraded the evidence once if the risk was serious and twice if the risk was deemed to be very serious and described the rationale for each judgement in footnotes to each table.

For each comparison, where possible, we reported the following outcomes: quality of life (change from baseline to six months), individual preference at six months, adverse events at six months, FEV_1 % predicted (change from baseline to six months), FVC % predicted (change from baseline to six months), sputum weight (change from baseline to six months), and number of pulmonary exacerbations at 12 months.

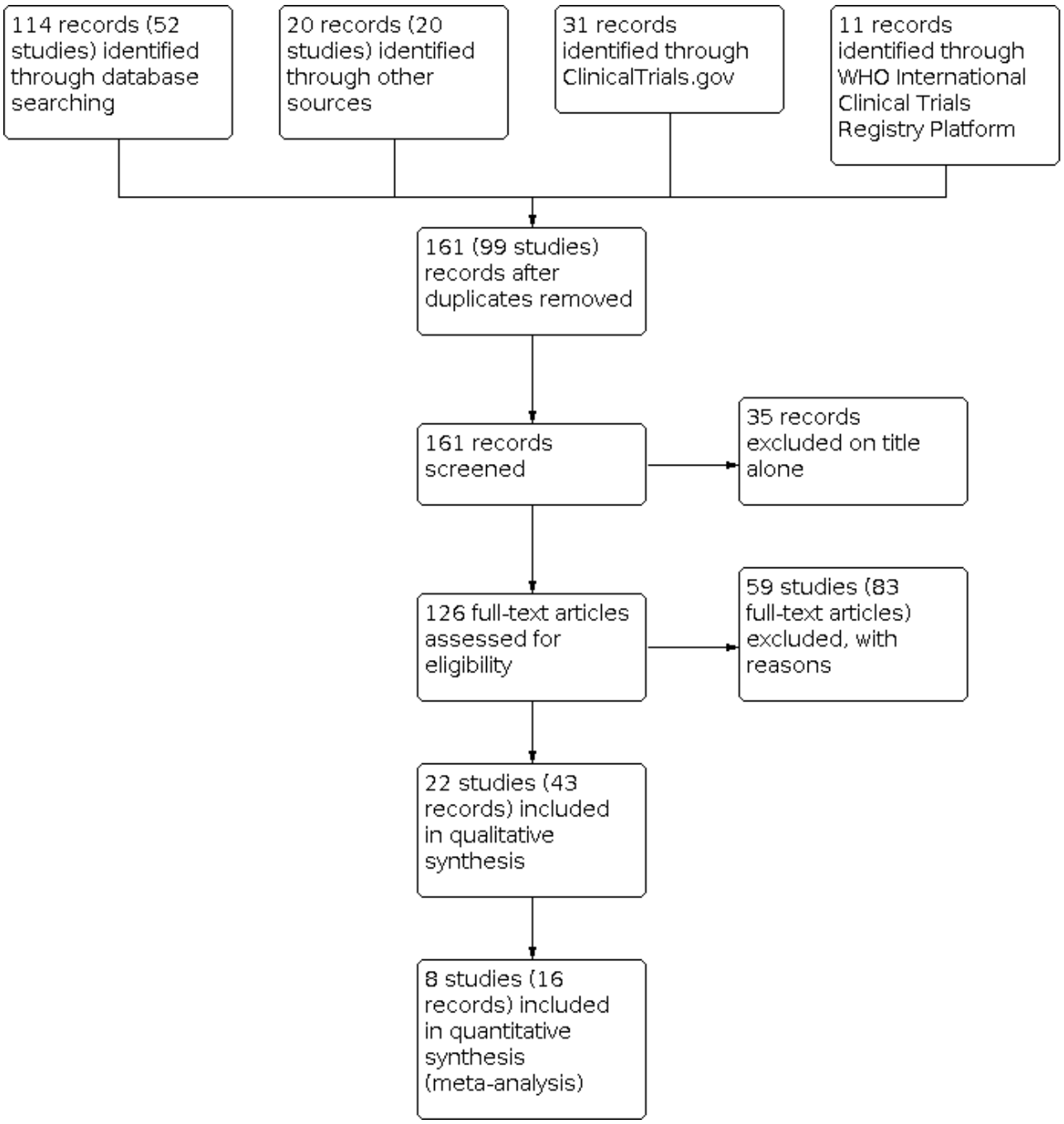
RESULTS

Description of studies

Results of the search

In total, we identified 161 citations representing 99 studies (Figure 1). The electronic searches of the CFGD Trials Register identified 114 citations representing 52 studies. We identified an additional 20 citations, representing 20 studies, by searching the reference lists of relevant articles. Our search of ClinicalTrials.gov yielded 31 citations, one of which had already been identified from the CFGD Trials Register. Our search of the WHO ICTRP yielded 11 citations, three of which were already captured in the ClinicalTrials.gov search. Of the 161 citations representing 99 studies, we excluded 35 at the title and abstract screening stage. We reviewed the full texts for 81 studies (126 citations). We included 22 studies (43 citations) and excluded 59 studies (83 citations) (see below).

Figure 1. Study flow diagram.



Included studies

We included 43 citations representing 22 studies. Full-text articles were available for 19 studies (Bilton 1992; Chatham 2004; Fauroux 1999; Gungor 2021; Hofmeyr 1986; Holland 2003; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Miller 1995; Milne 2004; Mortensen 1991; Osman 2010; Phillips 2004; Pryor 1979; Pryor 1994; Pryor 2010; Reisman 1988; Steven 1992; Webber 1985), while only abstracts were available for three studies (Howard 2000; Kofler 1994; Pike 1999). When multiple citations were available for a study, we extracted data from full-text articles. We reviewed all citations, and when applicable, also extracted date for additional outcomes not included in the full-text articles.

Of the 22 included studies, we included eight in the analysis: three randomised controlled parallel studies (Gungor 2021; Pryor 2010; Reisman 1988), four randomised cross-over studies with adequate washout periods (Hristara-Papadopoulou 2005; Miller 1995; Milne 2004; Phillips 2004), and one randomised cross-over study with an inadequate washout period for which we have first-arm data before the first cross-over period (Osman 2010). The remaining studies were randomised cross-over studies with inadequate washout periods, and we have attempted to obtain first-arm data collected before the first cross-over. We have contacted the study authors and are awaiting their responses.

Seven studies declared funding from either government agencies, patient organisations or charities (Bilton 1992; Fauroux 1999; Hofmeyr 1986; Mortensen 1991; Pryor 2010; Reisman 1988; Webber 1985), and two studies declared funding from these sources plus some industry sponsorship (Chatham 2004; Osman 2010). One study was soley sponsored by industry funding (Miller 1995). One trial specifically reported no funding was received (Gungor 2021), and the remaining 11 studies did not report or describe any funding (Holland 2003; Howard 2000; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Kofler 1994; Milne 2004; Phillips 2004; Pike 1999; Pryor 1979; Pryor 1994; Steven 1992).

We have included information on all 22 included studies in the sections Included studies and Risk of bias in included studies. We have included results on the eight studies included in the analysis in the Effects of interventions section.

Trial design

In 13 studies the intervention duration was less than one day (Bilton 1992; Fauroux 1999; Hofmeyr 1986; Holland 2003; Howard 2000; Miller 1995; Milne 2004; Mortensen 1991; Osman 2010; Phillips 2004; Pike 1999; Pryor 1994; Steven 1992). Three studies had an intervention duration between two days and one week (Chatham 2004; Pryor 1979; Webber 1985). Six studies had an intervention duration of longer than one month (Gungor 2021; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Kofler 1994; Pryor 2010; Reisman 1988). The duration of the intervention in the randomised controlled studies with a parallel design were six weeks, one year, and three years (Gungor 2021; Pryor 2010; Reisman 1988).

We defined adequate washout for cross-over studies to be a minimum of one day. A total of 19 of the 22 studies were randomised cross-over studies (Bilton 1992; Chatham 2004; Fauroux 1999; Hofmeyr 1986; Holland 2003; Howard 2000; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Kofler 1994; Miller 1995; Milne 2004; Mortensen 1991; Osman 2010; Phillips 2004; Pike 1999; Pryor 1979; Pryor 1994; Steven 1992; Webber 1985). Of these, only four studies had adequate washout periods (Hristara-Papadopoulou 2005; Miller 1995; Milne 2004; Phillips 2004).

Participants

There were a total of 559 participants across the 22 studies. The smallest study had seven participants (Milne 2004), while the largest had 75 participants (Pryor 2010). Age ranged from six years to 63 years across all studies, and the mean age was 18.7 years. Of the 506 participants in the 20 studies which reported the sex of participants, 298 (59%) were male. Two studies, only available in abstract form, did not report age or sex of participants (Howard 2000; Kofler 1994).

The participants in a number of the included studies were identified as being infected or colonised with bacteria. In four studies, all analysed participants were infected or colonised with *Pseudomonas aeruginosa* (Bilton 1992; Chatham 2004; Hofmeyr 1986; Mortensen 1991). In another study, approximately half of the participants were infected or colonised with *P aeruginosa* and *Burkholderia cepacia* (Fauroux 1999). In five studies, all participants had an exacerbation of bronchopulmonary infection (Hofmeyr 1986; Phillips 2004; Pryor 1979; Steven 1992; Webber 1985). The authors of one study noted that all of the participants had a history of chronic bronchopulmonary infection (Pryor 1994). One study excluded individuals who had acquired *B cepacia* within the last three months (Pryor 2010). One study included participants who were stable and did not present with exacerbations (Hristara-Papadopoulou 2007). One study did not report on participants' infection status (Hristara-Papadopoulou 2005).

One study stratified randomisation by age, sex, and pulmonary impairment (Reisman 1988) and another study stratified randomisation by pulmonary impairment and sputum expectorated (Pryor 2010). Stratification of results based on the degree of pulmonary impairment was performed in three studies (Fauroux 1999; Miller 1995; Mortensen 1991).

Interventions

Sixteen studies specifically named ACBT as an intervention (Bilton 1992; Chatham 2004; Gungor 2021; Holland 2003; Howard 2000; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Kofler 1994; Miller 1995; Milne 2004; Osman 2010; Phillips 2004; Pike 1999; Pryor 1994; Pryor 2010; Steven 1992). Of these studies, five studies did not describe the components of ACBT (Hristara-Papadopoulou 2005; Howard 2000; Kofler 1994; Pike 1999; Pryor 2010). Six studies included FET as an intervention, but reported FET to contain all of the components of ACBT as described in the Methods section of this review (Fauroux 1999; Hofmeyr 1986; Mortensen 1991; Pryor 1979; Reisman 1988; Webber 1985). We considered these six studies as including ACBT as an intervention.

Ten studies compared ACBT as a single technique (Gungor 2021; Howard 2000; Hristara-Papadopoulou 2005; Kofler 1994; Miller 1995; Milne 2004; Phillips 2004; Pike 1999; Pryor 2010; Steven 1992). Twelve studies compared ACBT in conjunction with other techniques (Bilton 1992; Chatham 2004; Fauroux 1999; Hofmeyr 1986; Holland 2003; Hristara-Papadopoulou 2007; Mortensen 1991; Osman 2010; Pryor 1979; Pryor 1994; Reisman 1988; Webber 1985). Five studies included postural drainage as a component of ACBT (Hristara-Papadopoulou 2007; Miller 1995; Mortensen 1991; Steven 1992; Webber 1985).

Outcomes

All nine outcomes of this review were reported on by at least one study. Sputum (weight or volume) was the most often reported outcome, discussed in 18 of the 22 studies (Bilton 1992; Chatham 2004; Fauroux 1999; Hofmeyr 1986; Holland 2003; Howard 2000; Hristara-Papadopoulou 2007; Miller 1995; Milne 2004; Mortensen 1991; Osman 2010; Phillips 2004; Pike 1999; Pryor 1979; Pryor 1994; Pryor 2010; Steven 1992; Webber 1985). The least reported outcomes, which were discussed in only one study each, were mortality (Gungor 2021) and adverse events (Gungor 2021).

Excluded studies

We excluded a total of 59 studies (83 citations).

We excluded 19 studies because they did not address ACBT (ACTRN12619001681145; Asher 1982; Bain 1988; Baldwin 1994; Chatham 1998; Davies 2012; Desmond 1983; Kofler 1998; McDonnell 1986; NCT00164138; NCT00404859; NCT00716664; NCT01943890; NCT02906826; O'Neill 2017; Rossman 1982; Sontag 2010; Sutton 1985; Ward 2018). We excluded 11 studies because they were not randomised (ACTRN12605000471684; Horsley 2007; Klig 1989; Oberwaldner 1986; Orlik 2000; Orlik 2001Pryor 1990; Rogers 1984; Salh 1989; Webber 1986; Wilson 1995). Four studies were review articles with no original data (Prasad 1998a; Prasad 2000; Thomas 1995; Williams 1994). Five studies did not include people with CF (ACTRN12614001233617; ChiCTR1800019989; Hasani 1991; Hasani 1994; van Hengstum 1987). Six studies did not have a comparison of interest (Braggion 1995; Stanford 2020; Verboon 1986; White 1997; Williams 2000; Znotina 2000). We excluded seven studies because the description of the FET intervention did not contain all components of ACBT (ACTRN12619000224123; Andreasson 1987; Falk 1984; Gursli 2017; NCT03078127; RBR-5g9f6w; Sutton 1983). One additional study was excluded because the intervention of interest was not randomised (Steen 1991).

We excluded six studies (10 citations) previously listed as awaiting classification. Five of the studies were associated with abstracts that provided insufficient information (Castle 1994; Falk 1993; Lannefors 1992; Parker 1984; Petrone 2009), and one study had a mixed population of participants with and without CF (van Hengstum 1988). To date we have not received any response to our requests for additional data to allow us to include these studies and, given the age of the studies, do not expect to receive relevant information now; therefore we have excluded these studies. If we receive any relevant information in future, we will re-assess these studies.

Risk of bias in included studies

We assessed risk of bias for sequence generation; allocation concealment; blinding of the study participants, personnel, and outcome assessors; incomplete outcome data (intention-to-treat analysis, adequate follow up); selective reporting within each study; and other potential sources of bias (compliance or adherence assessment; washout reporting). Please see the figures for a summary of judgements on the risk of bias of all included studies (Figure 2; Figure 3).

Figure 2. Risk of bias summary: review authors' judgements about risk of bias domains for each included study.

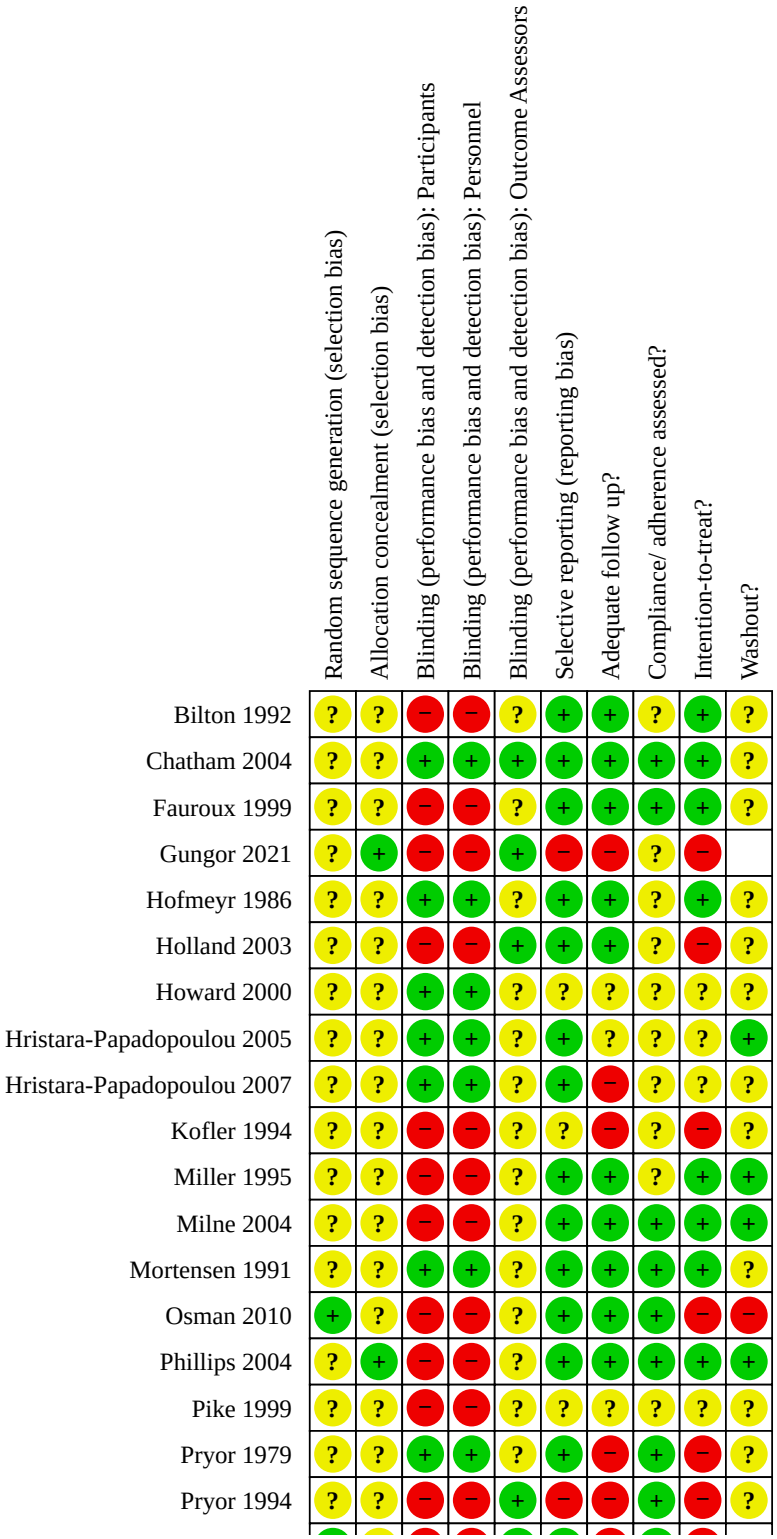


Figure 2. (Continued)

