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Interventions for improving adherence to airway clearance treatment and exercise in people with cystic fibrosis (Review)

Jones M, Moffatt F, Harvey A, Ryan JM

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[Intervention Review]

Interventions for improving adherence to airway clearance treatment and exercise in people with cystic fibrosis

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ABSTRACT

Background

Cystic fibrosis (CF) is a life-limiting genetic disorder predominantly affecting the lungs and pancreas. Airway clearance techniques (ACTs) and exercise therapy are key components of physiotherapy, which is considered integral in managing CF; however, low adherence is well-documented. Poor physiotherapy adherence may lead to repeated respiratory infections, reduced exercise tolerance, breathlessness, reduced quality of life, malaise and reduced life expectancy, as well as increased use of pharmacology, healthcare access and hospital admission. Therefore, evidence-based strategies to inform clinical practice and improve adherence to physiotherapy may improve quality of life and reduce treatment burden.

Objectives

To assess the effects of interventions to enhance adherence to airway clearance treatment and exercise therapy in people with CF and their effects on health outcomes, such as pulmonary exacerbations, exercise capacity and health-related quality of life.

Search methods

We searched the Cochrane Cystic Fibrosis Trials Register, compiled from electronic database searches and handsearching of journals and conference abstract books. Date of last search: 1 March 2023.

We also searched online trials registries and the reference lists of relevant articles and reviews. Date of last search: 28 March 2023.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-RCTs of parallel design assessing any intervention aimed at enhancing adherence to physiotherapy in people with CF versus no intervention, another intervention or usual care.

Data collection and analysis

Two review authors independently checked search results for eligible studies and independently extracted data. We used standard procedures recommended by Cochrane and assessed the certainty of evidence using the GRADE system.

Main results

Two RCTs (77 participants with CF; age range 2 to 20 years; 44 (57%) males) met the inclusion criteria of this review. One study employed an intervention to improve adherence to exercise and the second an intervention to improve adherence to ACT. Both studies measured

outcomes at baseline and at three months, but neither study formally assessed our primary outcome of adherence in terms of our planned outcome measures, and results were dependent on self-reported data.

Adherence to ACTs

One RCT (43 participants) assessed using specifically-composed music alongside ACTs compared to self-selected or no music (usual care). The ACT process consisted of nebuliser inhalation treatment, ACTs and relaxation or antibiotic nebuliser treatment. We graded all evidence as very low certainty.

This study reported adherence to ACTs using the Morisky-Green questionnaire and also participants' perception of treatment time and enjoyment, which may influence adherence (outcome not reported specifically in this review). We are uncertain whether participants who received specifically-composed music may be more likely to adhere at six and 12 weeks compared to those who received usual care, risk ratio (RR) 1.75 (95% confidence interval (CI) 1.07 to 2.86) and RR 1.56 (95% CI 1.01 to 2.40) respectively. There may not be any difference in adherence when comparing specifically-composed music to self-selected music at six weeks, RR 1.21 (95% CI 0.87 to 1.68) or 12 weeks, RR 1.52 (95% CI 0.97 to 2.38); or self-selected music to usual care at six weeks, RR 1.44 (95% CI 0.82 to 2.52) or 12 weeks, RR 1.03 (95% CI 0.57 to 1.86).

The music study also reported the number of respiratory infections requiring hospitalisation at 12 weeks, with no difference seen in the risk of hospitalisation between all groups.

Adherence to exercise

One RCT (24 participants) compared the provision of a manual of aerobic exercises, recommended exercise prescription plus two-weekly follow-up phone calls to reinforce exercise practice over a period of three months to verbal instructions for aerobic exercise according to the CF centre's protocol. We graded all evidence as very low certainty.

We are uncertain whether an educational intervention leads to more participants in the intervention group undertaking increased regular physical activity at three months (self-report), RR 3.67 (95% CI 1.24 to 10.85), and there was no reported difference between groups in the number undertaking physical activity three times per week or undertaking at least 40 minutes of physical activity. No effect was seen on secondary outcome measures of spirometry, exercise capacity or any CF quality of life domains. This study did not report on the frequency of respiratory infections (hospitalised or not) or adverse events.

Authors' conclusions

We are uncertain whether a music-based motivational intervention may increase adherence to ACTs or affect the risk of hospitalisation for a respiratory infection. We are also uncertain whether an educational intervention increases adherence to exercise or reduces the frequency of respiratory infection-related hospital admission. However, these results are largely based on self-reported data and the impact of strategies to improve adherence to ACT and exercise in children and adolescents with stable CF remains inconclusive.

Given that adherence to ACT and exercise therapy are fundamental to the clinical management of people with CF, there is an urgent need for well-designed, large-scale clinical trials in this area, which should conform to the CONSORT statement for standards of reporting and use appropriate, validated outcome measures. Studies should also ensure full disclosure of data for all important clinical outcomes.

PLAIN LANGUAGE SUMMARY

Which strategies might influence how accurately and how long people with cystic fibrosis complete chest physiotherapy and exercise?

Background

Cystic fibrosis (CF) is a progressive and life-limiting genetic condition that affects many systems in the body, especially the lungs. In the UK, 1 in every 2500 babies is diagnosed with CF. Physiotherapy is a very important part of treatment for people with CF. The two main goals of chest physiotherapy are to clear sticky mucus from the airways to prevent repeated infections and lung damage and to maintain physical fitness through exercise.

Chest physiotherapy can help prevent poor health and hospital admissions and may contribute to improving quality of life and life expectancy, but it is often considered a burden. People with CF may have to complete seven or more chest physiotherapy treatments a day, which can be time-consuming, tiring, and disruptive. As a result, people with CF may complete as little as 30% of their chest physiotherapy sessions, with rates often dipping during some stages in a person's life (such as adolescence). Although exercise is often viewed more positively by people with CF, they may not always carry out their exercises because of tiredness, feeling unwell, or a lack of time.

We wanted to explore what we can do to encourage people with CF to complete more of their planned chest physiotherapy or exercise. We were interested in a range of possible strategies including leaflets, videos, apps, rewards, motivational tools, exercise games, diaries, and text messages.

What did we do?

We looked for high-quality studies of people with CF (aged seven years and upwards). We planned to include any strategy aimed at improving adherence to chest physiotherapy or exercise compared to no strategy, usual care, or another type of strategy.

What did we find?

We found only two studies that we could include in our review. One was an educational study to improve adherence to exercise, and the second was a motivational study to increase adherence to chest physiotherapy.

In the exercise study (34 participants), those who received a written manual seemed to be more physically active at the end of the study, compared to those who were given verbal advice only, but we are not certain whether this was due to the manual. There were no other differences between groups in terms of quality of life, lung function, or exercise capacity.

In the chest physiotherapy study (43 participants), we are uncertain whether listening to specially-composed music during chest physiotherapy leads to more time spent completing treatments. We did not find that listening to music people chose themselves while doing physiotherapy led to completion of more treatment compared to not listening to any music. We did not find any real difference in hospital admissions due to chest infection between any of the groups.

What are the limitations of the evidence?

In both studies, the groups were very small and there were problems in trial design and reporting. This means that the reliability of the results might be affected. As a result, the evidence for strategies to improve adherence to physiotherapy and adherence to exercise was very uncertain. Whilst these studies suggest that some strategies may be helpful, future research needs to consider ways to accurately measure adherence. In the meantime, physiotherapists treating people with CF should follow local guidelines and national standards of care related to CF and treatment adherence.

How up to date is the evidence?

The evidence is current to 28 March 2023.

SUMMARY OF FINDINGS

Summary of findings 1. Motivational interventions to improve adherence to airway clearance treatment for people with CF - specifically-composed music versus no music

Motivational interventions to improve adherence to airway clearance treatment for people with CF - specifically-composed music versus no music

Patient or population: people with CF

Settings: community

Intervention: specifically-composed music as an adjunct to ACT

Comparison: no music during ACT

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No music	Specifically-composed music				
Adherence to treatment Morisky-Green questionnaire (number of participants showing full adherence) **Follow-up**: 3 months	600 per 1000	936 per 1000 (606 to 1000)	**RR 1.56** (1.01 to 2.40)	30 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	The Morisky-Green test is a dichotomous measure where there is perfect adherence versus some degree of non-adherence. The result favours specifically-composed music compared to no music. The data for this outcome were requested from the authors and were not published. Note: The follow-up at 3 months corresponds to the end of the intervention.
Frequency of hospitalisation for respiratory infection **Follow-up**: 3 months	400 per 1000	68 per 1000 (8 to 488)	**RR 0.17** (0.02 to 1.22)	30 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	The follow-up at 3 months corresponds to the end of the intervention.

Frequency of non-hospitalised respiratory infection	This outcome was not measured.	
FEV_1 % predicted (change from baseline)	This outcome was not measured.	
FVC % predicted (change from baseline) **Follow-up**: 3 months	This outcome was not measured.	
QoL (change from baseline)	This outcome was not measured.	
Exercise capacity (change from baseline)	This outcome was not measured.	