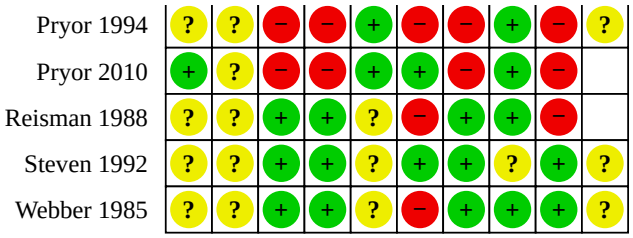
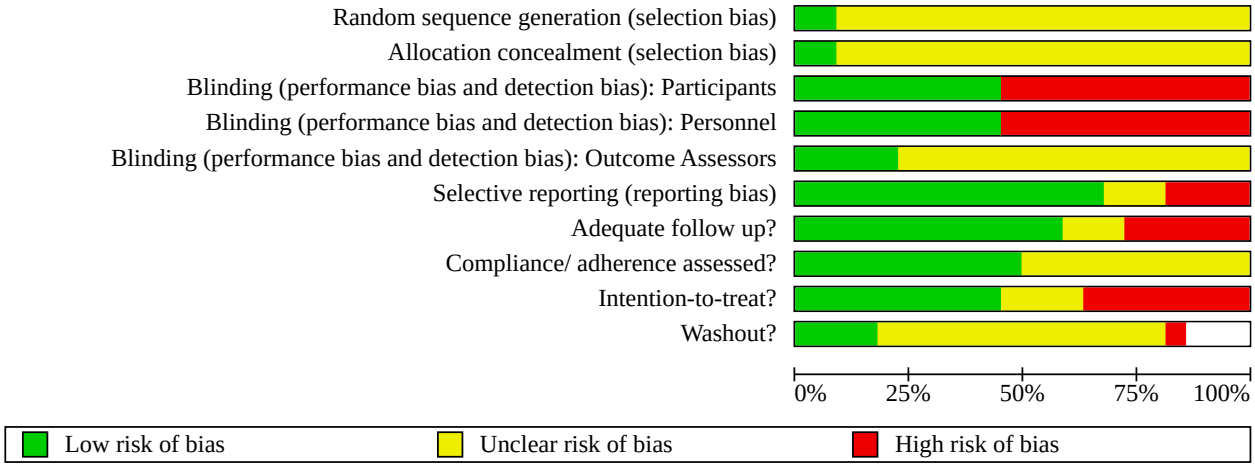


Figure 3. Risk of bias graph: review authors' judgements about risk of bias domains presented as percentages across all included studies.



Allocation

Sequence generation

In one of the 22 studies, which compared HFCWO with usual ACT, participants performed their usual ACT or HFCWO during alternate day treatment, and allocation to either treatment on day one was determined using a computer-generated randomisation table (Osman 2010). A further study used a computer-generated randomisation scheme to randomise participants to one of five airway clearance therapies (Pryor 2010). Thus, the risk of bias of sequence generation was low in these two studies.

In 20 of the 22 included studies, the authors did not specify how the random allocation was generated. The studies made statements that participants were randomly allocated to different treatment groups, but did not completely define the approaches. The risk of bias of sequence generation was unclear in these studies (Bilton 1992; Chatham 2004; Fauroux 1999; Gungor 2021; Hofmeyr 1986; Holland 2003; Howard 2000; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Kofler 1994; Miller 1995; Milne 2004; Mortensen 1991; Phillips 2004; Pike 1999; Pryor 1979; Pryor 1994; Reisman 1988; Steven 1992; Webber 1985).

Allocation concealment

Concealment of treatment allocation was reported in only two studies. Both studies used sealed envelopes during randomisation (Gungor 2021; Phillips 2004). We judged there to be a low risk of bias due to allocation concealment associated with these studies. In the remaining 20 studies, there was not sufficient information to make a judgement on allocation concealment; thus, the risk of bias of allocation concealment was unclear.

Blinding

Each intervention within the included studies was associated with a physical activity or mechanical devices (or both) which are necessary to the intervention. For this reason it was not feasible to blind the participants or personnel, as observed in all included studies. Lack of blinding may affect some outcomes more than others. We considered studies that did not blind participants or personnel and reported on subjective outcomes, such as personal preference or quality of life, to have a high risk of bias (Bilton 1992; Fauroux 1999; Gungor 2021; Holland 2003; Kofler 1994; Miller 1995; Milne 2004; Osman 2010; Phillips 2004; Pike 1999; Pryor 1994; Pryor 2010). We considered studies that did not blind participants or personnel and reported only on objective outcomes, such as lung function or sputum weight, to have a low risk of bias (Chatham 2004; Hofmeyr 1986; Howard 2000; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Mortensen 1991; Pryor 1979; Reisman 1988; Steven 1992; Webber 1985).

Five studies reported that the outcome assessors were blinded (Chatham 2004; Gungor 2021; Holland 2003; Pryor 1994; Pryor 2010). In one study it was noted that the laboratory researcher was

blinded to the treatment administered to participants (Chatham 2004). In the other four studies, the authors noted that an independent data collector, who was blinded to treatment order or treatment assignment, collected the measurements (Gungor 2021; Holland 2003; Pryor 1994; Pryor 2010). There is a low risk bias of blinding of outcome assessors associated with these four studies. In the remaining 17 studies the blinding of the outcome assessor is not specified, thus the risk of bias is unclear.

Incomplete outcome data

Intention-to-treat

The use of intention-to-treat analyses was unclear in four studies, therefore we also judged the related risk of bias to be unclear (Howard 2000; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Pike 1999). In eight studies, intention-to-treat analyses were not performed, and we judged these studies to have a high risk of bias because they did not include outcome data in the analysis from participants who withdrew (Gungor 2021; Holland 2003; Kofler 1994; Osman 2010; Pryor 1979; Pryor 1994; Pryor 2010; Reisman 1988). The remaining 10 studies are associated with a low risk of bias. In these studies, the participants were analysed in the groups to which they were randomised.

Adequate follow-up

It is unclear if follow-up was adequate in three studies (Hristara-Papadopoulou 2005; Howard 2000; Pike 1999), two of which were only available as conference abstracts (Howard 2000; Pike 1999). The risk of bias due to adequate follow-up is unclear in these two studies.

Follow-up was inadequate in six studies (Hristara-Papadopoulou 2007; Kofler 1994; Gungor 2021; Pryor 1979; Pryor 1994; Pryor 2010). In one study, seven out of 35 participants (20%) were not accounted for in the analysis (Hristara-Papadopoulou 2007). In another study, which is only available in abstract form, 10 out of 33 (30.30%) children with CF did not complete the program, and there was no description of reasons for loss to follow-up (Kofler 1994). In a further study, three out of 22 participants (14%) did not complete the study (Gungor 2021). In a fourth study, two out of 18 CF participants (11.11%) withdrew: one person developed a pneumothorax and the other person was unable to produce enough sputum for an accurate assessment (Pryor 1979). In the fifth study, four out of 24 (16.67%) participants withdrew from the study: two participants had their drug regimens changed during the study and two participants withdrew because of technical problems with the oximeter and collection of sputum (Pryor 1994). In the last study, 10 out of 75 participants (13.33%) were lost to follow-up: one died, one was accepted to the transplantation list, one required a limited pleurodesis for a pneumothorax, three were lost to follow-up, and three withdrew; the status of one of the participants was not reported (Pryor 2010). Since the loss to follow-up was greater than 10% in these six studies, they are associated with a high risk of bias.

In the remaining 13 studies the follow-up was adequate, thus there is a low risk of bias associated with follow-up in these studies. While all of the participants were accounted for in these 13 studies, authors in three studies reported having participants who withdrew for varying reasons (Holland 2003; Osman 2010, Reisman 1988). In one study, one out of 27 (3.70%) participants withdrew because of pain during respiratory muscle testing (Holland 2003). In another study, one out of 30 (3.33%) participants withdrew due to a hypoglycaemic episode (Osman 2010). In a third study, four out of 67 (5.97%) participants withdrew from the study: two participants from the ACBT + CCPT group relocated and another two participants from the ACBT group withdrew because of family anxiety associated with discontinuation of CCPT used with FET (Reisman 1988). Since the loss to follow-up was less than 10% in the studies with stated reasons for participant withdrawal, they were all associated with a low risk of bias.

Selective reporting

Since study protocols were unavailable for most studies to allow the comparison of planned and reported outcomes, we assessed selective reporting by comparing the outcomes outlined in the 'Methods' section with those outlined in the 'Results' section of the published papers.

The risk of bias from selective reporting was unclear in three studies that were only available as conference abstracts (Howard 2000; Kofler 1994; Pike 1999). Four studies were thought to potentially involve selective reporting, and we have judged there to be a high risk of bias associated with these studies (Gungor 2021; Pryor 1994; Reisman 1988; Webber 1986). In one study, different outcomes and results were reported in the paper than in the study protocol, which was posted in the trial registry (Gungor 2021). A second study stated that lung function measurements were recorded before and at 5, 10, 15 and 30 minutes after treatment (Pryor 1994); while the third study stated that lung function values were collected before and 30 minutes after the first daily treatment (Webber 1986). In both studies, the authors did not report actual data, only that there were no statistical differences in the lung function measurements collected at the start of treatment each day. The final study mentioned collecting sputum, but did not report on the results of sputum collection (Reisman 1988).

In the remaining 15 studies all outcomes outlined in the 'Methods' section were reported in the 'Results' section, or details were available on the trial registry website; thus, there is a low risk of bias from selective reporting associated with these studies.

Other potential sources of bias

Compliance Assessment

Compliance was assessed in 11 out of the 22 studies (Chatham 2004; Fauroux 1999; Milne 2004; Mortensen 1991; Osman 2010; Phillips 2004; Pryor 1979; Pryor 1994; Pryor 2010; Reisman 1988; Webber 1985). Compliance assessment involved the use of a diary in one study (Reisman 1988), monthly review in another study (Pryor 2010), and supervision in the remaining nine studies; the risk of bias is low in these 11 studies. In the remaining 11 studies it is unclear if compliance was assessed, thus the risk of bias assessment is unclear.

Washout

A total of 19 of the 22 included studies were randomised cross-over studies (Bilton 1992; Chatham 2004; Fauroux 1999; Hofmeyr 1986; Holland 2003; Howard 2000; Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Kofler 1994; Miller 1995; Milne 2004; Mortensen 1991; Osman 2010; Phillips 2004; Pike 1999; Pryor 1979; Pryor 1994; Steven 1992; Webber 1985). Of these, four had adequate washout periods (at least one day): two studies had a one-day washout period (Milne 2004; Phillips 2004), one study

had a seven-day washout period (Miller 1995), and one study had a two-month washout period (Hristara-Papadopoulou 2005); we therefore judged them to have a low risk of bias. One study, for which we were able to obtain first-arm data before the first cross-over, had no washout period; thus the risk of bias is high for this study (Osman 2010). The remaining 14 randomised cross-over studies did not describe a washout period, thus the risk of bias is unclear for these studies.

Effects of interventions

See: **Summary of findings 1** Summary of findings: ACBT compared with CCPT for people with cystic fibrosis; **Summary of findings 2** Summary of findings: ACBT compared with PEP mask therapy for people with cystic fibrosis; **Summary of findings 3** Summary of findings: ACBT compared with OD for people with cystic fibrosis; **Summary of findings 4** Summary of findings: ACBT compared with other breathing techniques for people with cystic fibrosis; **Summary of findings 5** Summary of findings: ACBT compared with exercise for people with cystic fibrosis

In this section, the results are given for the comparisons of ACBT with each comparator. Some comparators (i.e. PEP, oscillatory devices) include multiple techniques or devices, and the results of the comparison of ACBT with each technique or device are discussed separately. We have assessed and graded the certainty of the evidence for predefined outcomes (see above) in the summary of findings tables and definitions of these gradings provided (Summary of findings 1; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5).

ACBT versus CCPT or combinations

See Summary of findings 1.

Six randomised studies (189 participants) compared ACBT with CCPT. Three studies (108 participants) compared ACBT with ACBT + CCPT (Osman 2010; Reisman 1988; Webber 1985), one study (16 participants) compared ACBT + CCPT with CCPT (Pryor 1979), one study (35 participants) compared ACBT + respiratory exercises with CCPT + respiratory exercises (Hristara-Papadopoulou 2007), and one study (30 participants) compared ACBT with CCPT (Hristara-Papadopoulou 2005). One study was of parallel design (n = 63) (Reisman 1988), while the remaining studies were of cross-over design (Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Osman 2010; Pryor 1979; Webber 1985). We were only able to include the parallel study and two of the cross-over studies in the meta-analysis (Hristara-Papadopoulou 2005; Osman 2010; Reisman 1988). Four randomised cross-over studies had insufficient washout periods, but we obtained first-arm data (before the first cross-over) comparing ACBT with ACBT + CCPT from the Osman study investigators and included these data in the meta-analysis where possible (Osman 2010). The study consisted of multiple treatment groups of which ACBT and ACBT + CCPT were just two. Of the 29 participants in the study as a whole, one performed ACBT before the first cross-over and five performed ACBT + CCPT before the first cross-over, thus a comparison cannot be made in the analysis (Osman 2010). For the remaining studies with insufficient washout periods, we contacted the study authors to obtain necessary information and are awaiting their response. If new data become available, we will include these in an update of the review.

Primary outcomes

1. Quality of life

None of the included studies assessed this outcome.

2. Personal preference

None of the included studies assessed this outcome.

3. Mortality

None of the included studies assessed this outcome.

Secondary outcomes

1. Adverse events

None of the included studies assessed this outcome.

2. Exercise tolerance

None of the included studies assessed this outcome.

3. Lung function

a. FEV_1 in L or % predicted

i. FEV_1 (L)

A randomised cross-over study reported FEV_1 in L for ACBT compared to CCPT (Hristara-Papadopoulou 2005); there was no difference between groups after 12 months, MD 0.52 L (95% CI -0.25 to 1.29) (Analysis 1.1). In another cross-over study, ACBT and ACBT + CCPT had similar effects on FEV_1 in L, but the ACBT group had only one person, precluding formal analysis (Osman 2010).

ii. FEV_1 (% predicted per year)

The parallel study comparing ACBT with ACBT + CCPT reports the mean rate of decline in FEV_1 % predicted in each group. Participants in the ACBT alone group had mean (SD) rates of decline that differed significantly from baseline (-4.7 (7.1); $P < 0.001$); however, there was no statistically significant difference from baseline in the CCPT group (-1.9 (5.8)). The difference in mean rate of decline between groups was also reported not to be statistically significant $P < 0.08$ (Reisman 1988).

In a cross-over study, ACBT and ACBT + CCPT had similar effects on FEV_1 % predicted, but the ACBT group had only one person, precluding formal analysis (Osman 2010).

We have concerns due to the risk of bias and imprecise results, so are uncertain about this evidence.

b. FVC in L or % predicted

i. FVC (L)

One randomised cross-over study comparing ACBT to CCPT found no difference in FVC (L) between the two interventions after one year (Hristara-Papadopoulou 2005), MD 0.70 L (95% CI -0.15 to 1.55) (Analysis 1.2). In another cross-over study, FVC in L was higher after a session with ACBT + CCPT than with ACBT alone (Osman 2010). However, there was only one person in the ACBT group, precluding a formal analysis.

ii. FVC (% predicted per year)

The parallel study reported mean rate of decline in FVC % predicted in each group. Participants in both the ACBT alone group and the CCPT group had mean (SD) rates of decline that did not differ significantly from baseline: ACBT -1.6 (5.7) and CCPT 0.2 (4.9). Investigators reported no difference between groups in the mean rate of decline (Reisman 1988).

In another cross-over study, FVC % predicted was higher after a session with ACBT + CCPT than with ACBT alone (Osman 2010). However, there was only one person in the ACBT group, precluding a formal analysis.

We have concerns due to the risk of bias and imprecise results, so are uncertain about this evidence.

4. Sputum

Two studies comparing ACBT with ACBT + CCPT collected sputum; however the parallel study did not report any data for this outcome (Reisman 1988) and while the cross-over study reported similar weights of sputum with ACBT and with ACBT + CCPT, the ACBT group had only one person, precluding formal analysis (Osman 2010).

5. Oxygen saturation

One cross-over study comparing ACBT to CCPT reported a non-significant difference in saturated oxygen levels between the two therapies (Hristara-Papadopoulou 2005). A further cross-over study reported similar levels of oxygen saturation after ACBT and ACBT + CCPT, but the ACBT group had only one person, precluding formal analysis (Osman 2010).

6. Number of pulmonary exacerbations

The parallel study comparing ACBT with ACBT + CCPT presented hospitalisation data for pulmonary exacerbations and for non-pulmonary admissions separately (Reisman 1988). The authors noted that acute exacerbations were treated in the hospital and observed that nine out of 33 participants receiving ACBT and five out of 30 participants receiving ACBT + CCPT experienced pulmonary exacerbations. The nine participants in the ACBT group had 30 hospital admissions and 347 hospital days. One participant in the ACBT group accounted for 15 of the hospital admissions and 150 of the hospital days. The five participants in the ACBT + CCPT group had eight hospital admissions and 73 hospital days. Our analysis showed that group differences in the number of participants, hospital admissions, and hospital days did not reach statistical significance; for pulmonary exacerbations, RR 1.64 (95% CI 0.62 to 4.34) (Analysis 1.3; low-certainty evidence). The study authors also found no significant difference in pulmonary exacerbation rates between the two therapies. They presented the number of participants, hospital admissions, and hospital days for each therapy. We rated the certainty of evidence as low due to risk of bias concerns and imprecise results.

ACBT versus PEP or combinations

See Summary of findings 2.

Five studies (110 participants) compared ACBT with PEP: two studies (28 participants) compared ACBT with ACBT + PEP (Hofmeyr 1986; Mortensen 1991), a further two studies (53 participants) compared ACBT with PEP (Kofler 1994; Pryor 2010), and one study (29 participants) compared ACBT + CCPT with PEP (Osman 2010). One study was of parallel design (Pryor 2010) and four studies were cross-over studies with insufficient washout periods. We obtained first-arm data (before the first cross-over) from the Osman study comparing ACBT + CCPT with PEP and included these data in the meta-analyses where possible. This study consisted of multiple treatment groups of which ACBT + CCPT and PEP were just two. Of the 29 participants, five performed ACBT + CCPT before the first cross-over and one performed PEP before the first cross-over. For the remaining three studies with insufficient washout periods, we have contacted the study authors to obtain necessary information and are awaiting their response. If new data become available they will be included in an update of the review.

Primary outcomes

1. Quality of life

The 12-month, parallel study assessed quality of life using the Short Form-36 and the Chronic Respiratory Questionnaire (Pryor 2010). This study randomised 75 participants to one of five treatment groups, two of which were ACBT (n = 15) and PEP (n = 15). The authors reported no significant differences across the five treatment groups for either the physical domain (P = 0.99) or the mental domain (P = 0.27) of the Short Form-36, but both the physical and mental domains decreased after 12 months (P = 0.05 and P = 0.002, respectively). There were no significant differences at the end of the study across the five treatment groups for each of the four domains of the Chronic Respiratory Questionnaire: dyspnoea (P = 0.7), fatigue (P = 0.85), emotion (P = 0.39), and mastery (P = 0.82). The fatigue (P = 0.69), emotion (P = 0.39), and mastery (P = 0.37) domains showed no significant differences over time. However, there were small, clinically-important improvements in the dyspnoea ratings over the 12-month study for the ACBT (change of 0.7) and the PEP groups (change of 0.5). This study reported insufficient data for both the Short Form-36 and the Chronic Respiratory Questionnaire for inclusion in the meta-analysis. We rated the certainty of the evidence for quality of life when comparing ACBT with PEP mask therapy as very low because of the high risk of bias, the imprecise results, and the suspicion of publication bias.

None of the cross-over studies reported on quality of life.

2. Personal preference

The included studies did not assess this outcome.

3. Mortality

The included studies did not assess this outcome.

Secondary outcomes

1. Adverse events

The included studies did not assess this outcome.

2. Exercise tolerance

The parallel study assessed exercise tolerance using a modified shuttle test (Pryor 2010). Mean baseline scores for the ACBT and the PEP groups were 1005.4 m and 887.9 m. At the end of the study, there were no statistically significant differences across the five treatment groups (P = 0.52). The authors did not report any additional data on this outcome.

None of the cross-over studies reported on exercise tolerance.

3. Lung function

a. FEV_1 in L or % predicted

i. FEV_1 (L)

The parallel study and one cross-over study reported on this outcome (Osman 2010; Pryor 2010). In the parallel study, there was no significant difference in the final mean (SD) FEV_1 L between the ACBT group (1.94 (0.80)) and the PEP group (2.02 (1.17)) (Pryor 2010). We estimated the mean between-group difference in final values to be MD -0.08 L (95% CI -0.85 to 0.69) (Analysis 2.1). In the cross-over study, participants in the ACBT + CCPT group and the PEP group had similar levels of FEV_1 in L and % predicted (Osman 2010). However, the PEP group had only one person, precluding formal analysis.

b. FVC in L or % predicted

Across the five arms of the parallel study, the investigators reported no significant differences in terms of FVC (P = 0.54) (Pryor 2010). In the cross-over study, participants in the ACBT + CCPT group and the PEP groups had similar levels of FVC in L and % predicted (Osman 2010). However, the PEP group had only one person, precluding formal analysis.

4. Sputum

In a cross-over study, participants may have produced more sputum in terms of weight after ACBT + CCPT than after PEP therapy (Osman 2010). However, the PEP group had only one person, precluding formal analysis.

5. Oxygen Saturation

In the cross-over study, oxygen saturation was similar in the ACBT + CCPT and PEP groups (Osman 2010). However, the PEP group had only one person, precluding formal analysis.

6. Number of pulmonary exacerbations

The included studies did not assess this outcome.

ACBT versus oscillating devices or combinations

See Summary of findings 3.

Six studies (152 participants) compared ACBT with oscillating devices: one study (seven participants) compared ACBT with airway oscillating devices (AOD) (Milne 2004), one study (20 participants) compared ACBT with ACBT + AOD (Pryor 1994), one study (21 participants) compared ACBT with AOD + forced expiration (FE) (Pike 1999), one study (10 participants) compared ACBT with HFCC (Phillips 2004), one study (29 participants) compared ACBT + CCPT with AOD (flutter) and ACBT + CCPT to HFCC (HFCWO) (Osman 2010), and one study (65 participants) compared ACBT with two different AOD devices (Cornet and Flutter) (Pryor 2010). One parallel-designed study (Pryor 2010) and two cross-over studies with sufficient washout periods were included in the meta-analysis (Milne 2004; Phillips 2004). Three of the studies were of cross-over design but had insufficient washout periods (Osman 2010; Pryor 1994; Pike 1999). For one of these cross-over studies which had multiple treatment groups (of which ACBT + CCPT, AOD, and HFCC were just three), we obtained data from the study authors for results measured before the first cross-over and included these data in the meta-analysis (Osman 2010). Of the 29 participants in this study, five performed ACBT + CCPT before the first cross-over, two performed AOD before the first cross-over, and 15 performed HFCC before the first cross-over. For the remaining two cross-over studies with insufficient washout periods, we have contacted the study authors to obtain necessary information and are awaiting their response. If new data become available, they will be included in an update of the review.

Primary outcomes

1. Quality of life

The 12-month parallel study assessed quality of life using the Short Form-36 and the Chronic Respiratory Questionnaire (Pryor 2010). This study randomised 75 participants to one five treatment groups, which included ACBT (n = 15), Cornet (n = 15), and Flutter (n = 15). The authors reported no significant differences across the five treatment groups for either the physical domain (P = 0.99) or the mental domain (P = 0.27) of the Short Form-36, but both the physical and mental domains decreased after 12 months (P = 0.05 and P = 0.002, respectively). There were no significant differences at the end of the study across the five treatment groups for each of the four domains of the Chronic Respiratory Questionnaire: dyspnoea (P = 0.7), fatigue (P = 0.85), emotion (P = 0.39), and mastery (P = 0.82). The fatigue (P = 0.69), emotion (P = 0.39), and mastery (P = 0.37) domains showed no significant differences over time. However, the dyspnoea ratings improved among the Flutter (change of 1.3, moderate improvement) and ACBT (change of 0.7, small improvement) groups, but not among the Cornet group (change less than 0.5). We rated the certainty of the evidence comparing ACBT with oscillating devices in terms of quality of life as very low because of the high risk of bias, the imprecise results, and the suspicion of publication bias.

2. Personal preference

The two included studies had 17 participants, and each included a different therapy as a comparator. When comparing ACBT with AOD, one study reported that three participants (43%) preferred ACBT, two (29%) preferred AOD, and two (29%) had no preference between the two treatments (Milne 2004). When comparing ACBT with HFCC, one study reported that all 10 participants found ACBT comfortable, while six (60%) found HFCC uncomfortable (Phillips 2004). In addition, eight (80%) participants had difficulty clearing secretions using HFCC (Phillips 2004).

3. Mortality

None of the included studies assessed this outcome.

Secondary outcomes

1. Adverse events

None of the included studies assessed this outcome.

2. Exercise tolerance

One parallel study assessed exercise tolerance using a modified shuttle test (Pryor 2010). Mean baseline scores for the ACBT, Cornet, and Flutter groups were 1005.4 metres, 906.7 metres, and 1044.3 metres respectively. At the end of the study, there were no statistically significant differences across the five treatment groups (P = 0.52). The authors did not report any additional data on this outcome.

None of the cross-over studies reported on exercise tolerance.

3. Lung function

a. FEV_1 in L or % predicted

i. FEV_1 (L)

The parallel study reported that there was no significant difference in the final mean (SD) FEV_1 (L) between: the ACBT group, 1.94 L (0.80); the Cornet group, 1.90 (0.89) L; or the Flutter group, 2.43 (0.94) L (Pryor 2010). We estimated the mean between-group difference in final values between the ACBT and Cornet groups to be MD 0.04 L (95% CI -0.60 to 0.68) (Analysis 3.1) and between the ACBT and Flutter groups to be MD -0.49 L (95% CI -1.18 to 0.20) (Analysis 4.1).

The two cross-over studies with adequate washout periods provided no results for FEV_1 that were suitable for meta-analysis. In one study the authors reported a mean FEV_1 of 1.34 L after ACBT treatment and 1.38 L after AOD treatment (Milne 2004). In the second study, the authors reported a mean (range) FEV_1 of 1.55 L (0.87 to 2.84) after ACBT treatment and 1.48 L (0.73 to 2.76) after HFCC treatment (Phillips 2004). We have contacted both authors for additional information and are awaiting their responses.

In the cross-over study with first-arm data, raw data were provided for meta-analysis (Osman 2010). When comparing ACBT + CCPT with AOD, our analysis showed no significant difference between the two treatments, MD 0.11 L (95% CI -0.95 to 1.18) (Analysis 5.1). Similarly, when comparing ACBT + CCPT with HFCC, our analysis showed no significant difference between the two treatments, MD -0.06 L (95% CI -0.79 to 0.68) (Analysis 6.1).

ii. FEV_1 (% predicted)

In the cross-over study with first-arm data, raw data were provided for meta-analysis (Osman 2010). Our analyses showed no difference between interventions either when comparing ACBT + CCPT with AOD, MD 5.41% predicted (95% CI -15.62 to 26.44) (Analysis 5.2) or when comparing ACBT + CCPT to HFCC, MD 0.30% predicted (95% CI -15.63 to 16.23) (Analysis 6.2).

b. FVC in L or % predicted

i. FVC (L)

The 12-month parallel study reported that there were no significant differences in terms of FVC across the five arms (P = 0.54) (Pryor 2010).

The two cross-over studies with adequate washout periods provided no results on FVC that were suitable for meta-analysis. When comparing ACBT with AOD in one study, the authors reported a mean FVC of 2.98 L after ACBT treatment and 2.98 L after AOD treatment (Milne 2004). When comparing ACBT with HFCC in the second study, the authors reported a mean (range) FVC of 2.68 L (1.80 to 4.25) after ACBT treatment and 2.64 L (1.59 to 4.14) after HFCC treatment (Phillips 2004). We have contacted both authors for additional information and are awaiting their responses.

In the cross-over study with first-arm data, raw data were provided for meta-analysis (Osman 2010). Our analysis showed no significant difference between the two treatments either when comparing ACBT + CCPT with AOD, MD -0.47 L (95% CI -1.29 to 0.35) (Analysis 5.3) or when comparing ACBT + CCPT with HFCC, MD -0.36 L (95% CI -1.29 to 0.56) (Analysis 6.3).

ii. FVC (% predicted)

In the cross-over study with first-arm data, raw data were provided for meta-analysis (Osman 2010). Our analysis showed no significant difference between the two treatments either when comparing ACBT + CCPT with AOD, MD -6.49% (95% CI -22.81 to 9.84) (Analysis 5.4) or when comparing ACBT + CCPT with HFCC, MD -5.08% (95% CI -20.62 to 10.47) (Analysis 6.4).

4. Sputum

When comparing ACBT with AOD, our analysis showed no significant difference between the two treatments in terms of sputum weight, MD 1.56 g (95% CI -20.53 to 23.65) (Analysis 4.2). The study authors also reported no significant difference between the two treatments with regard to 24-hour sputum weights (Milne 2004). They presented 24-hour mean, SD, and the range of sputum weights post-treatment.

When comparing ACBT with HFCC, one study had a cross-over design with an adequate washout, but provided no relevant results on wet sputum weight for meta-analysis (Phillips 2004). The study authors noted that participants produced a significantly greater amount of sputum during treatment with ACBT than HFCC. Median sputum weight was 4.1 g during ACBT and 0.7 g during HFCC (P < 0.01). We have contacted the authors for additional information and are awaiting their response.

Our analysis showed no significant difference between the two treatments in terms of wet sputum weight when comparing ACBT + CCPT with AOD, MD 36.47 g (95% CI -16.71 to 89.65) (Analysis 5.5) or when comparing ACBT + CCPT with HFCC, MD 15.65 g (95% CI -39.70 to 71.00) (Analysis 6.5). The study authors noted that significantly more sputum was expectorated during ACBT + CCPT than with HFCC during treatment sessions and over a 24-hour period of time (including treatment), while the sputum expectorated at all other times (excluding treatment) was not statistically significant (Osman 2010).

5. Oxygen saturation

When comparing ACBT with HFCC, one study reported no significant differences in oxygen saturation (no further data reported) (Phillips 2004).

Our analysis of the first-arm data from the cross-over study (Osman 2010) showed no significant difference between the two treatments when comparing ACBT + CCPT with AOD, MD -0.81% (95% CI -2.26 to 0.65) (Analysis 5.6) or when comparing ACBT + CCPT with HFCC, MD -1.00% (95% CI -2.45 to 0.45) (Analysis 6.6).

6. Number of pulmonary exacerbations

None of the included studies assessed this outcome.

ACBT versus other breathing techniques

See Summary of findings 4.

One parallel study and two cross-over studies compared ACBT with other breathing techniques (Miller 1995; Osman 2010; Pryor 2010). The parallel study included 75 participants across five arms, two of which were ACBT and AD (Pryor 2010). We included one cross-over

study (n = 18) with a sufficient washout period in the meta-analysis comparing ACBT with AD (Miller 1995). The second cross-over study, with 29 participants, compared ACBT + CCPT with AD (Osman 2010). Although the study had an insufficient washout period, we obtained data from before the first cross-over from the study authors and included these data in the meta-analysis. The study consisted of multiple treatment groups of which ACBT + CCPT and AD were just two; of the 29 participants, five performed ACBT + CCPT before the first cross-over and five performed AD before the first cross-over.

Primary outcomes

1. Quality of life

The 12-month parallel study assessed quality of life using the Short Form-36 and the Chronic Respiratory Questionnaire (Pryor 2010). This study randomised 75 participants to one of five treatment groups, which included ACBT (n = 15) and AD (n = 15). The authors reported no significant differences across the five treatment groups for either the physical domain (P = 0.99) or the mental domain (P = 0.27) of the Short Form-36, but both the physical and mental domains decreased after 12 months (P = 0.05 and (P = 0.002, respectively). There were no significant differences at the end of the study across the five treatment groups for each of the four domains of the Chronic Respiratory Questionnaire: dyspnoea (P = 0.7), fatigue (P = 0.85), emotion (P = 0.39), and mastery (P = 0.82). The fatigue (P = 0.69), emotion (P = 0.39), and mastery (P = 0.37) domains showed no significant differences over time. However, there were small, clinically-important improvements in the dyspnoea ratings over the 12-month study period for the ACBT (change of 0.7) and the AD groups (change of 0.5). We rated the certainty of the evidence for quality of life when comparing ACBT with other breathing techniques as very low because of the high risk of bias, the imprecise results, and the suspicion of publication bias.

2. Personal preference

When comparing ACBT with AD, one cross-over study reported that nine participants (50%) preferred AD, while eight preferred (44%) ACBT (Miller 1995). One study participant (6%) had no preference between the two treatments.

3. Mortality

The included studies did not assess this outcome.

Secondary outcomes

1. Adverse events

The included studies did not assess this outcome.

2. Exercise tolerance

The parallel study assessed exercise tolerance using a modified shuttle test (Pryor 2010). Mean baseline scores for the ACBT and the AD groups were 1005.4 metres and 985.0 metres, respectively. At the end of the 12-month study period, there were no statistically significant differences across the five treatment groups (P = 0.52). The authors did not report any additional data on this outcome.

None of the cross-over studies reported on exercise tolerance.

3. Lung function

a. FEV_1 in L or % predicted

i. FEV_1 (L)

In the parallel study, there was no significant difference in the final mean (SD) FEV_1 between the ACBT group, 1.94 (0.80) L, and the AD group, 2.64 (1.22) L (Pryor 2010). We estimated the mean between-group difference in final values between the ACBT and AD groups to be -0.70 L (95% CI -1.49 to 0.09) (Analysis 7.1).