*The basis of the assumed risk and the corresponding risk is described in the comments. For lung function outcomes, absolute data was not presented in a format which could be analysed due to the crossover design of the study, therefore only analyses of percentage change from baseline were included in this review

Abbreviations: ACT: airway clearance technique; CF: cystic fibrosis; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; QoL: quality of life; RCT: randomised controlled trial; RR: risk ratio.

GRADE Working Group grades of evidence
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.

[a]Downgraded once due to risk of bias across several domains, including high risk of bias from lack of blinding and an unclear risk of bias around allocation concealment. There were also concerns around selective reporting and incomplete outcome data.
[b]Downgraded once due to imprecision caused by a very small sample size.
[c]Downgraded once due to indirectness (only children and adolescents included).

Summary of findings 2. Motivational interventions to improve adherence to airway clearance treatment for people with CF - self-selected music versus no music

Motivational interventions to improve adherence to airway clearance treatment for people with CF - self-selected music versus no music
Patient or population: people with CF
Settings: hospital or community
Intervention: music enjoyed by the participant (self-selected) as an adjunct to ACT

Comparison: no music during ACT

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No music	Music enjoyed by the participant				
Adherence to treatment Morisky-Green questionnaire (number of participants showing full adherence) **Follow-up**: 3 months	600 per 1000	618 per 1000 (342 to 1000)	**RR 1.03** (0.57 to 1.86)	28 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	The Morisky-Green test is a dichotomous measure where there is perfect adherence versus some degree of non-adherence. The data for this outcome were requested from the authors and were not published. Note: The follow-up at 3 months corresponds to the end of the intervention.
Frequency of hospitalisation for respiratory infection **Follow-up**: 3 months	400 per 1000	232 per 1000 (72 to 744)	**RR 0.58** (0.18 to 1.86)	28 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	Note: The follow-up at 3 months corresponds to the end of the intervention.
Frequency of non-hospitalised respiratory infection **Follow-up**: 3 months	This outcome was not measured.					
FEV_1 % predicted (change from baseline) **Follow-up**: 3 months	This outcome was not measured.					
FVC % predicted (change from baseline) **Follow-up**: 3 months	This outcome was not measured.					
QoL (change from baseline)	This outcome was not measured.					

Follow-up: 3 months					
Exercise capacity (change from baseline) **Follow-up**: 3 months	This outcome was not measured.				

*The basis of the **assumed risk** and the **corresponding risk** is described in the comments. For lung function outcomes, absolute data was not presented in a format which could be analysed due to the crossover design of the study, therefore only analyses of percentage change from baseline were included in this review

Abbreviations: ACT: airway clearance technique; CF: cystic fibrosis; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; QoL: quality of life; RCT: randomised controlled trial; RR: risk ratio.

GRADE Working Group grades of evidence
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.

[a]Downgraded once due to risk of bias across several domains, including high risk of bias from lack of blinding and an unclear risk of bias around allocation concealment. There were also concerns around selective reporting and incomplete outcome data.
[b]Downgraded once due to imprecision caused by a very small sample size.
[c]Downgraded once due to indirectness (only children and adolescents included).

Summary of findings 3. Motivational interventions to improve adherence to airway clearance treatment for people with CF - specifically-composed music versus self-selected music

Motivational interventions to improve adherence to airway clearance treatment for people with CF - specifically-composed music versus self-selected music

Patient or population: people with CF

Settings: community

Intervention: specifically-composed music as an adjunct to ACT

Comparison: music enjoyed by the participant (self-selected) as an adjunct to ACT

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				

	Music enjoyed by the participant	Specifically-composed music				
Adherence to treatment Morisky-Green questionnaire (number of participants showing full adherence) **Follow-up**: 3 months	615 per 1000	935 per 1000 (597 to 1000)	**RR 1.52** (0.97 to 2.38)	28 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	The Morisky-Green test is a dichotomous measure where there is perfect adherence versus some degree of non-adherence. The result slightly favours specifically-composed music compared to self-selected music. The data for this outcome were requested from the authors and were not published. Note: The follow-up at 3 months corresponds to the end of the intervention.
Frequency of hospitalisation for respiratory infection	231 per 1000	67 per 1000 (7 to 566)	**RR 0.29** (0.03 to 2.45)	28 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	
Frequency of non-hospitalised respiratory infection	This outcome was not measured.					
FEV_1 % predicted (change from baseline)	This outcome was not measured.					
FVC % predicted (change from baseline)	This outcome was not measured.					
QoL (change from baseline)	This outcome was not measured.					
Exercise capacity (change from baseline)	This outcome was not measured.					

*The basis of the **assumed risk** and the **corresponding risk** is described in the comments. For lung function outcomes, absolute data was not presented in a format which could be analysed due to the crossover design of the study, therefore only analyses of percentage change from baseline were included in this review

Abbreviations: ACT: airway clearance technique; CF: cystic fibrosis; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; QoL: quality of life; RCT: randomised controlled trial; RR: risk ratio.

GRADE Working Group grades of evidence

High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.

[a]Downgraded once due to risk of bias across several domains, including high risk of bias from lack of blinding and an unclear risk of bias around allocation concealment. There were also concerns around selective reporting and incomplete outcome data.
[b]Downgraded once due to imprecision caused by a very small sample size.
[c]Downgraded once due to indirectness (only children and adolescents included).

Summary of findings 4. Educational interventions to improve adherence to exercise for people with CF

Educational interventions to improve adherence to exercise for people with CF

Patient or population: people with CF

Settings: community

Intervention: exercise prescription plus manual with aerobic physical activity guidelines and 2-weekly follow-up phone calls

Comparison: initial verbal instruction regarding aerobic exercise in line with CF centre protocol

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Verbal instruction	Instruction plus follow-up				
Adherence to treatment (number of participants undertaking physical activity) **Follow-up**: 3 months	176 per 1000	646 per 1000 (218 to 1000)	RR 3.67 (95% CI 1.24 to 10.85)	34 (1 RCT)	⊕⊖⊖⊖ **very low**[a, b, c]	Investigators also reported that there was no difference between groups in the number of participants undertaking physical activity three times per week, RR 1.50 (95% CI 0.51 to 4.38) or those undertaking at least 40 minutes of physical activity per week, RR 1.00 (95% CI 0.30 to 3.36).
Frequency of hospitalisation for respiratory infection **Follow-up**: 3 months	Outcome not reported.					

Frequency of non-hospitalised respiratory infection **Follow-up**: 3 months	Outcome not reported.					
FEV_1 % predicted (change from baseline) **Follow-up**: 3 months	The mean FEV_1 % predicted increased in the verbal instruction group by 1.00%.	The mean change from baseline in FEV_1 % predicted was 2.80% lower in the instruction and follow-up group (10.69 lower to 5.09 higher).	MD -2.80 (95% CI -10.69 to 5.09)	34 (1 study)	⊕⊖⊖⊖ **very low**[a, b, c]	There was also no difference reported in the change from baseline in FEV_1 / FVC% between groups MD -1.40 (95% CI -8.66 to 5.86).
FVC % predicted (change from baseline) **Follow-up**: 3 months	The mean FVC % predicted increased in the verbal instruction group by 2.00%.	The mean change from baseline in FVC % predicted was 2.40% lower in the instruction and follow-up group (9.02 lower to 4.22 higher).	MD -2.40 (95% CI -9.02 to 4.22)	34 (1 study)	⊕⊖⊖⊖ **very low**[a, b, c]	See above for the change from baseline in FEV_1 / FVC%.
QoL (change from baseline) **Follow-up**: 3 months	See comments.			34 (1 RCT)	⊕⊖⊖⊖ **very low**[a, b, c]	There were no significant differences between groups in any domain of the CFQ (physical; emotional; social; treatment; respiratory; vitality; health; weight; body image; nutrition; digestive; social role).
Exercise capacity (change from baseline) VO_2 peak **Follow-up**: 3 months	The mean increase in VO_2 peak in the verbal instruction only group was 2.30 mL/kg/min.	The mean increase in VO_2 peak in the instruction and follow-up group was 1.20 mL/kg/min lower (7.26 lower to 4.86 higher).	MD -1.20 mL/kg/min (95% CI -7.26 to 4.86)	34 (1 RCT)	⊕⊖⊖⊖ **very low**[a, b, c]	The outcomes shuttle walking test, 6-minute walk, step test and CPET were not reported.

*The basis of the **assumed risk** and the **corresponding risk** is described in the comments. For lung function outcomes, absolute data was not presented in a format which could be analysed due to the crossover design of the study, therefore only analyses of percentage change from baseline were included in this review

Abbreviations: CF: cystic fibrosis; CFQ: cystic fibrosis questionnaire; CI: confidence interval; CPET: cardiopulmonary exercise testing; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MD: mean difference; QoL: quality of life; RCT: randomised controlled trial; RR: risk ratio; SD: standard deviation; VO_2 peak: peak oxygen uptake.