When comparing ACBT with AD, one study had a cross-over design with an adequate washout, but no results on FEV_1 suitable for meta-analysis were provided (Miller 1995). The study authors noted that there was no difference in pulmonary function between the two therapies. We have contacted the authors for additional information and are awaiting their response.

A further study compared ACBT + CCPT with AD (Osman 2010); our analysis showed no significant difference between the treatments, MD -0.51 L (95% CI -1.72 to 0.70) (Analysis 8.1).

ii. FEV_1 (%)

One study compared ACBT + CCPT with AD (Osman 2010); our analysis showed no significant difference between the treatments, MD -8.30% predicted (95% CI -35.22 to 18.62) (Analysis 8.2).

b. FVC in L or % predicted

i. FVC (L)

The 12-month parallel study reported that there were no significant differences in terms of FVC across the five arms (P = 0.54) (Pryor 2010).

When comparing ACBT with AD, one included study had a cross-over design with an adequate washout, but no results on FVC suitable for meta-analysis were provided (Miller 1995). The study authors noted that there was no difference in pulmonary function between the two therapies, yet more participants had improved FVC with ACBT than AD. Results for FVC were presented as the number of tests which showed an improvement. We have contacted the authors for additional information and are awaiting their response.

A further study compared ACBT + CCPT with AD (Osman 2010); our analysis showed no significant difference between the treatments, MD -0.85 L (95% CI -2.13 to 0.44) (Analysis 8.3).

i. FVC (%)

One study compared ACBT + CCPT with AD (Osman 2010); our analysis showed no significant difference between the treatments, MD -11.02% predicted (95% CI -32.84 to 10.80) (Analysis 8.4).

4. Sputum

Two studies reported on this outcome (Miller 1995; Osman 2010). When comparing ACBT with AD, our analysis of data from the Miller study showed no significant difference in sputum weights between the two therapies, MD -0.40 g (95% CI -3.93 to 3.13) (Analysis 7.2). The study authors presented the MD and standard error (SE) between the two treatments and also noted that there was no significant difference in sputum weights between the two therapies (Miller 1995).

In the second study, Osman compared ACBT + CCPT with AD (Osman 2010). Our analysis showed no significant difference in sputum

weights between the two therapies, MD -3.52 g (95% CI -68.49 to 61.46) (Analysis 8.6).

There were no statistically significant differences between treatments in terms of sputum weights.

5. Oxygen saturation

When comparing ACBT with AD, one cross-over study with an adequate washout noted that there was no difference in mean oxygen saturation between the two therapies, but provided no results which we could enter into a meta-analysis (Miller 1995). We have contacted the authors for additional information, and are awaiting their response.

One study compared ACBT + CCPT with AD (Osman 2010). Our analysis showed no significant difference in oxygen saturation between the two therapies, MD -1.08 % (-3.17 to 1.01) (Analysis 8.5).

6. Number of pulmonary exacerbations

The included studies did not assessed this outcome.

ACBT versus exercise or versus ACBT plus exercise

See Summary of findings 5.

One cross-over RCT compared ACBT with exercise (Bilton 1992), and one parallel RCT compared ACBT to ACBT plus exercise (Gungor 2021). Bilton 1992 included 18 participants and compared ACBT with exercise. This study had a cross-over design with an insufficient washout period; therefore, we did not include it in the meta-analysis. We have contacted study authors to obtain necessary information and are awaiting their response. If new data become available, we will include these in a future update of the review. In the parallel study, the participants received the intervention for six weeks, but were followed for six months. The study randomised 22 participants to either ACBT plus postural exercise or ACBT alone (Gungor 2021). Investigators have reported their results as a journal article and posted results on their clinical trial registry entry, but the reporting of these results is inconsistent between the two resources. We have primarily presented the results reported in the journal article, and noted when we report results that were extracted from the clinical trial registry entry.

Primary outcomes

1. Quality of life

One study (22 participants) assessed quality of life using the CFQ-Revised and scores did not change significantly from baseline over the course of the study (Gungor 2021). Median scores for the emotional function and treatment difficulties subdomains were not statistically significant between groups at six weeks (P = 0.093 on the emotional function subdomain and P = 0.062 on the treatment difficulties subdomain) or six months (P = 0.431 on the emotional function subdomain and P = 0.579 on the treatment difficulties subdomain). The study did not report on the between-group differences for the other subdomains. These measurements differ from the results on ClinicalTrials.gov which reports the mean (SE) score of all domains for each group. We rated our certainty of the evidence as very low because of our concerns with risk of bias, imprecision, and publication bias.

2. Personal preference

The included parallel study did not address this outcome (Gungor 2021).

3. Mortality

The included parallel study reported no deaths in either treatment group during the six months of follow-up (Gungor 2021). Mortality data were only reported in the clinical trials registry entry.

Secondary outcomes

1. Adverse events

The included parallel study reported no adverse events in either treatment group during the six months of follow-up (Gungor 2021). We rated our certainty of the evidence as very low because of our concerns with risk of bias and our very serious concerns with the imprecise results.

2. Exercise tolerance

The included parallel study used the modified shuttle test to assess exercise tolerance (Gungor 2021). The median distance covered by participants in both groups increased from baseline over the course of the study, but the differences in median distances between groups were not statistically significant at six weeks (990 m in the ACBT + exercise group versus 760 m in the ACBT alone group) or at six months (1235 m in the ACBT + exercise group versus 960 m in the ACBT alone group). These measurements differ from the results on ClinicalTrials.gov which reports the mean (SE) distance walked.

3. Lung function

a. FEV_1 in L or % predicted

i. FEV_1 % predicted

The median FEV_1 % predicted did not change significantly in either group during follow-up and there were no differences seen between groups at either six weeks (90.5% predicted in the ACBT + exercise group versus 86% predicted in the ACBT alone group) or six months (88.5% predicted in the ACBT + exercise group versus 95.5% predicted in the ACBT alone group; P = 0.873) (Gungor 2021). These measurements differ from the results on ClinicalTrials.gov which reports the mean (SD) values at each time point. We rated our certainty of the evidence as very low because of our concerns with the risk of bias and our very serious concerns with the imprecise results.

b. FVC in L or % predicted

The mean FVC % predicted did not change significantly in either group during follow-up and there were no differences seen between groups at either six weeks or six months (P = 0.749) (Gungor 2021). These measurements differ from the results on ClinicalTrials.gov which reports the mean (SD) values at each time point. We rated our certainty of the evidence as very low because of our concerns with the risk of bias and our serious concerns with the imprecise results.

4. Sputum

The included study did not address this outcome.

5. Oxygen saturation

The included study did not address this outcome.

6. Number of pulmonary exacerbations

One participant in the ACBT only group (1 out of 11 people; 9.1%) was hospitalised due to an exacerbation and was discontinued from the trial (Gungor 2021). There were no pulmonary exacerbations in the ACBT plus postural exercise group. We rated our certainty of the evidence as very low because of our concerns with risk of bias and our very serious concerns with the imprecise results.

ACBT versus other therapy

Five studies (106 participants) compared ACBT with other therapies. One study (26 participants) compared ACBT with ACBT + non-invasive ventilation (NIV) (Holland 2003), one study (16 participants) compared ACBT with ACBT + pressure support ventilation (PSV) (Fauroux 1999), one study (20 participants) compared ACBT with the test of incremental respiratory endurance (TIRE) (Howard 2000), one study (24 participants) compared ACBT with coughing (Steven 1992), and one study (20 participants) compared ACBT + CCPT with RIM (Chatham 2004). All five studies had a cross-over design with insufficient washout periods and hence none of these were included in the meta-analyses. We have contacted study authors to obtain necessary information and are awaiting their response. If new data become available they will be included in an update of the review.

DISCUSSION

Summary of main results

This review compared ACBT with other airway clearance therapies. Following searching and screening, we included 22 studies in the review. Of these, we were only able to include eight in the analyses; the remaining 14 studies are cross-over studies with inadequate washout periods. Due to the risk of a carry-over effect in cross-over studies, we only used data from the period before the first cross-over. When possible we have contacted the study authors and in some cases are still awaiting their responses. Of the eight studies that are included in the analysis, ACBT was compared with eight different therapies: AD, AOD, HFCC, PEP, ACBT + CCPT, CCPT + respiratory exercises, CCPT, and ACBT + postural exercise.

For each of the primary outcomes of this review (quality of life, personal preference, and mortality), we considered the certainty of the evidence to be low or very low. Each comparison for the primary outcomes was addressed by only one or two studies with either a high or an unclear risk of bias, imprecise results, and limited reporting of the study results. One of these studies was available only as a clinical trials registry entry. We were unable to assess the certainty of the evidence for many of the outcomes for many of the comparisons because of a lack of data.

ACBT versus CCPT

Six randomised studies (189 participants) were eligible for this comparison (Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007; Osman 2010; Pryor 1979; Reisman 1988; Webber 1985). None of the studies evaluated any of the primary outcomes. We found no difference in the effects on FEV_1 and FVC % predicted between ACBT and CCPT (Hristara-Papadopoulou 2005; Osman 2010; Reisman 1988). One study reported similar sputum weight in both groups (Osman 2010), and two studies reported similar levels of oxygen saturation in both groups (Hristara-Papadopoulou 2005; Osman 2010). There were no differences in the number of pulmonary exacerbations between people using ACBT and people using CCPT (low-certainty evidence) (Reisman 1988). None of the studies reported on adverse events or exercise tolerance.

ACBT versus PEP

Five studies (110 participants) are included in this comparison (Hofmeyr 1986; Kofler 1994; Mortensen 1991; Osman 2010; Pryor 2010).

We found no evidence of an effect on quality of life when comparing ACBT to PEP mask therapy (very low-certainty evidence); no study reported on the other two primary outcomes. One study found no difference between therapies in exercise tolerance using a modified shuttle test (Pryor 2010). We found no difference in the effects on FEV_1 and FVC % predicted (Osman 2010; Pryor 2010). In one study participants may have produced more sputum ACBT + CCPT than after PEP therapy, but there was only a single participant in the PEP group precluding formal analysis (Osman 2010). The same study reported similar levels of oxygen (Osman 2010). No study reported on adverse events or pulmonary exacerbations.

ACBT versus oscillating devices

Six studies (152 participants) compared ACBT with oscillating devices (Milne 2004; Osman 2010; Phillips 2004; Pike 1999; Pryor 1994; Pryor 2010).

In one study, there were no differences between the five treatment groups in any of the four domains of the Chronic Respiratory Questionnaire (very low-certainty evidence) (Pryor 2010). Two studies reported on personal preference after two days of treatment, but found no clear preference for any individual therapy (Milne 2004; Phillips 2004). One study found no difference between therapies in exercise tolerance using a modified shuttle test (Pryor 2010). Four studies assessed lung function and found no difference between treatments (Milne 2004; Osman 2010; Phillips 2004; Pryor 2010). Three studies did not identify any differences between groups in expectorated sputum (Milne 2004; Osman 2010; Phillips 2004); two of these studies additionally reported no differences in oxygen saturation (Osman 2010; Phillips 2004). No study reported mortality, adverse events or pulmonary exacerbations.

ACBT versus other breathing techniques

Three studies compared ACBT with other breathing techniques (Miller 1995; Osman 2010; Pryor 2010).

One study reported no differences between the five treatment groups in any of the four domains of the Chronic Respiratory Questionnaire (very low-certainty evidence) (Pryor 2010). A second study found no clear preference for a particular technique in a comparison of ACBT and AD (Miller 1995). Only one study reported on exercise tolerance and found no difference between treatments (Pryor 2010). None of the three studies in this comparison found any difference between groups in any measure of lung function (Miller 1995; Osman 2010; Pryor 2010). Two studies reported sputum weight and oxygen saturation; neither found any difference between treatment groups for either outcome (Miller 1995; Osman 2010). No study assessed mortality, adverse events or pulmonary exacerbations.

ACBT versus exercise

Two studies compared ACBT with exercise (Bilton 1992; Gungor 2021). One study had a cross-over design with an insufficient washout period, so we have not included the results in our analysis (Bilton 1992). We have concerns surrounding the results of the second study, which seem to differ between those published online at ClinicalTrials.gov and the published paper (Gungor 2021).

The study found no difference in quality of life but did not report personal preference (Gungor 2021). There were no deaths or adverse events in either treatment arm. The study also did not find any differences in any measure of lung function, although data were reported as median (IQR) in the published paper and mean (SD) on the trials registry. The study did not report on sputum or oxygen levels. One participant out of 11 in the ACBT-only group was hospitalised due to an exacerbation, but there were no pulmonary exacerbations in the ACBT plus postural exercise group (Gungor 2021).

ACBT versus other therapy

Five studies (106 participants) compared ACBT with other therapies: with ACBT + non-invasive ventilation (NIV) (Holland 2003), with ACBT + pressure support ventilation (PSV) (Fauroux 1999), with the test of incremental respiratory endurance (TIRE) (Howard 2000), with coughing (Steven 1992), and with RIM (Chatham 2004). All five studies had a cross-over design with insufficient washout periods and hence none of these were included in our analysis.

Overall completeness and applicability of evidence

This review includes analyses and a summary of 22 studies (eight studies in the quantitative analysis). The studies had different intervention groups, thus they could not be compared with each other. Two of the therapies of interest (hPEP and RIM) were not included as interventions in any of the studies. We included studies that assessed children and adults as well as those who have been hospitalised for exacerbations and those with stable conditions. Of the eight studies that were included in our analyses, three followed participants for at least one year (Hristara-Papadopoulou 2005; Pryor 2010; Reisman 1988); and four followed participants for less than one week (Miller 1995; Milne 2004; Osman 2010; Phillips 2004). All the studies included fewer than 100 participants.

Quality of the evidence

We were unable to assess the certainty of the evidence for many of the outcomes for many of the comparisons because of a lack of data. Overall, we rated the certainty of the evidence as low or very low. We downgraded the certainty because of concerns regarding study limitations, imprecise results, and suspected publication bias. Many of the studies were of short duration (less than one week), limiting our ability to draw conclusions about the effectiveness of the long-term use of ACBT (Summary of findings 1; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5).

With regards to sequence generation, allocation concealment, blinding (of outcome assessors), and washout periods, the majority of the studies are associated with an unclear risk of bias (Figure 3). A total of 20 out of the 22 studies reported that the participants were randomly allocated, but the methods of randomisation were not defined, thus the risk of bias for sequence generation is unclear in these studies. In the remaining two studies, there was a low risk of bias for sequence generation. Allocation concealment was reported in two of the 22 studies, and the remaining studies are associated with an unclear risk of bias for allocation concealment. Blinding of the outcome assessors was observed in five studies and was unclear in the remaining 17 studies (Figure 2). A washout period was not reported in 14 of the 19 randomised cross-over studies, thus they were associated with a unclear risk of bias. One of the randomised cross-over studies clearly did not have a washout period, thus it had a high risk of bias. Four of the 19 randomised cross-over studies had washout periods of at least a day, which we regarded as adequate and thus they were associated with low risk of bias (Figure 2).

In regards to intention-to-treat analysis, adequate follow up, selective reporting, and compliance assessment, the majority of the studies are associated with a low risk of bias (Figure 3). An intention-to-treat analysis was used in 10 out of the 22 studies. Follow-up was adequate with a of low risk of bias in 13 of the 22 studies. With regards to selective reporting, 16 out of the 22 studies had a low risk of bias, and we assessed the risk of bias due to compliance as low in 11 of the 22 studies (Figure 2).

Potential biases in the review process

It is unlikely that we have missed any studies that address ACBT. We have hand-searched all reference lists in the studies identified from the electronic searches, as well as the included studies presented both as full text articles and conference abstracts. In addition, because of the renaming of FET as ACBT in 1990 (Webber 1998), the electronic search included both terms (FET and ACBT) to capture all relevant studies. Also, all study authors that were contacted for additional information were sent a list of the studies included in the review and asked if they could provide the references of additional studies they thought may be relevant.

Bias may have been introduced because we only included studies of FET if FET was reported as containing all of the components of ACBT. As stated in the Types of interventions section, we used the definitions of the ACBT components as described by the Cystic Fibrosis Foundation and the Cystic Fibrosis Trust as standards in the process (Cystic Fibrosis Foundation 2023; Cystic Fibrosis Trust 2020b). Of the 53 excluded studies, seven were excluded solely because FET was not reported as including all of the components of ACBT (ACTRN12619000224123; Andreasson 1987; Falk 1984; Gursli 2017; NCT03078127; RBR-5g9f6w; Sutton 1983).

Agreements and disagreements with other studies or reviews

Consistent with previous Cochrane Reviews on airway clearance therapies for people with cystic fibrosis (Burnham 2021; Main 2005; McIlwaine 2019; Morrison 2020), we did not identify any advantage of ACBT compared to other airway clearance therapies.

AUTHORS' CONCLUSIONS

Implications for practice

There is little evidence to support or reject the use of active cycle of breathing technique (ACBT) over any other airway clearance therapy in people with cystic fibrosis (CF). It is our opinion that ACBT is comparable with other therapies in outcomes such as personal

preference, exercise tolerance, lung function, sputum weight, oxygen saturation, and number of pulmonary exacerbations.

Implications for research

The majority of studies in this review were cross-over studies with insufficient washout periods, increasing the risk of carry-over effects. More randomised controlled studies comparing ACBT with other airway clearance therapies are needed. Because of the concern of carry-over effects, cross-over study authors should allow adequate washout periods between treatments.