GRADE Working Group grades of evidence
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low certainty: we are very uncertain about the estimate.

[a]Downgraded once de to risk of bias (high risk due to blinding and selective reporting).
[b]Downgraded once due to indirectness (only children and adolescents included; study measures adherence to physical activity, which can be one type of ACT).
[c]Downgraded once due to imprecision (low number of participants).

BACKGROUND

Description of the condition

Cystic fibrosis (CF) is a life-limiting autosomal recessive genetic disorder, which affects exocrine glands (predominantly lungs and pancreas) throughout the body. A genetic mutation affecting the CF transmembrane regulator (CFTR) protein acts on chloride channels, leading to excessive reabsorption of sodium and water across cell membranes; this produces dehydrated extracellular fluid and subsequently thick secretions (Ratjen 2009). In the lungs, airway surface liquid depletion impairs mucociliary transport, making thick secretions difficult to clear; these accumulate, causing repeated respiratory tract infection, poor mucociliary clearance, persistent bacterial colonisation and irreversible damage (Hurt 2012). Indeed, respiratory failure is the predominant cause of morbidity and mortality in CF (Radtke 2022). Consequences of progressive respiratory disease (productive cough, haemoptysis, breathlessness and reduced exercise capacity) (Bott 2009; CF Trust 2020), plus pancreatic insufficiency characterised by poor absorption of protein and fat (Ratjen 2009), with subsequent malnutrition (O'Sullivan 2009), result in a reduced quality of life (QoL) (Britto 2004; CF Trust 2022; Dobbin 2005).

Physiotherapy is an integral and essential component of CF management, as highlighted in international consensus and physiotherapy guidelines (Bott 2009; CF Trust 2020; NICE 2017). Physiotherapy may comprise multimodal interventions (Wilson 2023), e.g. the management of musculoskeletal conditions and stress urinary incontinence (Button 2016); however, the cornerstone of treatment (and therefore the focus of this review) involves the assessment and management of airway clearance techniques (ACTs) (Burnham 2021; CF Trust 2020; Heinz 2022; McIlwaine 2014; McIlwaine 2019; Morrison 2020; Sherman 2019; Wilson 2019), with or without the use of non-invasive ventilation (Moran 2017) and cardiovascular capacity (exercise) (CF Trust 2020; Radtke 2022). There is significant variation in the range of ACTs and exercise options for people with CF (Wilson 2023), but the treatment regimen is invariably acknowledged as burdensome for the individual, and their carer(s), across the course of their life (Davies 2020; Maetz 2021; Raywood 2022; Sawicki 2013). The median number of treatments per day for an adult with CF is seven, which constitutes an average daily treatment duration of between 108 and 180 minutes (Dodd 2000; O'Donohoe 2014; Sawicki 2009). Consequently, given the reported time burden, non-adherence to physiotherapy is an ongoing challenge in the treatment of CF (O'Donohoe 2014; Raywood 2022). Self-reported adherence to airway clearance in adults with CF is low (Meyers 2006; Raywood 2022; Sherman 2019). The CF Trust estimates that between 30% and 70% of people with CF are non-adherent in at least some portion of their treatment plan (CF Trust 2020), with a documented decline of up to 50% in adherence in adolescence (Arias Llorente 2008; Goodfellow 2015; Raywood 2022). Interestingly, a greater number of people with CF consistently take their enzymes (65% to 95%); reported adherence to oral antibiotics is 67%, for inhaled antibiotics it is 31% to 53% (CF Trust 2020), and adherence is 27% to 46% for dornase alfa (Modi 2006; Daniels 2013). A systematic review of adherence to CF treatments assessed 11 low-quality studies with 1058 participants; 10 of the included studies evaluated adherence with questionnaires and one used daily telephone diaries (O'Donohoe 2014). Only two low-quality studies identified individual types of ACT. The review reported ACT adherence rates from 10 studies that ranged from 33.3% ± 43.15% to 91.2% by participant questionnaire (O'Donohoe 2014). Non-adherence to exercise (defined as planned, structured, and repetitive physical activity with the aim of improving or maintaining physical fitness) has also been described (Casperson 1985; Hurley 2021). However, it is suggested that the perception of exercise therapy is generally viewed more positively by individuals with CF given its focus on health promotion rather than illness management (Rand 2014). Factors such as the impact on activities of daily living and social functioning, treatment burden, accidental or purposeful forgetting, lack of perceived benefit and "being unpleasant" have been identified as influencing non-adherence (Arias Llorente 2008; Conway 1996; Dodd 2000; George 2010; Hurley 2021). Poor adherence to all aspects of CF treatment has been associated with an increased number of infective pulmonary exacerbations and the need for intravenous (IV) antibiotic therapy (Eakin 2011; Goodfellow 2015). The consequences of poor physiotherapy adherence (ACT and exercise) are significant both for individuals with CF (reduced QoL, malaise and mortality) and in terms of healthcare costs (Cutler 2018; Wildman 2014).

Description of the intervention

Individuals with CF require an extensive, complex treatment regimen focused on medication, ACTs and exercise participation (Bott 2009; CF Trust 2020; NICE 2017; Wilson 2023). Adherence is defined as "the extent to which a person's behaviour (i.e. taking medication, following a diet and/or executing lifestyle changes), corresponds to agreed recommendations from a healthcare provider" (WHO 2003). Adherence to and persistence with treatment in CF vary by specific intervention; adherence is generally poorer for ACTs when compared to most medication use (Myers 2006). Poor adherence to physiotherapy has been estimated to be about 60% (Bregnballe 2011; Oates 2019); it leads to an increase in episodes of acute infection and hospital admission, which may contribute to premature death (McLeod 2020; Meyers 2006). Barriers to physiotherapy (ACT and exercise) adherence in people with CF are multifactorial (Abbott 1994; Bregnballe 2011; Conway 1996; Geiss 1992; George 2010; Santuzzi 2020; Sawicki 2009), in particular, the high time-demand of daily management is evidenced (Arias Llorente 2008; Bernard 2004; Bregnballe 2011; Santuzzi 2020). Although adherence to physiotherapy treatment (ACT and exercise) varies between individuals, it is particularly poor in adolescents and young adults with CF (Arias Llorente 2008; Bregnballe 2011; Conway 1996; Davies 2020; Eakin 2011; George 2010; O'Donohoe 2014). Clinical variables (e.g. disease severity), demographic characteristics and knowledge about the condition have not been demonstrated as reliable predictors of treatment adherence (Sherman 2019). Contemporary work has considered the application of social cognitive theory, in particular the influence of psychosocial variables such as self-efficacy and self-confidence in overcoming barriers to treatment components, as well as the influence of subjective norms (Bishay 2016; George 2010; Sherman 2019).

Interventions that aim to enhance adherence to ACT and exercise in people with CF may improve functional and health-related QoL; these include psycho-educational interventions (leaflets, videos, apps aimed at increasing knowledge and understanding), psychotherapeutic or motivational interventions (cognitive behavioural therapy (CBT), contingent privileges or rewards, setting realistic expectations, motivational interviewing),

or organisational interventions (self-management diary, electronic reminders, technology-based interventions such as active gaming, apps, telecare) (Duff 2010). Evaluation of these strategies will provide evidence to inform clinical practice and improve healthcare outcomes for people with CF.

It is worthy of note that there is currently no 'gold standard' tool for the measurement of patient adherence to physiotherapist-prescribed self-management strategies. In a critical review of adherence to physiotherapy self-management strategies, the authors noted a diverse range of measures including self-report diaries, self-administered surveys, interviews and observational measures such as activity monitors or video capture (Peek 2015). The lack of a single valid and reliable measurement tool of adherence to physiotherapy self-management strategies may limit the ability to compare the effectiveness of interventions across studies (Bailey 2018).

How the intervention might work

The development of complex prophylactic management and treatment options for symptomatic relief has led to an increased median predicted survival age from young childhood to over 40 years of age (CFF 2014; Keogh 2018); however, although adherence to these interventions is essential for efficacy (Eakin 2011; Sawicki 2009), adherence to physiotherapy ACTs and exercise remains lower than to other treatments (Meyers 1999). Identifying patient-reported barriers to treatment adherence has been considered essential for developing approaches targeted at modifiable factors (Sherman 2019). Psycho-educational interventions target knowledge and understanding of the condition and treatment benefits and barriers; some studies have suggested that there are significant gaps in knowledge across people with CF and their families (Lonabaugh 2018), or that the information is suppressed as part of an individual's coping style (Duff 2010). Psychotherapeutic and motivational approaches are broadly aimed at reducing stress, improving coping styles and strategies, and exploring ambivalence or enhancing behaviour change in favour of adherence to the prescribed treatment regimen (Goldbeck 2014). Organisational interventions assist in the organisation and time management of treatments, e.g. providing active reminders or prompts, scheduling strategies, or tailoring treatments to lifestyle or life-stage, e.g. encouraging exercise through active video gaming.