The majority of included studies had immediate outcomes, as defined by intervention durations of less than one day. Long-term studies with interventions greater than one month are needed to more adequately assess the effects of the interventions. Such studies may provide more data for outcomes that are important to people with CF, including quality of life and personal preference.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Bilton 1992

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant used 4 treatment regimens in randomised order over 4 consecutive days. The treatments were ACBT, exercise, exercise followed by ACBT, and ACBT followed by exercise. Each day consist of 2 identical treatment sessions with each session lasting 20 minutes. Usual medications were unchanged.
Participants	18 enrolled; 18 evaluated; 13 male (72.7% male).

Bilton 1992 *(Continued)*

	Age: mean (21 years); median (NR); SD (NR); range (16 to 34 years). Inclusion criteria: NR. Exclusion criteria: NR. Characteristics: all participants were infected with *Pseudomonas aeruginosa.*
Interventions	ACBT: thoracic expansion exercise, breathing control and the FET. The intervention was conducted in a gravity-assisted position for 20 minutes. Exercise: cycling at 60% VO_2 max for 20 minutes. Exercise followed by ACBT: exercise for 10 minutes followed by 10 minutes of ACBT. ACBT followed by exercise: ACBT for 10 minutes followed by 10 minutes of exercise.
Outcomes	Outcome measures: participant preference, lung function, sputum weight. Additional outcomes: perceived effectiveness.
Notes	Funding: D. Bilton and J. Abbott were supported by the Cystic Fibrosis Trust.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"The subjects were studied on four consecutive days. The study period contained four treatment days. The order of these was randomly allocated to each patient."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Personnel	High risk	Not possible.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	"All 18 patients completed the study."
Compliance/ adherence assessed?	Unclear risk	Not reported.
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Unclear risk	No description of a washout period.

Chatham 2004

Study characteristics	
Methods	Study Type: RCT (cross-over). Each participant was randomly allocated to alternate day treatment for 4 days. Treatments were applied once a day. The 2 treatment regimens used were CCPT + ACBT and RIM. Inhaled or nebulised treatments, or both, were administered before all study interventions and usual medications were unchanged. All participants also received intravenous antibiotics for worsening respiratory symptoms.
Participants	20 enrolled; 20 evaluated; 10 male (50% male). Age: mean (NR); median (NR); SD (NR); range (NR). Inclusion criteria: adult participants. Exclusion criteria: NR. Characteristics: all 20 participants were infected with *Pseudomonas aeruginosa*.
Interventions	CCPT + ACBT: postural drainage (with percussion administered by a physiotherapist) and FET. There were periods of relaxed breathing and thoracic expansion exercises as described in ACBT. The session durations were 30 minutes. This intervention was identified as the standardised physiotherapy. RIM: maximum of 36 manoeuvres. Every 6 inspiratory efforts was accompanied by a short rest interval (maximum of 1 minute). The session duration varied among the participants. The RIM protocol required the use of the RT2 hand-held manometer.
Outcomes	Outcome measures: sputum weight. Additional outcomes: concentration of protein, concentration of interleukin-8 (IL-8), concentration of HNE, FFM.
Notes	FEV_1 % predicted results were provided for the group whose alternate day treatment began with CCPT + ACBT and for the group whose alternate day treatment began with RIM. Results were not provided for each intervention group separately. Funding: A.A. Ionescu and L.S. Nixon were supported by CF Trust UK project grants. Other support was from the Astra Foundation UK and GlaxoSmithKline UK.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Participants were randomly allocated to alternate day treatment ....."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as sputum weight.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for subjective outcomes, such as sputum weight.

Chatham 2004 *(Continued)*

Blinding (performance bias and detection bias) Outcome Assessors	Low risk	"The laboratory researcher was blind to the treatment administered to patients."
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	All participants were accounted for.
Compliance/ adherence assessed?	Low risk	"All treatment sessions were performed under supervision..."
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Unclear risk	No description of a washout period.

Fauroux 1999

Study characteristics	
Methods	Study Type: RCT (cross-over). Each participant used 2 treatment regimens in randomised order over 2 days. The treatments were FET and FET + PSV. Each day consisted of 2 different treatment sessions with each session lasting 20 minutes. Usual medications were unchanged.
Participants	16 enrolled; 16 evaluated; 7 male (43.8% male). Age: mean (13 years); median (NR); SD (4 years); range (6 to 18 years). Inclusion criteria: age greater than 6 years; clinically stable. Exclusion criteria: NR. Characteristics: 9 participants were colonized with *Pseudomonas aeruginosa*, 7 were colonised with *Burkholderia cepacia*, 6 were on inhaled bronchodilators, 7 were on corticosteroids, 11 were on rhDNase, 1 participant was on a lung transplant list and had been receiving PSV for the previous 6 years.
Interventions	FET: As described in Pryor 1979. FET + PSV: FET manoeuvres with PSV applied during inspiration and resting periods. PSV required the use of a nasal mask and the pressure support generator ARM25.
Outcomes	Outcome measures: participant preference, lung function, sputum weight, oxygen saturation. Additional outcomes: heart rate; respiratory rate; maximal expiratory pressure; maximal inspiratory pressure; PEF; FEF at 50%, 25% and 25-75%; airway resistance % predicted value.
Notes	Results were stratified by pulmonary disease severity. Funding: Association Francaise de Lutte contre la Mucoviscidose (AFLM).

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"During the study, each patient received two chest physiotherapy sessions in random order on two different days..."

Fauroux 1999 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	"All the patients completed the protocol."
Compliance/ adherence assessed?	Low risk	A physiotherapist supervised the sessions.
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Unclear risk	No description of a washout period.

Gungor 2021

Study characteristics	
Methods	Study type: RCT. Parallel design. Duration: 6 weeks. Location: single centre in Turkey.
Participants	22 participants enrolled; 19 analysed; 11 male (57.8% male). Age, mean (SD): 9.36 (2) years). Inclusion criteria: aged 6 to 14 years old, FEV_1 > 30% Exclusion criteria: presence of cor pulmonale, spinal fracture history, currently under intravenous medication, severe gastroesophageal reflux.
Interventions	Each intervention was applied by a therapist once per week for 6 weeks. ACBT: 3 phases - breathing control, chest expansion exercise, and huff coughing. ACBT + postural exercise: ACBT as above plus postural exercise, which included thoracic vertebra mobilization, pectoral stretching, scapula and thoracic extension strengthening, and core stability exercises.

Gungor 2021 *(Continued)*

Outcomes	Outcome measures: exercise tolerance (modified shuttle test), quality of life (CFQ-R), FEV_1, FVC, mortality, adverse events, pulmonary exacerbations. Additional measures: postural stability, spinal deformity, FEV_1/FVC, PEF.
Notes	Funding: Authors received no financial support and declared no conflicts of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not currently available.
Allocation concealment (selection bias)	Low risk	"The patients ... were equally randomized into two groups according to the sealed opaque envelope system with blocking."
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as quality of life. The lack of blinding may have less of an effect on objective outcomes, such as lung function and mortality.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as quality of life. The lack of blinding may have less of an effect on objective outcomes, such as lung function and mortality.
Blinding (performance bias and detection bias) Outcome Assessors	Low risk	All evaluations were performed by a blinded independent rehabilitation specialist.
Selective reporting (reporting bias)	High risk	There are major discrepancies between the outcomes reported in the study protocol, the NCT registry entry, and the paper. For instance, FVC is mentioned in the paper, but not in the study protocol or NCT registry entry.
Adequate follow up?	High risk	In ACBT + postural exercise group, 1/11 participants (9%) was lost to follow-up. In the ACBT only group, 1/11 participants (9%) was lost to follow-up and 1/11 (9%) was hospitalised.
Compliance/ adherence assessed?	Unclear risk	Not currently available.
Intention-to-treat?	High risk	Study used a per-protocol analysis.

Hofmeyr 1986

Study characteristics

Methods	Study type: RCT (cross-over). Each participant used 3 treatment regimens in randomised order over 3 consecutive days. The treatments were FET (gravity-assisted position), PEP + FET (gravity-assisted position) and PEP + FET (sitting position). Each regimen was used for a 24-hour period which included 4 treatment sessions. The mean time for each session was 21 minutes (range:10 to 31). The mean time for each intervention on a treatment day was 83 minutes/day (range: 59 to 105). Bronchodilators were continued before physiotherapy if this was a part of the participants' normal regimen. 15 participants were receiving intravenous antibiotic treatment and 3 were receiving oral antibiotic treatment.

Hofmeyr 1986 *(Continued)*

Participants	18 enrolled; 18 evaluated; 12 male (66.7% male). Age: mean (22.5 years); median (NR); range (13 to 37 years). Inclusion criteria: producing at least 20g of sputum in 24 hours; fit enough to carry out own chest physiotherapy. Exclusion criteria: participants with pneumothorax or a history of pneumothorax. Characteristics: all 18 participants had an exacerbation of their bronchopulmonary infection.
Interventions	FET (gravity-assisted position): 4 deep inspirations with relaxed expiration, breathing control, FET, and coughing as needed. PEP + FET (gravity-assisted position): 6 breaths with PEP, breathing control, FET, and coughing as needed. PEP required the use of a PEP mask, one-way valve, and manometer. PEP + FET (sitting position): 6 breaths with PEP, breathing control, FET, and coughing as needed. PEP required the use of a PEP mask, one-way valve, and manometer.
Outcomes	Outcome measures: lung function, sputum weight, oxygen saturation.
Notes	The lowest and highest points of SaO_2 were provided. Funding: Cystic Fibrosis Research Trust

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Each patient used the three treatment regimens in randomised order over three consecutive days..."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	All participants were accounted for.
Compliance/ adherence assessed?	Unclear risk	Not discussed.
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Unclear risk	No description of a washout period.

Holland 2003

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant used 2 treatment regimens in randomised order over 2 consecutive days. The treatments were ACBT and ACBT + NIV. Each day consisted of 2 treatment sessions with each session lasting 30 minutes. Bronchodilator and rhDNase were used on study days. The study had a run-in period of 2 days.
Participants	27 enrolled; 26 evaluated; 21 male (80.8% male). Age: mean (27 years); median (NR); SD (6.4 years); range (NR). BMI mean: 20.6 kg/m^2. Inclusion criteria: aged 18 years or over; admitted to a university hospital with an acute exacerbation of CF; producing more than 20 g sputum in 24 hours. Exclusion criteria: required continuous NIV, decreased level of consciousness, pneumothorax, symptomatic gastro-oesophageal reflux requiring modification of treatment, major haemoptysis (200 mL or more over 24 hours), oxygen saturation less than 90% on room air at study entry, started home antibiotic treatment before day 5 of admission. Characteristics: 26 participants were infected with *Pseudomonas aeruginos*a, none were colonized with *Burkholderia cepacia*.
Interventions	ACBT: a sequence of 6 thoracic expansion exercises, breathing control, 6 thoracic expansion exercises, breathing control, FET, and coughing as needed. ACBT + NIV: ACBT with NIV administered during the entire duration of the treatment. NIV required the use of a nasal mask and bilevel device.
Outcomes	Outcome measures: participant preference; lung function; sputum weight; oxygen saturation. Additional outcomes: inspiratory and expiratory muscle strength; breathlessness.
Notes	Funding: Not described.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"A within-subject cross-over design was used with subjects randomly allocated to treatment order."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.

Holland 2003 *(Continued)*

Blinding (performance bias and detection bias) Outcome Assessors	Low risk	"All measurements were obtained by an independent data collector who was blinded to treatment order."
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	One of 27 participants withdrew at the start of the study because of pain experienced during respiratory muscle testing. The loss to follow up was 3.70% (< 10%).
Compliance/ adherence assessed?	Unclear risk	Not reported.
Intention-to-treat?	High risk	Participants lost to follow up were not included in the analysis.
Washout?	Unclear risk	No description of a washout period.

Howard 2000

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant was randomly allocated to alternate day treatment for 2 days. The 2 treatment regimens used were ACBT and TIRE. There was a run-in period of 10 days.
Participants	20 enrolled; number evaluated (NR); gender split (NR). Age: Details NR. Inclusion criteria: NR. Exclusion criteria: NR. Characteristics: 5 participants had FEV_1 less than 30% predicted, 8 participants had FEV_1 30% to 70% predicted, 7 participants had FEV_1 > 70% predicted.
Interventions	ACBT: physiotherapy using ACBT. TIRE: TIRE at 80% of sustained maximum inspiratory pressure until failure was indicated by a computer.
Outcomes	Outcome measures: sputum weight.
Notes	Funding: Not described.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"...patients were randomly allocated..."
Allocation concealment (selection bias)	Unclear risk	Not discussed.

Howard 2000 *(Continued)*

Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as sputum weight.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as sputum weight.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Unclear risk	Not reported.
Adequate follow up?	Unclear risk	Not reported.
Compliance/ adherence assessed?	Unclear risk	Not reported.
Intention-to-treat?	Unclear risk	Unclear. Only available as an abstract.
Washout?	Unclear risk	No description of a washout period.

Hristara-Papadopoulou 2005

Study characteristics	
Methods	Study type: RCT. Cross-over design with 2-month washout period. Duration: 1 year. Location: Greece. Each participant used 2 treatment regimens in a randomised order for 1 year, with a 2-month washout period.
Participants	30 children and young people with CF enrolled; 30 evaluated; 16 male (53% male). Age, mean (SD): 13.13 (4.01) years. Characteristics: all 20 participants were infected with *Pseudomonas aeruginosa*.
Interventions	ACBT: 1 breath control cycle, breast expansion, and forced exhale; includes a 3-month learning period; performed under the supervision of physiotherapists or parents for 25 minutes/day. CCPT: positioning, tremors, pressings or vibrations, and cough applied by physiotherapists or parents for 15 minutes/day.
Outcomes	Outcome measures: FEV_1, FVC, SaO_2 Additional outcomes: Maximum expiratory flow rate, FEF_{50}
Notes	We believe that the author of this paper is actually Alexandra Hristara-Papadopoulou and there was an error in the citation. It is highly unlikely that there are two people working in the same department in the same institution who have the same name except for a single letter.

Hristara-Papadopoulou 2005 *(Continued)*

Funding: Not described.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported in study.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function and oxygen saturation.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not reported in study.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Unclear risk	Not reported in study.
Compliance/ adherence assessed?	Unclear risk	Not reported in study.
Intention-to-treat?	Unclear risk	Not reported in study.
Washout?	Low risk	2 months.

Hristara-Papadopoulou 2007

Study characteristics

Methods	Study type: RCT. Cross-over design. Each participant used 2 treatment regimens in randomised order for 3 months. Duration: 3 months. Location: single centre in Greece.
Participants	35 participants enrolled; 28 evaluated; 14 male (40% male). Age, mean (SD): 12.4 (3.9) years; range 8 to 20 years. Inclusion and exclusion criteria: NR. Characteristics: all participants were stable and did not present with exacerbations of symptoms.

Hristara-Papadopoulou 2007 *(Continued)*

Interventions	ACBT: diaphragmatic breathing (5 to 10 times), thoracic breathing (4 times deep breathing + 5 seconds of holding breath), percussion, pressure vibration, FET, or huffing, cough, and active respiratory exercises (unilateral and bilateral, 10 minutes). The intervention was performed in a drainage position. Each session lasted 55 minutes. CCPT with respiratory exercises: PD, percussion, pressure-vibration, cough and active respiratory exercises (unilateral and bilateral, 10 minutes). Each session lasted 60 minutes.
Outcomes	Outcome measures: sputum volume. Additional outcomes: sputum colour
Notes	The same author team undertook the earlier year-long study in the same institution using the same comparison in children with CF. We do not know whether some children who participated in the earlier study also participated in this later study, potentially being counted twice in the results. Funding: Not described.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"All children received the same 2 methods of respiratory physiotherapy ... in random order of respiratory physiotherapy for approximately 3 months" States random order but does not state how sequence was generated.
Allocation concealment (selection bias)	Unclear risk	Not discussed..
Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as sputum volume.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as sputum volume.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed
Selective reporting (reporting bias)	Low risk	All outcomes outlined in methods are reported in results.
Adequate follow up?	High risk	Study does not account for the missing 7 participants.
Compliance/ adherence assessed?	Unclear risk	Not discussed.
Intention-to-treat?	Unclear risk	Not discussed..
Washout?	Unclear risk	No description of a washout period.

Kofler 1994

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant was randomly allocated to alternate 4-month treatments for 8 months. The 2 treatment regimens used were ACBT and PEP. Each group followed conventional therapy for CF (including antibiotics and enzymes).
Participants	33 enrolled; 23 evaluated; gender split (NR). Age: NR. Inclusion criteria: NR. Exclusion criteria: NR. Characteristics: NR.
Interventions	ACBT: no description. PEP: no description.
Outcomes	Outcome measures: participant preference, lung function.
Notes	Funding: Not described.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Paper states "children with cystic fibrosis were randomly assigned".
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Unclear risk	Not discussed.
Adequate follow up?	High risk	10 of 33 CF children (> 10%) did not complete the program, and there was no description of those participants lost to follow up. The loss to follow up was 30.30% (> 10%). Only available as an abstract.
Compliance/ adherence assessed?	Unclear risk	Not reported.

Kofler 1994 *(Continued)*

Intention-to-treat?	High risk	Participants lost to follow up were not included in the analysis. Only available as an abstract.
Washout?	Unclear risk	No description of a washout period.