Why it is important to do this review

Physiotherapy is generally considered to be an integral and essential component of the management of CF (Bott 2009; CF Trust 2020; NICE 2017). The consequences of poor physiotherapy adherence may be potentially significant both for individuals with CF (repeated respiratory infection, reduced exercise tolerance, breathlessness, reduced QoL, malaise and reduced life expectancy) and in terms of healthcare costs (increased use of pharmacology, primary care access and hospital admission). As such, evidence-based strategies to inform clinical practice and improve adherence to physiotherapy management are believed to be significant for improving QoL for the individual and reducing economic burden; this area of research has been raised as a priority by the James Lind Alliance Priority Cystic Fibrosis Setting Partnership (Rowbotham 2019). The need to assess the efficacy of strategies to improve adherence to physiotherapy management is of paramount importance to optimise healthcare outcomes.

Highly effective cystic fibrosis transmembrane regulator (CFTR) modulator therapies are life-changing for people living with CF, many of whom have found the burden of treatment for their condition difficult to bear. Early evidence suggest that CFTR modulator therapies may result in lower rates of cough and infective exacerbations (CFF 2021) and an improved prognosis (Nissenbaum 2020). The availability of these highly effective treatments may affect the need for physiotherapy and influence the judicious and evidence-based total or partial withdrawal of treatments such as physiotherapy, which have previously proved burdensome.

OBJECTIVES

To assess the effects of interventions to enhance adherence to airway clearance treatment and exercise therapy in people with CF and their effects on health outcomes, such as pulmonary exacerbations, exercise capacity and health-related QoL.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) and quasi-RCTs. We did not include observational studies, case studies and cross-over RCTs.

Types of participants

Adults and children (from aged seven years upwards) with CF. The lower limit of seven years was a post hoc protocol change after we became aware that specialist units anticipate that children with CF are likely to manage their physiotherapy independently (with potential supervision, but not active involvement, of parents) from the age of seven years rather than eight years, which we originally stated. We included populations of either gender, any ethnicity, any stage of disease and based in either a hospital or community setting.

Types of interventions

We included any intervention aimed at enhancing adherence to physiotherapy versus no intervention, usual care or another intervention aimed at enhancing adherence to physiotherapy. We did not compare adherence to two different physiotherapy regimens.

Interventions could include:

1. educational (increasing knowledge and understanding);
2. behavioural (CBT, contingent privileges or rewards, setting realistic expectations);
3. organisational (self-management diary, electronic reminders); or
4. technology (active gaming, apps, telecare).

We planned to evaluate adherence using these interventions to one or more of the following components of physiotherapy management; cardiovascular capacity (exercise) with or without the use of non-invasive ventilation, and airway clearance with or without the use of non-invasive ventilation.

Types of outcome measures

We assessed the following primary and secondary outcome measures.

Primary outcomes

1. Adherence
   a. electronic monitoring (% of completed treatments)
   b. confirmed observed participation by parent or carer or healthcare professional (% of completed treatments)
   c. self-reported diary (% of completed treatments)

Secondary outcomes

1. Frequency of hospitalisation for respiratory infection (requirement for non-routine intravenous (IV) antibiotics)
2. Frequency of non-hospitalised respiratory infection (requirement for home unplanned, rescue or non-routine IV antibiotics)
3. Lung function
   a. forced expiratory volume at one second (FEV_1) (L and % predicted)
   b. forced vital capacity (FVC) (L and % predicted)
   c. FEV_1/FVC %
   d. lung clearance index (LCI)
4. QoL measures using a disease-specific tool (e.g. Cystic fibrosis Health-Related Quality of Life questionnaire (Quittner 2005)) or a non-specific tool (e.g. Short Form 36 (SF-36) (SF-36))
5. Adverse events (any adverse advent associated with the intervention reported by authors, e.g. haemoptysis, pneumothorax, respiratory distress, death)
6. Exercise capacity, as assessed by
   a. shuttle walking test (SWT);
   b. 6-minute walk;
   c. step test; or
   d. cardio-pulmonary exercise testing (CPET) and the maximum oxygen consumption an individual can use in 1 minute per kg of body weight (ml/kg/min) (VO_2 peak)

Search methods for identification of studies

We searched for all relevant published and unpublished trials without restrictions on language, year or publication status.

Electronic searches

The Cochrane Cystic Fibrosis and Genetic Disorders Group's Information Specialist conducted a search of the Group's Cystic Fibrosis Trials Register for relevant studies using the following terms: (physiotherapies & exercising AND treatment adherence):kw.

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 latest search: 1 March 2023.

We additionally searched the following electronic databases and registers to identify published articles and additional studies for inclusion in this review. We present the database search strategies in the appendices (Appendix 1).

1. MEDLINE Ovid (1946 to 24 February 2023)
2. SCOPUS Elsevier (1823 to 28 February 2023)
3. AMED EBSCO (Allied and Complementary Medicine; 1985 to 27 February 2023)
4. PsychINFO APA Publishing (1806 to February 2023)
5. CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1982 to 27 February 2023)

We also searched online trials registries: 28 March 2023.

1. The World Health Organization (WHO) International Clinical Trials Registry Platform (trialsearch.who.int/)
2. US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov)
3. ISRCTN registry (www.isrctn.com)

Searching other resources

We checked the bibliographies of included studies and any relevant systematic reviews identified for further references to relevant studies.

We searched the following conference proceedings (2010 to 2020).

1. American Thoracic Society (ATS) International Conference (www.thoracic.org)
2. European Respiratory Society (ERS) International Congress (www.ersnet.org)
3. British Thoracic Society (summer and winter meetings) (www.brit-thoracic.org.uk)
4. UK Cystic Fibrosis Conference (UKCFC) (www.cysticfibrosis.org.uk)

Data collection and analysis

Two review authors (MOJ and FM) employed standard methods recommended by Cochrane.

Selection of studies

Two review authors (MOJ and FM) independently checked the search results, initially screening the titles and abstracts. We immediately excluded any study that did not meet the review's inclusion criteria if it was clear from the title or abstract. We retrieved full papers for any study where eligibility was unclear and for any study that appeared to meet the inclusion criteria. We translated any papers that were not written in English. There were no disagreements, but if any should occur in future updates of the review, we will resolve these through discussion and consensus. Where we do not achieve resolution, a third author (AH) will consider the paper(s) in question (Lefebvre 2022). We kept a full record of decisions and their rationale.

Data extraction and management

Two review authors (MOJ and FM) independently extracted data using a standardised form, which included:

1. study design;
2. sample size (intervention and control groups);
3. country of origin;
4. study population (age, gender);
5. details of the intervention (educational (increasing knowledge and understanding); behavioural (CBT, contingent privileges or rewards, setting realistic expectations); organisational (self-management diary, electronic reminders); or technology (active gaming, apps, telecare)
6. results for outcomes (primary and secondary outcomes as described above) and adverse events split by time point;
7. risk of bias assessments.

There were no discrepancies between authors, However, if discrepancies between authors occur in future updates of the review, we will resolve these by consensus; if we are unable to reach agreement, a third author (AH) will consider the paper. Where papers did not present sufficient data to enter a study into the meta-analysis, we contacted study authors to request access to the missing data.

We planned to compare data between the intervention and control group at the end of the intervention period, plus at the end of intervention and any follow-up period. We have reported data from all time periods, e.g. immediate or short term (less than one month); medium term (one to six months); and long term (more than six months). If studies had reported multiple measures, we planned to use data taken at the time point closest to these thresholds. For one study, investigators reported data at both six and 12 weeks; we have presented both of these time points separately, although they would both actually fall under the medium-term grouping (Montero-Ruiz 2020). This study also evaluated multiple interventions, and we have reported the results for each comparison separately. We looked at the effect of any intervention on the adherence to ACT and the adherence to exercise separately.

Assessment of risk of bias in included studies

Two review authors (MOJ and FM) independently assessed and agreed the risk of bias (ROB) in the included study using the Cochrane ROB 1 assessment tool outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017). Where the quality of study was unclear, we attempted to contact the study authors for clarification.

We assessed ROB based on the following Cochrane criteria, summarising ROB for each outcome of interest within a study and using judgements of yes, no or unclear.

1. Adequate sequence generation
2. Adequate allocation concealment
3. Adequate blinding of assessors
4. Incomplete outcome data adequately assessed
5. Free of suggestion of selective outcome reporting
6. Free of other bias

We recognised that the nature of the interventions means it is not possible to blind participants. Similarly, it may be possible that therapists or clinicians are not blinded in studies of this kind of intervention; in this situation we planned not to assess these criteria, but to reflect the potential impact of incomplete blinding in the discussion of the results.