Miller 1995

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant used 2 treatment regimens in randomised order over 2 days. The treatments were ACBT and AD. Each day consisted of 2 identical treatment sessions with each session lasting 30 minutes. There was a 1-week washout period between the 2 treatment days. Pre-treatment included nebulised bronchodilators for some participants, and saline for others.
Participants	18 enrolled; 18 evaluated; 10 male (55.6% male) Age: mean (NR); median (NR); SD (NR); range (11 to 32 years). Inclusion criteria: age greater than or equal to 11 years; clinically stable participants not receiving intravenous antibiotics. Exclusion criteria: NR. Characteristics: all 18 participants were clinically stable at the time of the study and not receiving intravenous antibiotics.
Interventions	ACBT: a postural drainage regimen was performed with ACBT (including breathing control, deep breathing, and forced expirations). AD: breathing control in conjunction with cough suppression to mobilise mucus. After multiple cycles, sputum was expectorated. The position was either sitting or supine.
Outcomes	Outcome measures: participant preference; lung function; sputum secretion; oxygen saturation. Additional outcomes: heart rate; xenon-133 gas ventilation study.
Notes	Funding: MedicAid provided the Optimist nebulisers.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Eighteen patients with cystic fibrosis took part in a randomised two-day cross-over trial."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may

Miller 1995 *(Continued)*

		have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	All participants were accounted for.
Compliance/ adherence assessed?	Unclear risk	Not reported.
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Low risk	1-week washout period.

Milne 2004

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant was randomised to alternate-day treatment on 2 days. Each day consist of 2 identical treatment sessions with each session lasting 15 minutes. There was a 1-day washout period between the 2 treatment days. The 2 treatment regimens used were ACBT and AOD (flutter). Nebulisation therapy was administered before all study interventions.
Participants	7 enrolled; 7 evaluated; 4 male (57.1% male). Age: mean (28 years); median (NR); SD (NR); range (16 to 42 years). Inclusion criteria: participants admitted for a course of intravenous antibiotics, participants old enough to perform lung function test. Exclusion criteria: pneumothorax or frank haemoptysis; participant admitted for terminal care. Characteristics: NR.
Interventions	ACBT: thoracic expansions; controlled breathing; FET; and coughing in a sitting position. AOD (flutter): the device was place in the participant's mouth. Participants exhaled 10 to 15 times through the flutter and then performed FET. AOD required the use of a flutter device.
Outcomes	Outcome measures: participant preference; lung function; sputum weight.
Notes	Funding: Not described

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Participants were randomised to two groups..."

Milne 2004 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	All participants were accounted for.
Compliance/ adherence assessed?	Low risk	"The researcher supervised the physiotherapy sessions.".
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Low risk	1-day washout period.

Mortensen 1991

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant was randomised to 3 groups over 3 days. The groups included a control (spontaneous coughing) group, an FET group, and a PEP + FET group. Each treatment day consisted of one session lasting 20 minutes. Usual medications were unchanged, including bronchodilators, mucolytic drugs and antibiotics taken before treatments.
Participants	10 enrolled; 10 evaluated; 6 male (60% male). Age: mean (NR); median (20 years); SD (NR); range (15 to 26 years). Height: mean (NR); median (165.5 cm); range (154 to 185 cm) Inclusion criteria: NR. Exclusion criteria: NR. Characteristics: all 10 participants were infected with *Pseudomonas aeruginosa* and were non-smokers.
Interventions	Control (spontaneous coughing): spontaneous coughing. FET: FET; breathing control; and postural drainage (including thoracic expansion exercises, relaxation, breathing control).

Mortensen 1991 *(Continued)*

	PEP + FET: tidal volume breathing with PEP followed by FET and coughing. The intervention was conducted in a sitting position. PEP required the use of a PEP mask, 1-way valve, and manometer.
Outcomes	Outcome measures: lung function, sputum weight. Additional measures: number of huffs; urine content; tracheobronchial clearance.
Notes	Funding: Danish Medical Research Council and the National Union for the Fight Against Lung Diseases

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"The study was a randomised, single-blinded cross-over trial."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Unclear. Not enough information was presented to make an assessment.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	All participants were accounted for.
Compliance/ adherence assessed?	Low risk	"Physiotherapy treatments were supervised by a physiotherapist".
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Unclear risk	No description of a washout period.

Osman 2010

Study characteristics

Methods	Study type: RCT (cross-over). Each participant was randomised to alternate day treatment over 4 consecutive days. The treatments regimens were HFCWO and usual therapy. Participants received either HFCWO on days 1 and 3 and their usual ACT on days 2 and 4 or vice versa. Treatment session were 2 times daily for 30 min. All nebulised and inhaled medications were taken before treatment sessions.
Participants	30 enrolled; 29 evaluated; 21 male (72% male). Age: mean (29.4 years); median (NR); SD (8.4 years); range (NR).

Osman 2010 *(Continued)*

	Height: mean (171 cm); median (NR); SD (9 cm); range (NR) Inclusion criteria: FEV_1 ≥ 20% predicted, age ≥ 16 years, infective pulmonary exacerbations. Exclusion criteria: current severe haemoptysis, rib fractures, pregnancy, inability to give consent, persons whose usual ACT was HFCWO. Characteristics: NR.
Interventions	HFCWO (The Vest): This is the same as HFCC. Each participant was fitted with the appropriate sized vest. Participants remained in a upright sitting position throughout the 30 minute treatment session. HFCWO was applied for 8 minutes at each of 3 frequencies in sequence (10, 13, and 15 Hz) with each frequency followed by a 2-minute resting period. Participants were instructed to huff or cough as they felt necessary to expectorate secretions. ACBT with modified PD&P and with modified PD alone: In accordance with the guidelines of the International Physiotherapy Group for Cystic Fibrosis (International Physiotherapy Group for CF 2009). AD in sitting and with modified PD: In accordance with the guidelines of the International Physiotherapy Group for Cystic Fibrosis (International Physiotherapy Group for CF 2009). PEP: In accordance with the guidelines of the International Physiotherapy Group for Cystic Fibrosis (International Physiotherapy Group for CF 2009). Not stated if using mask or mouthpiece. Flutter: In accordance with the guidelines of the International Physiotherapy Group for Cystic Fibrosis (International Physiotherapy Group for CF 2009).
Outcomes	Outcome measures: participant preference; lung function; sputum weight; oxygen saturation. Additional measures: perceived efficacy; comfort; incidence of urinary leakage.
Notes	In the published article, all usual therapies are group together, including ACBT, and compared to HFCWO. HFCWO was described by the study authors as The Vest, which is an HFCC device. The study authors were contacted and provided us with raw data for each participant including what their usual therapies were and all first-arm data before the first cross-over. Funding: Robert Luff Foundation and Hill-Rom Ltd.

Risk of bias

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 (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	It is noted that an independent observer, blinded to the method of airway clearance used, performed spirometry, weighed the sputum samples, and collected visual analogue scales regarding perceived efficacy, comfort, and uri-

Osman 2010 *(Continued)*

		nary leakage. It is not noted whether an independent observer assessed oxygen saturation.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were report in the results.
Adequate follow up?	Low risk	One of the participants withdrew due to a hypoglycaemic episode. The loss to follow up was 3.33% (< 10%).
Compliance/ adherence assessed?	Low risk	Each airway clearance treatment sessions was supervised by a physiotherapist to ensure optimisation and standardization.
Intention-to-treat?	High risk	Participants lost to follow up were not included in the analysis.
Washout?	High risk	There was no washout period. Raw data were obtained from the study authors before first crossover.

Phillips 2004

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant used 2 treatment regimens in randomised order over 2 days. Each day consisted of 2 identical treatment sessions each lasting 20 minutes. There was a 1-day washout period between the 2 treatment days. The treatment regimens used were ACBT and HFCC.
Participants	10 enrolled; 10 evaluated; 7 male (70% male). Age: mean (13.7 years); median (14 years); SD (NR); range (9 to 16 years). Inclusion criteria: acute respiratory exacerbation. Exclusion criteria: pneumothorax or haemoptysis; any vision, hearing or balance disturbance; chest trauma. Characteristics: NR.
Interventions	ACBT: relaxed breathing control; 3-4 thoracic expansion exercises; and FET. HFCC: 4x 2-phase cycles of 600 oscillations per minute for 3 minutes followed by 60 oscillations per minute for 2 minutes. HFCC required the use of the Hayek Oscillator 1000.
Outcomes	Outcome measures: participant preference; lung function; sputum weight.
Notes	Funding: Not described

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear.
Allocation concealment (selection bias)	Low risk	Sealed envelopes were used.

Phillips 2004 *(Continued)*

Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Study reported, "An independent, blinded observer measured the weight of wet sputum." The study did not report if those assessing other outcomes were blinded.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	All participants were accounted for.
Compliance/ adherence assessed?	Low risk	Both treatments were supervised.
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Low risk	1-day washout period.

Pike 1999

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant used 2 treatment regimens in randomised order over 2 days. Each day consisted of 2 identical treatment sessions. The 2 treatment regimens used were ACBT and AOD (Flutter) + FE.
Participants	21 enrolled; 21 evaluated; 12 male (57.1% male). Age: mean (NR); median (26 years); SD (NR); range (NR). Inclusion criteria: NR. Exclusion criteria: NR. Characteristics: NR.
Interventions	ACBT: no description. AOD (Flutter) + FE: no description.
Outcomes	Outcome measures: participant preference; lung function; sputum weight; oxygen saturation.
Notes	Funding: Not described
Risk of bias	

Bias	**Authors' judgement**	**Support for judgement**

Pike 1999 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	The participants were randomised, but method not described.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Study reported that "sputum weight, pulmonary function, and oxygen saturation were measured by an independent observer."
Selective reporting (reporting bias)	Unclear risk	Not discussed.
Adequate follow up?	Unclear risk	Not discussed.
Compliance/ adherence assessed?	Unclear risk	Not reported.
Intention-to-treat?	Unclear risk	Unclear. Only available as an abstract.
Washout?	Unclear risk	No description of a washout period.

Pryor 1979

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant used 2 treatment regimens in randomised order over 4 days. The treatments were CCPT and FET. The frequency of the treatment sessions varied. 12 participants needed treatment 4x daily, 3 needed treatment 3x daily, 1 needed treatment 2x daily. Usual medications were unchanged.
Participants	18 enrolled; 16 evaluated; 8 male (50% male). Age: mean (20.5 years); median (NR); SD (NR); range (14 to 28 years). Inclusion criteria: NR. Exclusion criteria: admitted for terminal care. Characteristics: all 18 participants had an acute exacerbation of their bronchopulmonary infection.
Interventions	CCPT: postural drainage (breathing expansion exercises, coughing, and percussion); chest percussion; and shaking. FET + CCPT: Postural drainage and FET with expansion breathing exercise; coughing; and percussion and chest compression.

Pryor 1979 *(Continued)*

Outcomes	Outcome measures: lung function; sputum weight. Additional outcomes: rate of sputum production.
Notes	Analysis included part I of the study only. Part II compares ACBT (self-administered) to ACBT (physiotherapist administered). This is not a comparison of interest in this review. Funding: Not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The treatments were given in random order.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function and sputum weight.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	High risk	Two of 18 participants withdrew from the study: 1 developed pneumothorax and the other was unable to produce enough sputum for an accurate assessment. The loss to follow-up was 11.11% (> 10%).
Compliance/ adherence assessed?	Low risk	"Three physiotherapists took part in the treatment sessions throughout the study."
Intention-to-treat?	High risk	Participants lost to follow up were not included in the analysis.
Washout?	Unclear risk	No description of a washout period.

Pryor 1994

Study characteristics

Methods	Study type: RCT (cross-over). The treatments were randomised and remained the same for a 24-hour period. There were 3 sessions in a day (2 monitored and 1 unmonitored). The treatments were ACBT and ACBT + AOD (flutter). Usual medications were unchanged.
Participants	24 enrolled; 20 evaluated; 14 male (70% male).

Pryor 1994 *(Continued)*

	Age: mean (24.4 years); median (NR); SD (NR); range (16 to 36 years). Inclusion criteria: participants admitted to the hospital as clinically stable (clinical stability was measured by the absence of any clinical changes such as fever, FEV_1, FVC, FEF_{50}, FEF_{75}, ability to do their own chest physiotherapy); available for 2 consecutive days as close to discharge as possible. Exclusion criteria: participants admitted to the hospital for terminal care or with a pneumothorax or frank haemoptysis. Characteristics: all 24 participants had a history of bronchopulmonary infection.
Interventions	ACBT: breathing control; thoracic expansion; FET. ACBT + AOD (flutter): flutter for the first 10 minutes of the session; ACBT for the remainder.
Outcomes	Outcome measures: participant preference; sputum weight; oxygen saturation.
Notes	Sputum weight is reported for both the morning and afternoon sessions. Only baseline information is extractable for lung function. Funding: Not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Treatment regimens were randomised..."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as sputum weight and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as patient preference. The lack of blinding may have less of an effect on objective outcomes, such as sputum weight and oxygen saturation.
Blinding (performance bias and detection bias) Outcome Assessors	Low risk	"The measurement of the monitored session were taken by independent observers."
Selective reporting (reporting bias)	High risk	It is stated that lung function measurements were recorded before and at 5, 10, 15 and 30 minutes after treatment, but results of lung function measurement are not provided.
Adequate follow up?	High risk	4 of 24 participants withdrew from the study; 2 participants had their drug regimens changed during the study and another 2 participants withdrew because of technical problems with the oximeter and collection of sputum. The loss to follow up was 16.67% (> 10%).
Compliance/ adherence assessed?	Low risk	The treatment sessions were monitored.
Intention-to-treat?	High risk	Participants lost to follow up were not included in the analysis.

Pryor 1994 *(Continued)*

Washout?	Unclear risk	No description of a washout period.

Pryor 2010

Study characteristics	
Methods	`Study type: RCT (parallel design).
Participants	75 participants with CF Age: median (range) 27 (17 to 63) years. Gender split: 47 males and 28 females. Inclusion criteria: 16 years of age or older, $FEV_1 \geq 25\%$ predicted. Exclusion criteria: evidence of current respiratory exacerbation, past history of pneumothorax, current severe haemoptysis, awaiting lung or heart transplantation, pregnancy, and recent (within 3 months) acquisition of *Burkholderia cepacia*.
Interventions	ACBT versus AD versus cornet versus flutter versus PEP (exact device not clear i.e. mask or mouth-piece).
Outcomes	Measured monthly for 1 year: FEV_1; FVC; MEF_{25}; RV/TLC%; BMI; exercise capacity (modified shuttle test); QoL.
Notes	Lung function data available for 65 participants. The author has been contacted about obtaining additional data, and we are awaiting their response. Funding: An award from the Clinical Research Committee, Royal Brompton & Harefield Charitable Trust Foundation, provided the equipment and the Debbie Shearer Fund financed travel for the proponents of AD (Belgium) and PEP (Denmark) to visit Royal Brompton Hospital; and the travel expenses of the physiotherapists training subjects on the AD arm of the study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomisation was computerized and used a random number sequence stratified by FEV1% predicted..."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as quality of life. The lack of blinding may have less of an effect on objective outcomes, such as lung function.
Blinding (performance bias and detection bias) Personnel	High risk	Blinding was not possible. The lack of blinding may have a high risk of bias for subjective outcomes, such as quality of life. The lack of blinding may have less of an effect on objective outcomes, such as lung function.
Blinding (performance bias and detection bias) Outcome Assessors	Low risk	"The measurements of lung function and body mass index at 0, 6, and 12 months and the statistical analyses were undertaken by observers (physiolo-

Pryor 2010 *(Continued)*

		gists and statistician) blind to the regimen to which the subjects had been randomised."
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	High risk	10 of 75 (13%) of participants were lost to follow up. Additionally, 13 participants changed their airway clearance technique, but the details on this are not provided.
Compliance/ adherence assessed?	Low risk	"Subjects were requested to attend monthly, for a review of their ACT..."
Intention-to-treat?	High risk	Participants who were lost to follow up were not included in the analysis.

Reisman 1988

Study characteristics	
Methods	Study type: RCT (parallel design). Participants were stratified according to sex, age, and pulmonary function. Within each stratum, participants were then randomised to 1 of the treatment groups. The treatments were FET and CCPT + FET. In both groups participants took pancreatic enzyme supplements, antistaphylococcal antibiotics, and inhaled β2-bronchodilators. 3 year study.
Participants	67 enrolled; 63 evaluated; 38 male (60.3 % male). Age: no mean; SD; median or range reported. Inclusion criteria: 7 < years to < 21 years; FEV_1 > 40% of the predicted value for height and sex; participants with mild to moderate pulmonary disease only. Exclusion criteria: participants involved in any other studies.
Interventions	FET: maximal and normal inspirations, forced expiration, and breathing control. CCPT + FET: postural drainage; percussion; and FET.
Outcomes	Outcome measures: lung function; number of pulmonary exacerbations.
Notes	Participants were stratified by age, sex, and pulmonary impairment. Funding: Supported in part by grant aid from the Canadian Federal Department of Health and Welfare.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Subjects were randomly assigned within each stratum to one of two groups."
Allocation concealment (selection bias)	Unclear risk	Not discussed.