Measures of treatment effect

For continuous variables, we calculated the mean difference (MD) between groups at follow-up with 95% confidence intervals (CIs). We planned to calculate the standardised mean difference (SMD) with 95% CIs as the measure of treatment effect, if different studies had used different measures for the same outcome. If these data had been unavailable, we planned to use the mean (and SD) change from baseline for each group. For dichotomous outcomes, we calculated the risk ratio (RR) with 95% CIs as the measure of treatment effect. We used the number of events in each group postintervention to calculate the RR.

The included trials measured adherence as a binary outcome. We therefore calculated the risk ratio (RR) with 95% CI to compare adherence between groups. All other outcomes we identified were measured on a continuous scale.

Unit of analysis issues

If trials reported data at multiple time points, we have presented these individually in the current review. For future updates, where studies report multiple measures, we will consider taking this approach or using only the data taken at the time point closest to our stated thresholds (see above). If the studies used multiple interventions, we summarised the results for outcomes separately. We analysed and present comparisons of different interventions separately. An included study may be designed such that investigators compare two different adherence interventions against a control group, but as it is likely the two arms will have different participants, we analysed the two interventions separately. If the participants are the same for both arms, this may result in double-counting.

The unit of analysis is the participant; cross-over studies are not eligible for inclusion in the review, as once a participant has been exposed to an adherence intervention, changes in behaviour may persist even though the intervention is removed.

Dealing with missing data

Where insufficient data were available to enter a study into a meta-analysis, we contacted the study authors to request access to the missing data. We did not impute missing data. Where data are missing, and we could not obtain these from the study authors, we acknowledged this as a limitation.

Assessment of heterogeneity

We were not able to combine data from different studies, and therefore we did not assess heterogeneity. For future updates of this review, we will assess heterogeneity and its impact using the Chi^2 test and the I^2 statistic (Deeks 2022). We will interpret I^2 values as follows.

1. 0% to 40%: might not be important
2. 30% to 60%: may represent moderate heterogeneity
3. 50% to 90%: may represent substantial heterogeneity

4. 75% to 100%: considerable heterogeneity

However, we will interpret the importance of observed I^2 values with reference to the magnitude of effects and the strength of evidence for heterogeneity as obtained from the Chi^2 test.

Assessment of reporting biases

We have assessed selective outcome reporting as detailed in Assessment of risk of bias in included studies. When sufficient data are available in future updates (i.e. at least 10 studies), we will explore possible publication bias and small study effects using funnel plots and test for funnel plot asymmetry using Egger's test (Egger 1997).

Data synthesis

Where sufficient data were available, we planned to present data for each outcome using a random-effects meta-analysis. We planned to use a random-effects model as we expected there to be variation between studies in terms of participants and interventions. We planned to conduct separate meta-analyses to examine effects of:

1. interventions to improve adherence to airway clearance treatment; and
2. interventions to improve adherence to exercise, compared to no treatment or usual care.

Where a study examined the effects of multiple treatment arms (i.e. Montero-Ruiz 2020), we included participants from each arm in separate meta-analyses. Where sufficient data were not available for a given outcome, we have described the findings narratively.

Subgroup analysis and investigation of heterogeneity

We planned to undertake a subgroup analysis according to age, i.e. children (7 to 12 years of age), adolescents (12 to 18 years) and adults (18 years and over), if the available data had allowed. Where studies included children and adolescents (e.g. 7 to 18 years) or adolescents and adults (e.g. 12 years and over), and we were unable to extract data for each age group, we planned to conduct separate subgroup analyses for children and adolescents, or adolescents and adults. We will do this in future updates, if data allow.

Sensitivity analysis

If sufficient data are available in future, we plan to conduct sensitivity analyses on the basis of ROB, specifically the effect of excluding studies at overall high ROB. We defined overall high risk of bias as having a judgement of a high ROB against at least one criterion. A lack of data means this has not been possible in this version of the review.

Summary of findings and assessment of the certainty of the evidence

The summary of findings tables provide key information concerning the certainty of evidence, the magnitude of effect of the interventions examined, and the sum of available data on all important outcomes for a given comparison (Schünemann 2022a). This will provide patient-important outcomes for decision-making by healthcare professionals and caregivers. We used the GRADE approach to evaluate the literature and reflect the extent to which we are confident that an estimate of the effect is correct (Schünemann 2022b). We have generated a table for each comparison that we present in the review. The outcomes presented in each table include, in order of priority:

1. adherence to treatment (% completed treatments) (reported using SMD for all results combined in the medium term (from one to six months));
2. frequency of hospitalisation in the medium term (from one to six months);
3. frequency of non-hospitalised respiratory infection in the medium term (from one to six months);
4. change from baseline in FEV_1 % predicted in the medium term (from one to six months);
5. change from baseline in FVC % predicted in the medium term (from one to six months);
6. change from baseline in QoL (using a disease-specific tool, e.g. Cystic Fibrosis Quality of Life Questionnaire, or a non-specific tool (SF-36)) (reported using SMD for all results combined in the medium term (from one to six months));
7. change from baseline in exercise capacity (by either shuttle walking test, six-minute walk, Step Test or CPET) (reported using SMD for all results combined in the medium term (from one to six months)).

RESULTS

Description of studies

For further information, please refer to the tables (Characteristics of included studies; Characteristics of excluded studies).

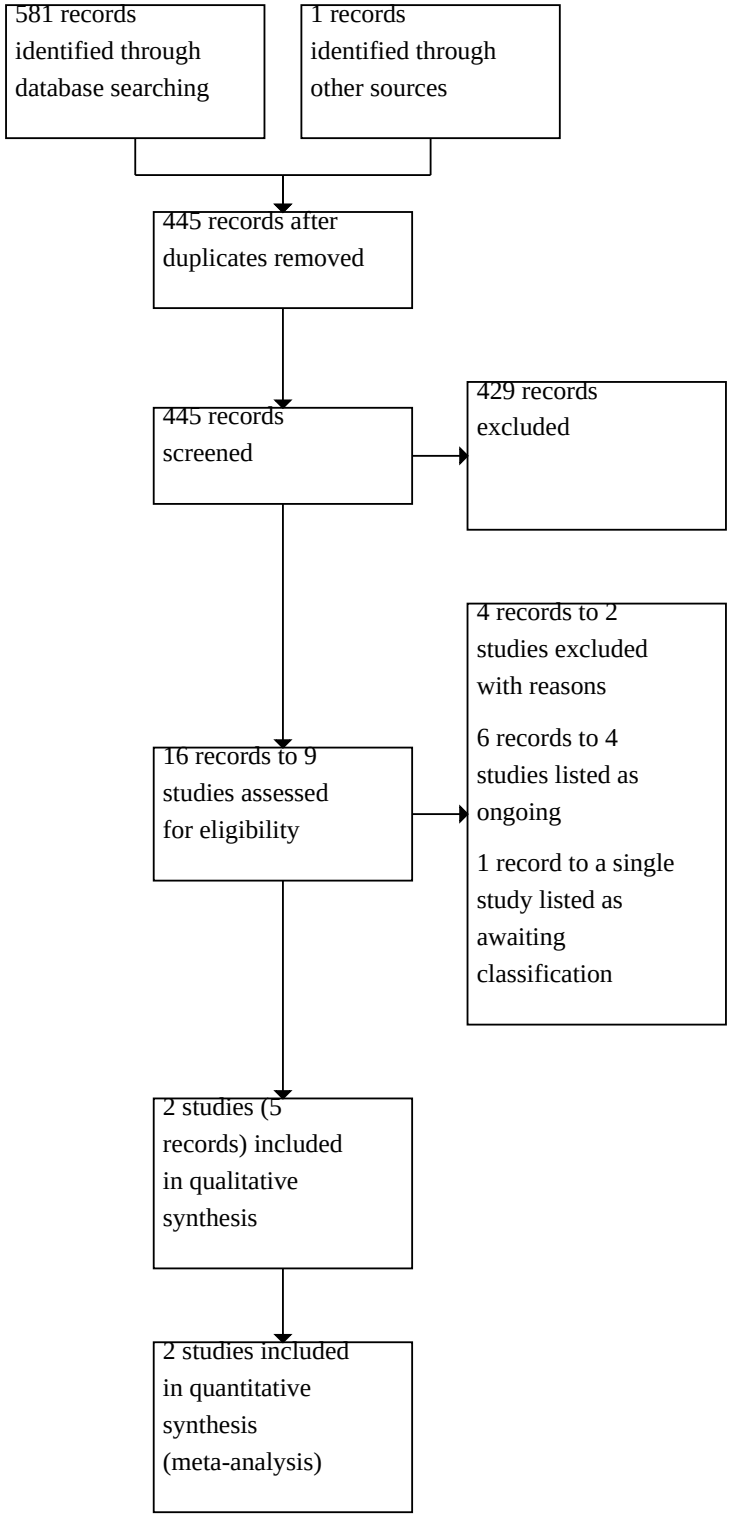
Results of the search

Two authors (MOJ and FM) independently screened the 445 unique records identified for evaluation in the searches. A total of 429 records did not meet the selection criteria on initial screening of title and abstract, and we therefore excluded these immediately. These papers did not meet the inclusion criteria to specifically assess the effectiveness of an adherence-promotion intervention for physiotherapy treatment (airway clearance and exercise therapy), but evaluated two different airway clearance interventions or exercise protocols.