Reisman 1988 *(Continued)*

Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function and the number of pulmonary exacerbations.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function and the number of pulmonary exacerbations.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	High risk	Not all of the outcomes outlined in the methods section were reported in the results. For instance, sputum was collected but results were not reported.
Adequate follow up?	Low risk	4 of 67 participants withdrew from the study: 2 participants from the CCPT + FET group relocated and another 2 participants from the FET group withdrew because of family anxiety associated with discontinuation of conventional chest physiotherapy (used with FET). The loss to follow up was 5.97% (<10%).
Compliance/ adherence assessed?	Low risk	"... they were asked to keep a diary reporting adherence to their own physiotherapy regimens.".
Intention-to-treat?	High risk	Lost to follow-up participants were not included in the analysis.

Steven 1992

Study characteristics	
Methods	Study type: RCT (cross-over). Each participant used 3 treatment regimens for 24-hour periods in randomised order over 3 consecutive days.The treatments were coughing, ACBT (gravity-assisted position), and ACBT (sitting). The frequency of the treatment sessions varied between 2 to 4 times per day. The mean duration of the treatment sessions was 22 minutes.
Participants	24 enrolled; 24 evaluated; 16 male (66.7% male). Age: mean (25 years); median (NR); SD (NR); range (17 to 33 years). Inclusion criteria: participants who were clinically stable; producing more than 20 g of sputum in 24 hours; and fit enough to carry out their own chest physiotherapy. Exclusion criteria: participants with a pneumothorax; frank haemoptysis; or an FEV_1 which increased more than 15% after bronchodilators. Characteristics: all 24 participants had an exacerbation of their bronchopulmonary infection.
Interventions	Coughing (sitting): coughing and breathing control. ACBT (gravity-assisted position): postural drainage and ACBT; including breathing control, thoracic expansion, and FET. ACBT (sitting): ACBT including breathing control; thoracic expansion; and FET.
Outcomes	Outcome measures: lung function; sputum weight; oxygen saturation.

Steven 1992 *(Continued)*

Notes	Funding: Not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Each patient used each of the three treatment regimens for a 24 hour period, in randomised order, over three consecutive days."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as lung function, sputum weight, and oxygen saturation.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	Low risk	All outcomes outlined in the methods section were reported in the results.
Adequate follow up?	Low risk	All participants were accounted for.
Compliance/ adherence assessed?	Unclear risk	Not reported.
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Unclear risk	No description of a washout period.

Webber 1985

Study characteristics

Methods	Study type: RCT (cross-over). Each participant used 2 treatment regimens in randomised order over 4 consecutive days. The treatments were FET and FET + self-percussion. The treatment regimen remained unchanged for a 24-hour period. 6 participants needed treatment 4x daily, 8 needed treatment 3 x daily, 2 needed treatment 2 x daily.The individual treatment time ranged from 10-38 minutes, while the daily treatment times ranged from 51-107 minutes. 12 participants received intravenous antibiotic treatment and four received oral antibiotic treatment. 4 participants did not use chest compression.
Participants	16 enrolled; 16 evaluated; 10 male (62.5% male). Age: mean (21.1 years); median (NR); SD (NR); range (13 to 35 years). Inclusion criteria: NR. Exclusion criteria: NR.

Webber 1985 *(Continued)*

	Characteristics: all 18 participants were admitted with an acute exacerbation of their bronchopulmonary infection.
Interventions	FET: postural drainage including thoracic expansion and FET including breathing control. FET + self-percussion: postural drainage including thoracic expansion; self-percussion; and FET including breathing control.
Outcomes	Outcome measures: sputum weight.
Notes	Funding: Cystic Fibrosis Research Trust

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Treatment days were randomised."
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Participants	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as sputum weight.
Blinding (performance bias and detection bias) Personnel	Low risk	Blinding was not possible. However, the risk of bias from a lack of blinding may be low for objective outcomes, such as sputum weight.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not discussed.
Selective reporting (reporting bias)	High risk	Lung function results were not reported.
Adequate follow up?	Low risk	All participants were accounted for.
Compliance/ adherence assessed?	Low risk	Treatment regimens were performed under the supervision of 3 physiotherapists.
Intention-to-treat?	Low risk	Participants were analysed in the groups to which they were randomised.
Washout?	Unclear risk	No description of a washout period.

ACBT: active cycle of breathing technique
AD: autogenic drainage
AOD: airway oscillating devices
BMI: body mass index
CCPT: conventional chest physiotherapy
CF: cystic fibrosis
CFQ-R: Cystic Fibrosis Questionnaire - Revised
FE: forced expiration
FEF: forced expiratory flow
FET: forced expiratory technique
FEV_1: forced expiratory volume at one second
FFM: fat-free mass

FVC: forced vital capacity
HFCC: high-frequency chest compression
HFCWO: high-frequency chest wall oscillation
HNE: human neutrophil elastase
Hz: herz
NIV: non-invasive ventilation
NR: not reported
PD: postural drainage
PD&P: postural drainage and percussion
PEF: peak expiratory flow
PEP: positive expiratory pressure
PSV: pressure support ventilation
QoL: quality of life
RCT: randomised controlled trial
rhDNase: dornase alfa
RIM: resistance inspiratory manoeuvre
SaO_2: oxygen saturation
SD: standard deviation
TIRE: test of incremental respiratory endurance
VO_2: oxygen consumption

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

Study	Reason for exclusion
ACTRN12605000471684	Not an RCT.
ACTRN12614001233617	Study does not include people with CF.
ACTRN12619000224123	Study used FET which did not include all components of ACBT.
ACTRN12619001681145	Study does not evaluate ACBT.
Andreasson 1987	Study used FET which did not include all components of ACBT.
Asher 1982	Study did not address ACBT.
Bain 1988	Study did not address ACBT.
Baldwin 1994	Study did not address ACBT.
Braggion 1995	A cross-over RCT, but no comparison of interest as all participants received FET after treatment periods.
Castle 1994	To date we have not received any response to our requests for additional data to allow us to include this study. Given its age, we do not expect to receive relevant information now. Therefore we have excluded the study, but if we receive any relevant information in future, we will re-assess this decision.
Chatham 1998	Study did not address ACBT.
ChiCTR1800019989	Study does not include people with CF.
Davies 2012	This study was excluded because it did not address ACBT.
Desmond 1983	Study did not address ACBT.
Falk 1984	A cross-over RCT, but FET did not include all components of ACBT.

Study	Reason for exclusion
Falk 1993	To date we have not received any response to our requests for additional data to allow us to include this study. Given its age, we do not expect to receive relevant information now. Therefore we have excluded the study, but if we receive any relevant information in future, we will re-assess this decision.
Gursli 2017	A cross-over RCT, which did not describe the components of FET.
Hasani 1991	This article did not address CF.
Hasani 1994	This article did not address CF.
Horsley 2007	A non-randomised study with no outcome of interest.
Klig 1989	A non-randomised cross-over study.
Kofler 1998	Study did not address ACBT.
Lannefors 1992	To date we have not received any response to our requests for additional data to allow us to include this study. Given its age, we do not expect to receive relevant information now. Therefore we have excluded the study, but if we receive any relevant information in future, we will re-assess this decision.
McDonnell 1986	Study did not address ACBT.
NCT00164138	This study was excluded because it did not address ACBT.
NCT00404859	Study did not address ACBT.
NCT00716664	Study did not address ACBT.
NCT01943890	Study did not address ACBT.
NCT02906826	Study did not address ACBT.
NCT03078127	A cross-over study using FET, which did not include all components of ACBT.
O'Neill 2017	Study did not address ACBT.
Oberwaldner 1986	Non-randomised controlled study.
Orlik 2000	Non-randomised controlled study.
Orlik 2001	Non-randomised controlled study.
Parker 1984	To date we have not received any response to our requests for additional data to allow us to include this study. Given its age, we do not expect to receive relevant information now. Therefore we have excluded the study, but if we receive any relevant information in future, we will re-assess this decision.
Petrone 2009	To date we have not received any response to our requests for additional data to allow us to include this study. Given its age, we do not expect to receive relevant information now. Therefore we have excluded the study, but if we receive any relevant information in future, we will re-assess this decision.
Prasad 1998a	A review on physiotherapy treatments in CF, thus there were no original data.

Study	Reason for exclusion
Prasad 2000	A review on physiotherapy treatments in CF, thus there were no original data.
Pryor 1990	A non-randomised study.
RBR-5g9f6w	Study used FET, which did not include all components of ACBT.
Rogers 1984	Not an RCT.
Rossman 1982	Study did not address ACBT.
Salh 1989	A non-randomised cross-over study.
Sontag 2010	Study did not address ACBT.
Stanford 2020	No comparison of interest.
Steen 1991	While the majority of the arms were randomised, the intervention of interest was not randomised.
Sutton 1983	Cross-over RCT using FET, which did not include all components of ACBT.
Sutton 1985	Did not address ACBT.
Thomas 1995	A review on physiotherapy treatments in CF, thus there were no original data.
van Hengstum 1987	Did not address CF.
van Hengstum 1988	Results were presented for the 8 participants involved in the study (6 with CF and 2 with agammaglobulinaemia). We contacted the study authors to obtain data for CF participants separately, but have not received any reply so are not able to include this study.
Verboon 1986	Cross-over RCT did not include a comparison of interest. The 2 treatments only differed by PD, which is considered a component of ACBT in our definition.
Ward 2018	Study does not evaluate ACBT.
Webber 1986	A non-randomised study.
White 1997	Cross-over RCT which did not include a comparison of interest. Participants were randomised to receive ACBT or ACBT without thoracic expansion.
Williams 1994	A review on physiotherapy treatments in CF, thus there were no original data.
Williams 2000	Cross-over RCT with no comparison of interest. CF participants were randomised to therapy-assisted ACBT or independent ACBT.
Wilson 1995	A non-randomised cross-over study.
Znotina 2000	No comparison of interest. RCT comparing PEP/ oscillating PEP + FET with a physiotherapist (Group A) or without a physiotherapist (Group B).

ACBT: active cycle of breathing technique
CF: cystic fibrosis
FET: forced expiration technique
PD: postural drainage
PEP: positive expiratory pressure

RCT: randomised controlled trial

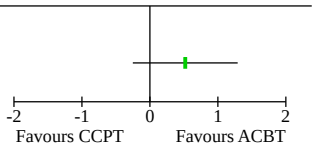
DATA AND ANALYSES

Comparison 1. ACBT versus CCPT

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 FEV $_1$ (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1.1 At 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2 FVC (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2.1 At 1 year	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.3 Pulmonary exacerbation	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.3.1 At 3 years	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

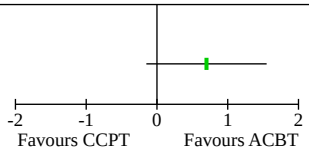
Analysis 1.1. Comparison 1: ACBT versus CCPT, Outcome 1: FEV $_1$ (L)

Study or Subgroup	ACBT Mean [L]	ACBT SD [L]	ACBT Total	CCPT Mean [L]	CCPT SD [L]	CCPT Total	Mean Difference IV, Fixed, 95% CI [L]
1.1.1 At 1 year							
Hristara-Papadopoulou 2005	2.24	1.15	15	1.72	1	15	0.52 [-0.25 , 1.29]



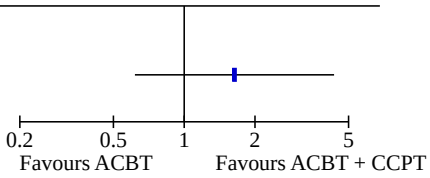
Analysis 1.2. Comparison 1: ACBT versus CCPT, Outcome 2: FVC (L)

Study or Subgroup	ACBT Mean	ACBT SD	ACBT Total	CCPT Mean	CCPT SD	CCPT Total	Mean Difference IV, Fixed, 95% CI
1.2.1 At 1 year							
Hristara-Papadopoulou 2005	2.67	1.26	15	1.97	1.11	15	0.70 [-0.15 , 1.55]



Analysis 1.3. Comparison 1: ACBT versus CCPT, Outcome 3: Pulmonary exacerbation

Study or Subgroup	ACBT Events	ACBT Total	ACBT + CCPT Events	ACBT + CCPT Total	Risk Ratio M-H, Fixed, 95% CI
1.3.1 At 3 years					
Reisman 1988	9	33	5	30	1.64 [0.62 , 4.34]

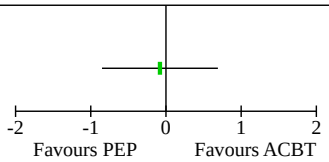


Comparison 2. ACBT versus PEP

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 FEV $_1$ (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1.1 Up to 1 week	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 2.1. Comparison 2: ACBT versus PEP, Outcome 1: FEV $_1$ (L)

Study or Subgroup	ACBT Mean	ACBT SD	ACBT Total	PEP Mean	PEP SD	PEP Total	Mean Difference IV, Fixed, 95% CI
2.1.1 Up to 1 week							
Pryor 2010	1.94	0.8	13	2.02	1.17	13	-0.08 [-0.85 , 0.69]

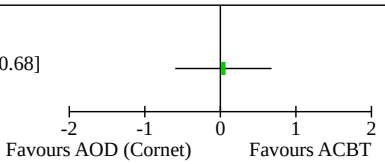


Comparison 3. ACBT versus AOD (Cornet)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 FEV $_1$ (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1.1 Up to 1 week	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 3.1. Comparison 3: ACBT versus AOD (Cornet), Outcome 1: FEV $_1$ (L)

Study or Subgroup	ACBT Mean	ACBT SD	ACBT Total	AOD (Cornet) Mean	AOD (Cornet) SD	AOD (Cornet) Total	Mean Difference IV, Fixed, 95% CI
3.1.1 Up to 1 week							
Pryor 2010	1.94	0.8	13	1.9	0.89	14	0.04 [-0.60 , 0.68]

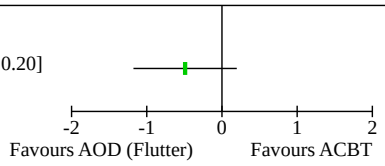


Comparison 4. ACBT versus AOD (Flutter)

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
4.1 FEV $_1$ (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1.1 Up to 1 week	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.2 Sputum weight	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.2.1 Up to 1 week	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

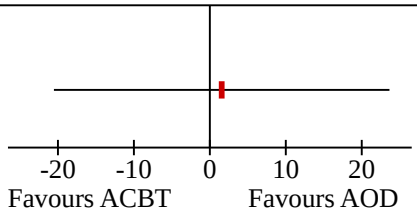
Analysis 4.1. Comparison 4: ACBT versus AOD (Flutter), Outcome 1: FEV $_1$ (L)

Study or Subgroup	ACBT Mean	ACBT SD	ACBT Total	AOD (Flutter) Mean	AOD (Flutter) SD	AOD (Flutter) Total	Mean Difference IV, Fixed, 95% CI
4.1.1 Up to 1 week							
Pryor 2010	1.94	0.8	13	2.43	0.94	12	-0.49 [-1.18 , 0.20]



Analysis 4.2. Comparison 4: ACBT versus AOD (Flutter), Outcome 2: Sputum weight

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI
4.2.1 Up to 1 week			
Milne 2004	1.56	11.27	1.56 [-20.53 , 23.65]

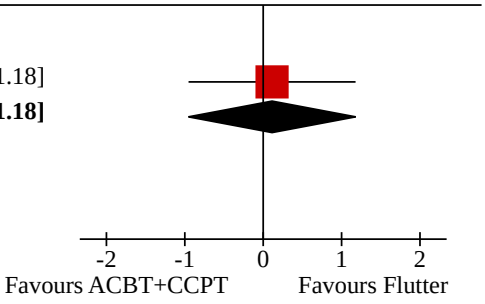


Comparison 5. ACBT + CCPT versus AOD (Flutter)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 FEV $_1$ (L)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.95, 1.18]
5.2 FEV $_1$% predicted	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.2.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	5.41 [-15.62, 26.44]
5.3 FVC (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.3.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.4 FVC % predicted	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.4.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.5 Sputum weight	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.5.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.6 Oxygen saturation	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.6.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

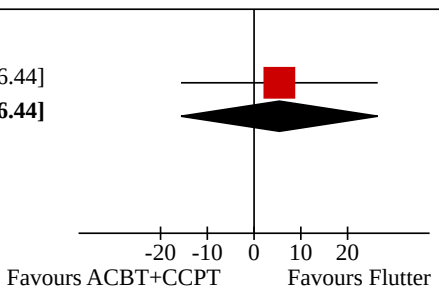
Analysis 5.1. Comparison 5: ACBT + CCPT versus AOD (Flutter), Outcome 1: FEV $_1$ (L)

Study or Subgroup	MD	SE	Weight	Mean Difference IV, Fixed, 95% CI
5.1.1 Day 1				
Osman 2010	0.113	0.5435269	100.0%	0.11 [-0.95 , 1.18]
Subtotal (95% CI)			**100.0%**	**0.11 [-0.95 , 1.18]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.21 (P = 0.84)				



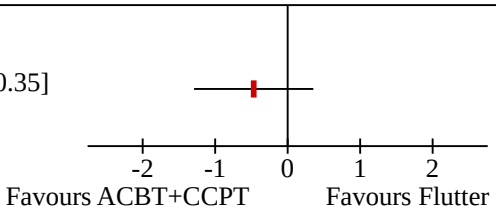
Analysis 5.2. Comparison 5: ACBT + CCPT versus AOD (Flutter), Outcome 2: FEV $_1$% predicted

Study or Subgroup	MD	SE	Weight	Mean Difference IV, Fixed, 95% CI
5.2.1 Day 1				
Osman 2010	5.41	10.73134894	100.0%	5.41 [-15.62 , 26.44]
Subtotal (95% CI)			**100.0%**	**5.41 [-15.62 , 26.44]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.50 (P = 0.61)				