We assessed 16 records of nine studies for eligibility. Of these, we have listed one study (single record) as awaiting assessment; this is an unpublished study evaluating a behavioural play intervention in children with CF (De Marchis 2017). We have listed a further four studies (six records) as ongoing trials, which are unable to be included at this time (Curran 2020; Lang 2019; NCT04249999; NCT05239611) (see below for details). The authors retrieved nine records for four completed studies and reviewed these in full (Bingham 2012; del Corral 2020; Hommerding 2015; Montero-Ruiz 2020). We subsequently included two full studies (five references) (Hommerding 2015; Montero-Ruiz 2020) and excluded two full studies (four references) (Bingham 2012; del Corral 2020).

Details of the screening process can be found in the PRISMA diagram (Figure 1).

Figure 1.



Included studies

We included two studies assessing children and adolescents with CF aged 2 to 20 years in this review (Hommerding 2015; Montero-Ruiz 2020).

Study design

Both studies were RCTs of parallel design with a duration of three months.

One study comprised two arms (Hommerding 2015), while the second study had three arms (Montero-Ruiz 2020). Power calculations were performed for both studies. In one study, the calculation was based on the physical score of the QoL questionnaire, resulting in a suggested total sample size of 30 (Hommerding 2015). In the second study, the calculation was based on the perception of time taken to complete ACT; and a total of 39 participants were deemed necessary to enable a valid response to the research question (Montero-Ruiz 2020). Both studies were single-centre; one study recruited participants from a hospital CF clinic in Rio Grande do Sul, Brazil (Hommerding 2015), and the second from a hospital paediatric pulmonology department in Malaga, Spain (Montero-Ruiz 2020).

Participants

Studies enrolled a total of 77 participants. Both studies enrolled children and adolescents with CF, with ages ranging from two to 20 years. A total of 44 participants (57%) were male. Whilst our inclusion criteria specified participants aged seven years and over, we included one study where some participants were younger than the threshold we had established (Montero-Ruiz 2020). Whilst it was not clear from the paper how many participants were younger than seven years of age, the average age of the participants in each of the groups (treatment, control and placebo) was seven or older; therefore, we decided to include the study.

One study required participants not to have had an infective exacerbation in the 15 days prior to the start of the study (Hommerding 2015). The second study reported a baseline Bhalla score of between 9 and 25 in participants (Montero-Ruiz 2020). The Bhalla score is a tool for assessing the severity and course of CF based on imaging findings; the score range is 3 to 25, where lower scores indicate more severe disease.

Interventions

One study compared a three-month educational intervention (comprising a manual of aerobic exercises, recommended exercise prescription, plus two-weekly follow-up phone calls to reinforce exercise practice) to standard verbal instructions recommending aerobic exercise in line with the CF centre protocol (Hommerding 2015). No further details of the verbal instruction were presented.

The second study assessed the use of music alongside ACTs for three months. The first group listened to specifically-composed music, the second group listened to any music of their choice which they enjoyed, and the third group completed their usual ACT routine without music (Montero-Ruiz 2020). The ACTs comprised three sections: nebuliser inhalation treatment, ACTs, and relaxation or antibiotic nebuliser treatment, if necessary. The specific ACTs used could include huffing, coughing, percussion, or vibrations. The specifically-composed music was intended to enhance enjoyment, promote relaxation, hold interest to facilitate deep breathing during nebulisation treatment, provide appropriate rhythmic support for ACTs used to aid mucus clearance, and offer a distraction from time spent on the ACT routine. It utilised instrumental music played on percussion instruments and was divided into three stages. Stage one was associated with nebulisation treatment and therefore included relaxing music (≤ 65 beats per minute (bpm), 13 minutes duration). Stage two was moderately rhythmical music used for ACT and bronchial clearance (mean 112.4 bpm, 23 minutes duration). The final stage was for relaxation and nebulisation (if required), and was a four-minute variation of stage one.

Outcomes

Both studies measured outcomes at baseline and immediately postintervention (i.e. at three months). In the educational study, self-reported data on exercise practice, regularity and interest were also collected at the two-week follow-up call (Hommerding 2015). In the music study, data were additionally collected at six weeks (Montero-Ruiz 2020). Neither of the included studies considered adherence as a primary outcome.

Only one study reported the primary outcome measure of this review (a marker of adherence) in terms of a percentage change in physical activity over time (Hommerding 2015). The music study reported adherence to ACT using the Morisky-Green Medication Adherence Scale that was adapted by the research team to consider ACT instead of pharmacotherapy. This measurement tool uses a series of questions with a yes/no dichotomous answer that reflects the patient's adherence to treatment. It is not clear from the data supplied if the 4-item or 8-item version was used, nor which cut-off scores were used to define adherent versus non-adherent participants. This study also reported on participants' enjoyment using a Likert scale with a choice of additional descriptive words and the perception of the time taken to complete their ACT alongside the actual time taken to complete the ACT (Montero-Ruiz 2020). While not reported in this review, these factors may influence adherence.

One study reported three measures of spirometry as the change from baseline: FEV_1 % predicted, FVC % predicted and FEV_1/FVC % predicted (Hommerding 2015). This study also reported measures of ergo-spirometry (heart rate at rest, oxygen saturation at rest, peak oxygen consumption, treadmill time and treadmill speed) (Hommerding 2015). The second study reported on respiratory infections requiring hospitalisation (Montero-Ruiz 2020). Hommerding 2015 also evaluated anthropometric measures (change in BMI and skinfold thickness) as well as QoL using the Cystic Fibrosis Questionnaire (CFQ) for the domains of physical, emotional, social, treatment, respiratory, vitality, health, weight, body image, nutrition, digestive and social role (Quittner 2005).

Excluded studies

We excluded two studies after a review of the full papers (Bingham 2012; del Corral 2018). One study was a cross-over RCT and therefore not eligible for inclusion (Bingham 2012). We excluded the second study as it compared different physical activity interventions and not different interventions or strategies to increase adherence (the intervention to promote adherence was the weekly telephone check which was given to both groups). Additionally, it excluded participants who were not able to attend at least 80% of the intervention sessions and participants who met

any exclusion criteria during the six weeks of the study (del Corral 2018).

Studies awaiting classification

We identified one study that is awaiting classification (De Marchis 2017). It was published as an abstract only, with limited information available. Investigators enrolled 30 children (aged 6 to 18 years) with CF that had been diagnosed with a sweat test and who were hospitalised for a pulmonary exacerbation. The children were randomly assigned to either a psychomotor intervention (games) or a physical exercise programme. Investigators assessed the six-minute walk test (6MWT), FEV_1, QoL using the revised version of the CFQ (CFQ-R; Quittner 2009) and preference using a Likert scale De Marchis 2017).

Ongoing studies

We identified four ongoing studies with published protocols but no available data (Curran 2020; Lang 2019; NCT04249999; NCT05239611).

Study design

All four ongoing trials are RCTs of parallel design based in single centres (Curran 2020; Lang 2019; NCT04249999; NCT05239611). Two are being run in Europe (Curran 2020; NCT04249999), one in Australia (Lang 2019) and one in the USA (NCT05239611). Duration of trials ranges from three months (NCT05239611) to 12 months with a further six months follow-up (Lang 2019).

Participants

One trial is in children (Lang 2019), two in adults only (Curran 2020; NCT05239611) and one in a mixed population aged from 12 to 35 years (NCT04249999). Sample size ranges from 30 participants (NCT05239611) to 110 participants (Lang 2019).

Interventions

All trials use a technological intervention (fitness tracker or telehealth platform with feedback) to standard care or fitness tracker without feedback.

Outcomes

The trials state a wide range of outcomes using different outcome measures.

Three trials are measuring lung function; three state FEV_1 (% predicted) (Curran 2020; NCT04249999; NCT05239611) and one trial additionally states FEV_1 L, FVC L and FVC % predicted (NCT04249999). One trial is measuring oxygen consumption (Curran 2020) and one trial ventilation defect percentage as detected by 129Xenon magnetic resonance imaging (MRI) (NCT05239611).

All four trials are assessing exercise: one using a daily step count and aerobic power (Curran 2020) and three using other self-reported measures of physical activity (Curran 2020; Lang 2019; NCT04249999), two using a modified SWT (Lang 2019; NCT05239611) and one formally measuring adherence to the exercise programme (NCT05239611).

Three trials are measuring some aspect of QoL: all three using the CFQ-R (Curran 2020; Lang 2019; NCT04249999), two additionally reporting on sleep quality (Curran 2020; NCT04249999), one reporting shortness of breath (Curran 2020), and the third assessing self-reported cough (Lang 2019). One trial is reporting on anxiety and depression (NCT04249999). Additionally, two trials are measuring the quality of the service or intervention (Lang 2019; NCT04249999).

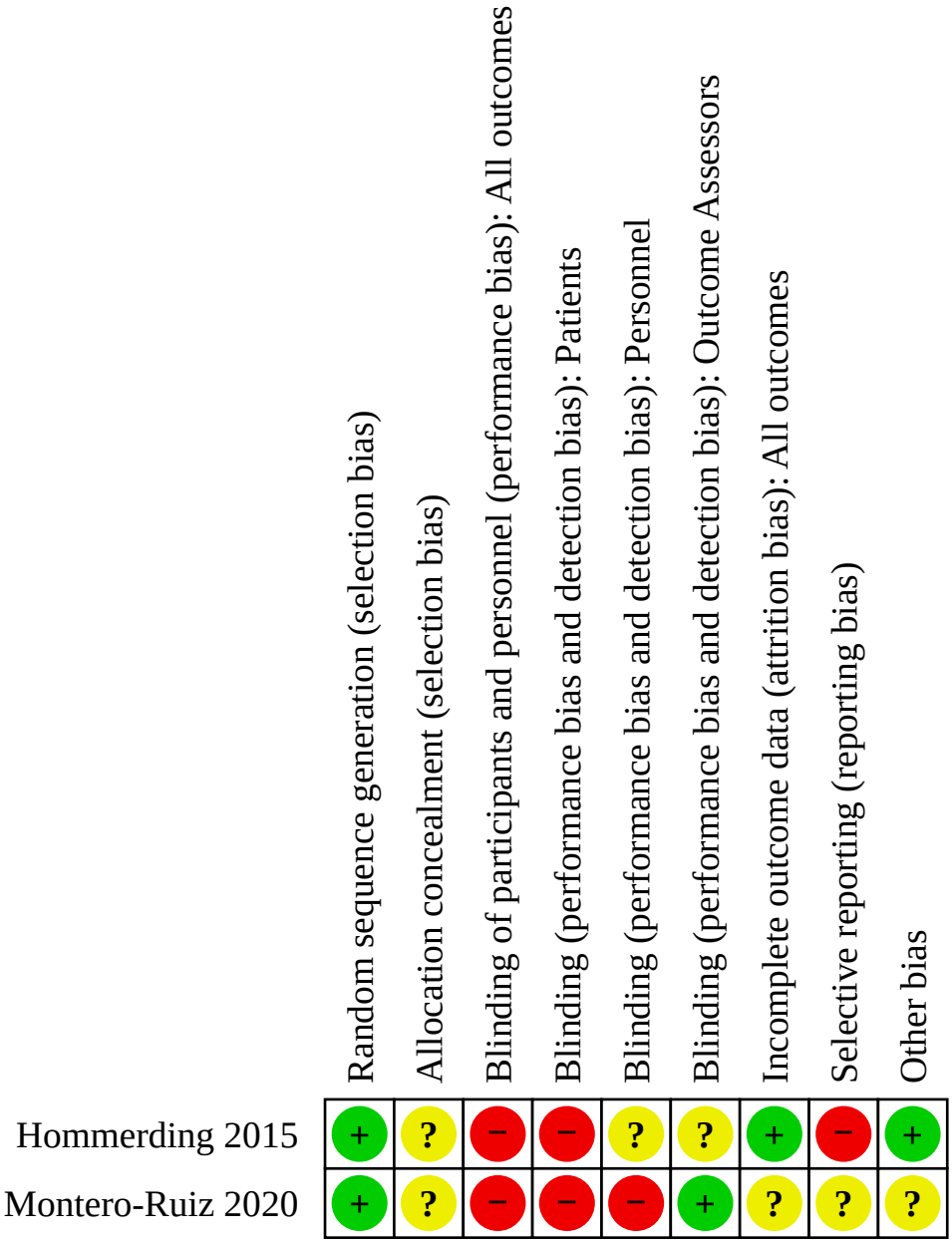
In terms of exacerbations, one trial is reporting on the time to next exacerbation (Curran 2020) and one on hospitalisations (Lang 2019).

One trial is reporting BMI and grip strength (Curran 2020). Finally, one trial is assessing economic feasibility (Lang 2019).

Risk of bias in included studies

We noted some variation in risk of bias across the two included studies. Some judgements were limited by inadequate reporting, which made determining the true quality of the study design difficult. Details are outlined in the risk of bias summary (Figure 2).

Figure 2.



Allocation

There was a low risk of allocation bias due to generation of sequence in both studies since they both used a computer-based program (Hommerding 2015; Montero-Ruiz 2020). Neither study reported details of the concealment of allocation, and we judged this domain to have an unclear risk of bias (Hommerding 2015; Montero-Ruiz 2020).

Blinding

Both studies were at high risk for blinding of the participants and personnel responsible for delivering the intervention. It was not possible to blind participants to the intervention in either study, and personnel were not blinded to participants' group allocation (Hommerding 2015; Montero-Ruiz 2020). While the lack of blinding of participants and personnel is unlikely to affect

objective outcomes such as respiratory infections, it may affect the subjective outcome measures assessed in this review.

In one study, participants in the intervention group received a manual regarding exercise prescription which the control group did not receive (Hommerding 2015). In the second study, one of the intervention groups listened to music specifically composed for the group to accompany ACT and the other group listened to their own music, while the control group did not listen to any music (Montero-Ruiz 2020).

In one study, there was low risk of blinding of outcome assessment (detection bias), as outcome assessors were blinded to group allocation (Montero-Ruiz 2020). However, in the second study, there was unclear risk of detection bias, as it was not stated if outcome assessors were blinded to group allocation (Hommerding 2015).

Incomplete outcome data

We judged one study as being at low risk of attrition bias (Hommerding 2015), while we judged the second as being at unclear risk of attrition bias (Montero-Ruiz 2020). Although both studies reported data from all participants who completed the study (Hommerding 2015; Montero-Ruiz 2020), in one study 11 participants withdrew prior to trial completion (attrition 20.4%) (Montero-Ruiz 2020). However, the authors note that this was less than the initial estimates for the study (15 participants) and withdrawals were similar across all three groups ensuring that final sample sizes were sufficiently powered (Montero-Ruiz 2020).

Selective reporting

We judged one study as being at high risk of reporting bias; this study reports on self-reported physical exercise practice, and it was not clear what unit was self-reported or how investigators evaluated these data (Hommerding 2015). We judged the second study as having an unclear risk of reporting bias, as it reported improvements in adherence, but did not present the data relating to between-group changes until requested (Montero-Ruiz 2020). Furthermore, authors did not report which version of the Morisky-Green questionnaire was used, or if it had been validated for use in this population.

Other potential sources of bias

In one study, some of the participants were below the age stated in the inclusion criteria (seven years old); however, the mean age was greater than seven (Montero-Ruiz 2020).

Effects of interventions

See: **Summary of findings 1** Motivational interventions to improve adherence to airway clearance treatment for people with CF - specifically-composed music versus no music; **Summary of findings 2** Motivational interventions to improve adherence to airway clearance treatment for people with CF - self-selected music versus no music; **Summary of findings 3** Motivational interventions to improve adherence to airway clearance treatment for people with CF - specifically-composed music versus self-selected music; **Summary of findings 4** Educational interventions to improve adherence to exercise for people with CF

Adherence to ACT

We included a single three-arm study (43 participants) of adherence to ACT, which employed a motivational intervention (Montero-Ruiz 2020). We graded the certainty of the evidence for those outcomes included in the summary of findings tables. For the definitions of these gradings, please refer to Summary of findings 1, Summary of findings 2 and Summary of findings 3.

Primary outcomes

1. Adherence

The included study did not assess our primary outcome of adherence in terms of the measures we planned (Montero-Ruiz 2020). However, it did measure adherence using the Morisky-Green questionnaire. This questionnaire was originally designed to evaluate medication adherence, but has previously been modified to assess adherence to prescribed physical activity in chronic respiratory disease (Jiménez-Reguera 2020).

Participants who received specifically-composed music were more likely to adhere at six weeks than those who received usual care (i.e. no music) (RR 1.75, 95% CI 1.07 to 2.86; Analysis 1.1). This was also true at 12 weeks (RR 1.56, 95% CI 1.01 to 2.40; very low-certainty evidence; Analysis 1.1). However, due to grading the evidence as very low certainty, we are uncertain of this effect.

There was no evidence that participants who received self-selected music were more likely to adhere to treatment compared to those who received usual care at six weeks (RR 1.44, 95% CI 0.82 to 2.52; Analysis 1.2) or 12 weeks (RR 1.03, 95% CI 0.57 to 1.86; very low-certainty evidence; Analysis 1.2).