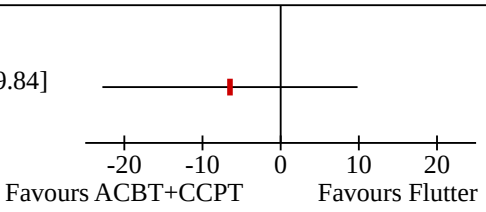
Analysis 5.3. Comparison 5: ACBT + CCPT versus AOD (Flutter), Outcome 3: FVC (L)

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI
5.3.1 Day 1			
Osman 2010	-0.4685	0.4198032	-0.47 [-1.29 , 0.35]



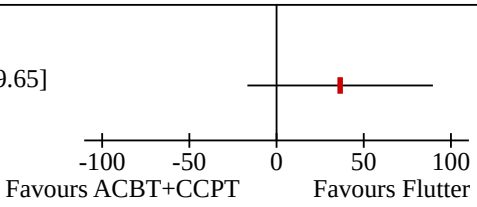
Analysis 5.4. Comparison 5: ACBT + CCPT versus AOD (Flutter), Outcome 4: FVC % predicted

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI
5.4.1 Day 1			
Osman 2010	-6.485	8.32740806	-6.49 [-22.81 , 9.84]



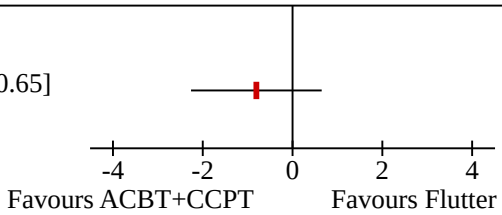
Analysis 5.5. Comparison 5: ACBT + CCPT versus AOD (Flutter), Outcome 5: Sputum weight

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
5.5.1 Day 1				
Osman 2010	36.473	27.1341342	36.47 [-16.71 , 89.65]	



Analysis 5.6. Comparison 5: ACBT + CCPT versus AOD (Flutter), Outcome 6: Oxygen saturation

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
5.6.1 Day 1				
Osman 2010	-0.806	0.742318	-0.81 [-2.26 , 0.65]	



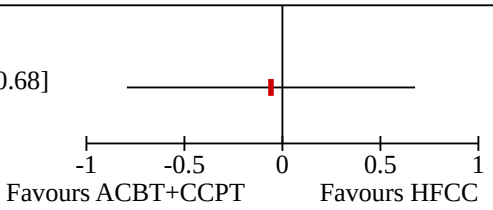
Comparison 6. ACBT + CCPT versus HFCC (HFCWO)

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
6.1 FEV $_1$ (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.2 FEV $_1$% predicted	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.2.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.3 FVC (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.3.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.4 FVC % predicted	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.4.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.5 Sputum weight	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.5.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.6 Oxygen satura-tion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
6.6.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

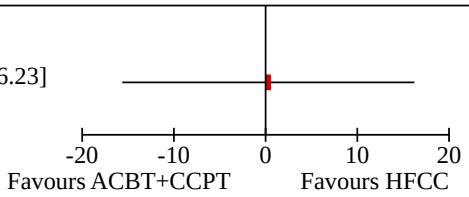
Analysis 6.1. Comparison 6: ACBT + CCPT versus HFCC (HFCWO), Outcome 1: FEV $_1$ (L)

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
6.1.1 Day 1				
Osman 2010	-0.058333	0.3750345	-0.06 [-0.79 , 0.68]	



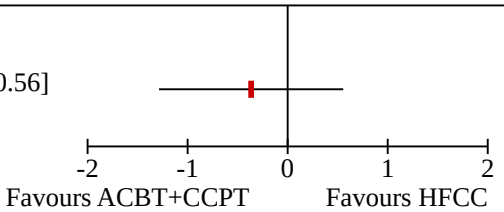
Analysis 6.2. Comparison 6: ACBT + CCPT versus HFCC (HFCWO), Outcome 2: FEV $_1$% predicted

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
6.2.1 Day 1				
Osman 2010	0.296666667	8.127649995	0.30 [-15.63 , 16.23]	



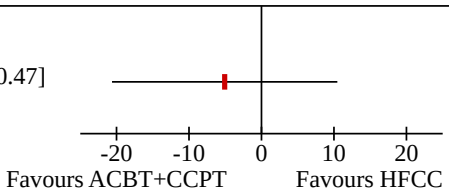
Analysis 6.3. Comparison 6: ACBT + CCPT versus HFCC (HFCWO), Outcome 3: FVC (L)

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
6.3.1 Day 1				
Osman 2010	-0.365	0.4697215	-0.36 [-1.29 , 0.56]	



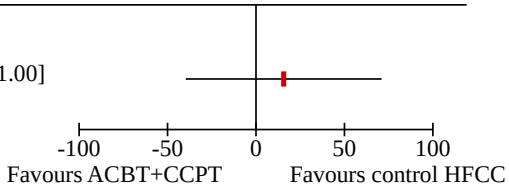
Analysis 6.4. Comparison 6: ACBT + CCPT versus HFCC (HFCWO), Outcome 4: FVC % predicted

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
6.4.1 Day 1				
Osman 2010	-5.076666667	7.930537523	-5.08 [-20.62 , 10.47]	



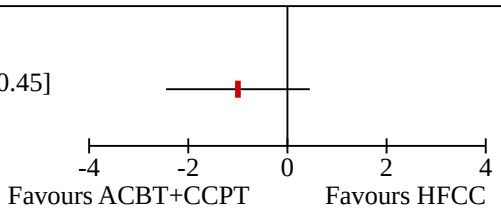
Analysis 6.5. Comparison 6: ACBT + CCPT versus HFCC (HFCWO), Outcome 5: Sputum weight

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
6.5.1 Day 1				
Osman 2010	15.6473333	28.2399127	15.65 [-39.70 , 71.00]	



Analysis 6.6. Comparison 6: ACBT + CCPT versus HFCC (HFCWO), Outcome 6: Oxygen saturation

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
6.6.1 Day 1				
Osman 2010	-0.99833	0.7393557	-1.00 [-2.45 , 0.45]	

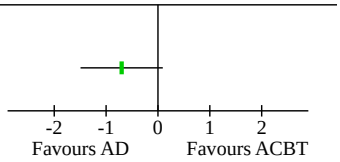


Comparison 7. ACBT versus AD

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 FEV_1 (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1.1 Up to 1 week	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.2 Sputum weight	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.2.1 Up to 1 week	1		Mean Difference (IV, Fixed, 95% CI)	-0.40 [-3.93, 3.13]

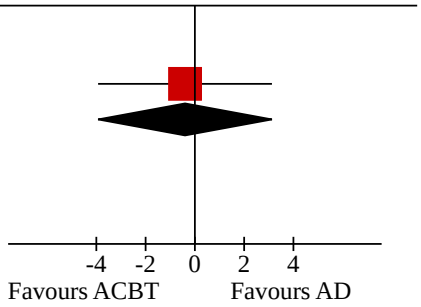
Analysis 7.1. Comparison 7: ACBT versus AD, Outcome 1: FEV $_1$ (L)

Study or Subgroup	ACBT Mean	ACBT SD	ACBT Total	AD Mean	AD SD	AD Total	Mean Difference IV, Fixed, 95% CI
7.1.1 Up to 1 week							
Pryor 2010	1.94	0.8	13	2.64	1.22	13	-0.70 [-1.49 , 0.09]



Analysis 7.2. Comparison 7: ACBT versus AD, Outcome 2: Sputum weight

Study or Subgroup	MD	SE	Weight	Mean Difference IV, Fixed, 95% CI
7.2.1 Up to 1 week				
Miller 1995	-0.4	1.8	100.0%	-0.40 [-3.93 , 3.13]
Subtotal (95% CI)			**100.0%**	**-0.40 [-3.93 , 3.13]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.22 (P = 0.82)				



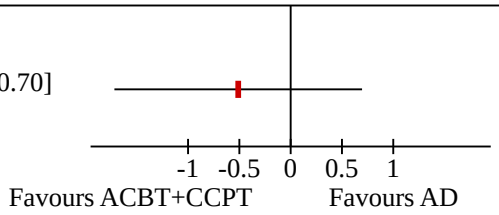
Comparison 8. ACBT + CCPT versus AD

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
8.1 FEV $_1$ (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.2 FEV $_1$% predicted	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.2.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.3 FVC (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.3.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.4 FVC % predicted	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.4.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.5 Oxygen satura-tion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.5.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.6 Sputum weight	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
8.6.1 Day 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

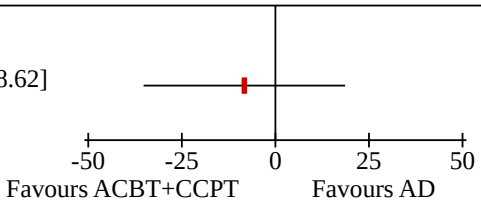
Analysis 8.1. Comparison 8: ACBT + CCPT versus AD, Outcome 1: FEV $_1$ (L)

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
8.1.1 Day 1				
Osman 2010	-0.511	0.6157232	-0.51 [-1.72 , 0.70]	



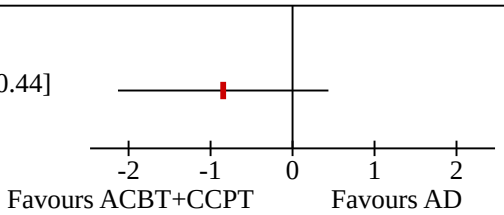
Analysis 8.2. Comparison 8: ACBT + CCPT versus AD, Outcome 2: FEV $_1$% predicted

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
8.2.1 Day 1				
Osman 2010	-8.3	13.73470786	-8.30 [-35.22 , 18.62]	



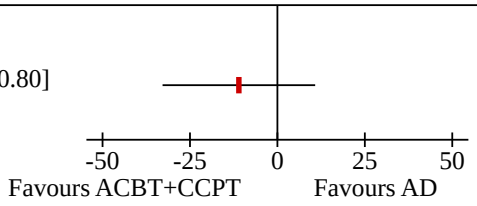
Analysis 8.3. Comparison 8: ACBT + CCPT versus AD, Outcome 3: FVC (L)

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
8.3.1 Day 1				
Osman 2010	-0.846	0.654892	-0.85 [-2.13 , 0.44]	



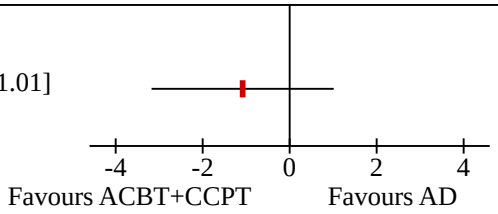
Analysis 8.4. Comparison 8: ACBT + CCPT versus AD, Outcome 4: FVC % predicted

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
8.4.1 Day 1				
Osman 2010	-11.02	11.1324722	-11.02 [-32.84 , 10.80]	



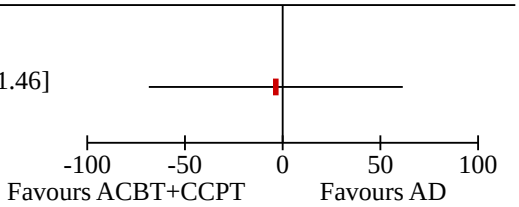
Analysis 8.5. Comparison 8: ACBT + CCPT versus AD, Outcome 5: Oxygen saturation

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
8.5.1 Day 1				
Osman 2010	-1.081	1.0683263	-1.08 [-3.17 , 1.01]	



Analysis 8.6. Comparison 8: ACBT + CCPT versus AD, Outcome 6: Sputum weight

Study or Subgroup	MD	SE	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
8.6.1 Day 1				
Osman 2010	-3.516	33.151755	-3.52 [-68.49 , 61.46]	



APPENDICES

Appendix 1. Search strategies for online trials registries

Database	Search terms	Date last searched
ClinicalTrials.gov	"cystic fibrosis" AND "active cycle of breathing technique" OR "forced expiration technique" OR "huff"	3 April 2021

(Continued)

World Health Organization International Clinical Trials Registry Platform (WHO ICTRP)	"cystic fibrosis" AND"active cycle of breathing technique" OR"forced expiration technique" OR "huff"	3 April 2021

WHAT'S NEW

Date	Event	Description
30 January 2023	New citation required but conclusions have not changed	With the inclusion of a new study, we were able to provide limited additional evidence on the effects of ACBT versus exercise. Some of the conclusions have been reworded based on current Cochrane guidance. Two authors are no longer able to contribute to the review and have been added to the acknowledgements (NAM, OAO).
30 January 2023	New search has been performed	A search of the Cochrane Cystic Fibrosis and Genetic Disorders (CFGD) Review Group's Cystic Fibrosis Trials Register identified 24 references potentially eligible for inclusion in the review. Searches of clinical trials registers yielded 42 references. Of these, three were duplicates and four references were captured in the search of the Cochrane Cystic Fibrosis and Genetic Disorders Review Group's Cystic Fibrosis Trials Register. Three studies were included, each with a single reference; two from the CFGD Group's register search (Hristara-Papadopoulou 2005; Hristara-Papadopoulou 2007) and one from the clinical trials registers (Gungor 2021). Five were additional references to already included studies (Fauroux 1999; Holland 2003; Osman 2010; Phillips 2004; Pryor 2010). Seven were additional references to six already excluded studies (Asher 1982; Braggion 1995; Chatham 1998; Gursli 2017; Rossman 1982; Steen 1991). Four new studies (10 references) from the CFGD Group's register search were excluded (Davies 2012; Horsley 2007; O'Neill 2017; Stanford 2020), along with 13 studies identified from the clinical trials registers. We have excluded the six studies that were awaiting assessment pending further information which had been requested from the investigators; to date we have not received any replies and so have excluded these studies now (Castle 1994; Falk 1993; Lannefors 1992; Parker 1984; Petrone 2009; van Hengstum 1988). We have added the summary of findings tables, per current guidance from Cochrane. Some of the conclusions have been reworded based on the new guidance.

HISTORY

Protocol first published: Issue 3, 2009
Review first published: Issue 11, 2010

Date	Event	Description
30 June 2016	New citation required but conclusions have not changed	A new author (Lisa Wilson) has joined the review team. Despite the inclusion of new data from the Pryor study, our conclusions have not changed.
30 June 2016	New search has been performed	A search of the Cystic Fibrosis and Genetic Disorders Group's Cystic Fibrosis Trials Register identified four new references potentially eligible for inclusion in this update. One was the full paper to an abstract previously listed as awaiting classification, but which has now been included (Pryor 2010). The second reference was to a study that has been excluded (Gursli 2017). Two references to one study have been listed as 'Awaiting classification' (Petrone 2009). Two studies previously listed as 'Awaiting classification' have now been excluded as we do not believe them to have been randomised (Orlik 2000; Orlik 2001).
22 October 2012	New citation required but conclusions have not changed	Despite the inclusion of new data, there is still insufficient evidence to support or reject the use of active cycle of breathing technique (ACBT) over any other airway clearance therapy and hence our conclusions have not changed.
22 October 2012	New search has been performed	The Cysitic Fibrosis Trial Register was search and no new references were identified. One study, which was initially listed under 'Studies awaiting classification', has now been included (Osman 2010). The study authors, who we had previously contacted for additional information, provided us with raw data for each participant clarifying which treatment they received and first-arm data before the cross-over. There was no washout period.

CONTRIBUTIONS OF AUTHORS

Karen Robinson provided the link with the Cochrane Cystic Fibrosis and Genetic Disorders Editorial Base.

Protocol

All authors were responsible for drafting the protocol.

Original review

The Editorial Base and all authors developed the search strategy and searched for studies. Naomi Mckoy obtained copies of studies, entered data into RevMan and carried out the analysis. All authors were responsible for selecting which studies to include, extracting data, interpreting the analysis and drafting the final review.

Updated review 2022

Karen Robinson, Ian Saldanha, and Lisa Wilson were involved in updating the review.

DECLARATIONS OF INTEREST

Lisa Wilson declares no known potential conflict of interest.

Ian Saldahna declares no known potential conflict of interest.

Karen Robinson declares no known potential conflict of interest.

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- CF Foundation, USA

  Partially funded by the Cystic Fibrosis Foundation.
- 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.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We reorganised the comparator interventions. They were previously listed separately, but we have grouped them for ease of analysis and in accordance with other physiotherapy reviews of the Cochrane CFGD Group into the following:

- Conventional chest physiotherapy (CCPT) (postural drainage, percussion, chest shaking, huffing, and coughing; excludes the use of exercise, FET, PEP, or other mechanical devices);
- PEP (PEP mask therapy, high pressure PEP mask therapy);
- Oscillatory devices (airway oscillating devices, high frequency chest compression devices);
- Breathing techniques (excluding ACBT, but including autogenic drainage);
- Exercise;
- Other therapy (resistive inspiratory manoeuvre).

In line with current Cochrane guidance, we have generated summary of findings tables for each comparison listed above and have graded the evidence using the GRADE criteria.

We have added sputum volume as an outcome.

In addition to our electronic searching and hand searching, we have searched the ClinicalTrials.gov and WHO ICTRP clinical trial registries.

INDEX TERMS

Medical Subject Headings (MeSH)

*Chest Wall Oscillation; *Cystic Fibrosis [therapy]; Mucus; Quality of Life; Respiratory Therapy [methods]

MeSH check words

Adolescent; Adult; Child; Humans; Middle Aged; Young Adult