There was no evidence that adherence differed between those who received specifically-composed music or self-selected music at six weeks (RR 1.21, 95% CI 0.87 to 1.68; Analysis 1.3) or 12 weeks (RR 1.52, 95% CI 0.97 to 2.38; very low-certainty evidence; Analysis 1.3).

Secondary outcomes

1. Frequency of hospitalisation for respiratory infection

Hospital admission data were collected for each group during the intervention period and authors calculated the number of respiratory infections requiring hospitalisation at three months (Montero-Ruiz 2020). We graded all the evidence as very low certainty. We found no evidence of a difference in the risk of hospitalisation between those in the specifically-composed music group and the usual care (i.e. no music) group (RR 0.17, 95% CI 0.02 to 1.22; Analysis 1.4). We also found no evidence of any difference in the risk of hospitalisation between those in the self-selected music group and the usual care group (RR 0.58, 95% CI 0.18 to 1.86; Analysis 1.5) or between those in the specifically-composed music group and the self-selected music group (RR 0.29, 95% CI 0.03 to 2.45; Analysis 1.6).

2. Frequency of non-hospitalised respiratory infection

Outcome not reported.

3. Lung function

Outcome not reported.

4. QoL measures using a disease-specific tool

Outcome not reported.

5. Adverse events

The authors reported that no adverse events occurred in any group during the study.

6. Exercise capacity

Outcome not reported.

Adherence to exercise

We have included one study (34 participants) in this comparison. This study compared an educational intervention to standard verbal instructions for aerobic exercise in line with the CF centre protocol (Hommerding 2015). We graded the certainty of the evidence for those outcomes included in the summary of findings tables. For the definitions of these gradings, please refer to Summary of findings 4.

Primary outcomes

1. Adherence

The included study did not formally assess our primary outcome of adherence in terms of the measures we planned. However, as a marker of adherence, data were available from self-reports of physical activity practice for the number of participants engaging in physical activity at the end of the study period, how many participants were undertaking physical activity three times per week and how many participants were undertaking at least 40 minutes of physical activity. We are uncertain whether an educational intervention leads to more participants in the intervention group undertaking increased regular physical activity at three months (self-report) (RR 3.67, 95% CI 1.24 to 10.85; very low-certainty evidence; Analysis 2.1). However, it was noted that no group data were provided relating to the n (%) who were physically active at baseline, nor to which group they were allocated. We found no evidence of any difference between groups in the number of participants undertaking physical activity three times per week (RR 1.50, 95% CI 0.51 to 4.38; Analysis 2.2) or undertaking at least 40 minutes of physical activity (RR 1.00, 95% CI 0.30 to 3.36; Analysis 2.3).

Secondary outcomes

1. Frequency of hospitalisation for respiratory infection

Outcome not reported.

2. Frequency of non-hospitalised respiratory infection

Outcome not reported.

3. Lung function

a. FEV_1 (% predicted)

There was no evidence of any difference in the change from baseline in FEV_1 % predicted between the intervention and control group at three months (MD -2.80, 95% CI -10.69 to 5.09; very low-certainty evidence; Analysis 2.4).

b. FVC (% predicted)

There was also no evidence of any difference in the change from baseline in FVC % predicted between the intervention and control group at three months (MD -2.40, 95% CI -9.02 to 4.22; very low-certainty evidence; Analysis 2.5).

c. FEV_1/FVC %

There was no evidence of any difference in the change from baseline in FEV_1 / FVC% between the intervention and control group at three months (MD -1.40, 95% CI -8.66 to 5.86; Analysis 2.6).

d. LCI

Outcome not reported.

4. QoL measures using a disease-specific tool

We found no evidence of any differences in any domain of the CFQ between intervention (IG) and control groups (CG) at three-month follow-up (very-low certainty evidence):

Domain	Median (range) score	P value
Physical	IG 0 (0 to 0) versus CG 0 (0 to 13)	P = 0.65
Emotional	IG 0 (0 to 6) versus CG 0 (8 to 0)	P = 0.10
Social	IG 0 (7 to 2) versus CG 0 (1 to 9)	P = 0.38
Treatment	IG 0 (0 to 0) versus CG 0 (16 to 0)	P = 0.65
Respiratory	IG 0 (-8 to 0) versus CG 0 (10 to 4)	P = 0.81
Vitality	IG 8 (16 to 0) versus CG 4 (14 to 22)	P = 0.28
Health	IG 0 (44 to 0) versus CG 0 (11 to 11)	P = 0.69
Weight	IG 0 (66 to 0) versus CG 0 (0 to 0)	P = 0.26
Body image	IG 0 (0 to 5) versus CG 5 (0 to 22)	P = 0.41

Nutrition	IG 0 (0 to 0) versus s CG 0 (16 to 0)	P = 0.48
Digestive	IG 0 (0 to 0) versus CG 0 (0 to 8)	P = 0.28
Social role	IG 0 (0 to 0) versus CG 0 (6 to 25)	P = 0.82

5. Adverse events

No adverse events were reported.

6. Exercise capacity

Investigators did not report on the SWT, the 6-minute walk test or the step test.

d. CPET and VO_2 peak

CPET was not reported.

There was no evidence of a difference in the change in VO_2 peak between the intervention and control group at three months (MD -1.20 mL/kg/min, 95% CI -7.26 to 4.86; very-low certainty evidence; Analysis 2.7).

DISCUSSION

The aim of this systematic review was to assess the effects of interventions to enhance adherence to ACT and exercise therapy in people with CF and their effects on health outcomes, such as pulmonary exacerbations, exercise capacity, health-related QoL, and healthcare costs.

Summary of main results

We found two small RCTs which met our inclusion criteria, one looking at adherence to ACT and the second looking at adherence to exercise (Hommerding 2015; Montero-Ruiz 2020).

Adherence to ACT

Self-reported data from a single small three-month study of 43 adolescents with CF, aged from two to 17 years suggests that the use of a motivational intervention may improve adherence to ACT (Montero-Ruiz 2020). Groups listening to the same specifically custom-composed music were more likely to adhere to treatment compared to no music or self-selected music at both six and 12 weeks (Analysis 1.1; Analysis 1.3), but there was no difference in adherence seen when comparing self-selected music to no music or when comparing the two music groups to each other (Analysis 1.2; Analysis 1.3). It should be noted, however, that in this study investigators included both ACT and inhalation therapy under the term 'physiotherapy treatment' and it is not clear which elements of the treatment (ACT or inhalation therapy) was most affected by the motivational intervention. A reduction in the frequency of respiratory infection-related hospital admission was also reported, but no difference was seen between the different groups; no data were reported on non-hospitalised respiratory infections. The authors reported that no adverse events occurred in any of the groups during the study. The study did not report on lung function, QoL, or exercise capacity (Montero-Ruiz 2020).

Adherence to exercise

Self-reported data from one small educational study in 34 children, adolescents and young adults aged 7 to 20 years with stable CF, suggests that the use of an educational intervention may be a marker to adherence to exercise therapy after three months of the intervention (Hommerding 2015). Investigators reported observing a "significant increase" in self-reported regular physical activity following the provision of verbal and written guidelines plus a two-weekly follow-up phone call to participants (n = 17) compared to initial verbal instruction alone (n = 17), and our analysis correspondingly showed results favouring guidelines plus follow-up communication (Analysis 2.1), but there was no evidence of a difference between groups in the number of participants undertaking physical activity three times per week or undertaking at least 40 minutes of activity. Eleven participants were active at baseline; however, it was noted that no group data for the number (%) who were physically active at baseline were presented. Furthermore, it is not clear which group the 11 participants we allocated to and therefore, whether any change in physical activity can be attributed to the intervention. This educational intervention also did not result in any change in lung function (FEV_1, FVC, FEV_1/FVC%), exercise capacity (VO_{2peak}), or any CF-related QoL domains (physical; emotional; social; treatment; respiratory; vitality; health; weight; body image; nutrition; digestive; social role). This study did not report on the frequency of respiratory infections (hospitalised or not) or adverse events (Hommerding 2015).

Overall completeness and applicability of evidence

Based on two small, single-centre studies whose participants were no older than 20 years of age and which both had potential risks of bias (Figure 2), it is difficult to generalise findings to the overall CF population or influence clinical practice. Results from both these studies are dependent on self-reported data, which may be unreliable. Furthermore, one study reported on the frequency of hospital admission during the three-month intervention period (Montero-Ruiz 2020), given that there may be seasonal variations in pulmonary exacerbations in CF (Chatterjee 2016), this limited time frame may not provide a comprehensive picture. Neither of the included studies followed-up participants beyond the end of the intervention, therefore no conclusions can be drawn regarding long-term effectiveness. The decision to include a study that incorporated some participants who were under seven years old may have also affected the results as younger children are more reliant on their parents for treatment and therefore any changes in behaviour will vary due to the level of parental input (Montero-Ruiz 2020). Large, multi-centred RCTs utilising objective outcomes to assess strategies to improve long-term adherence in people with CF are required, and future trials may draw on studies of adherence to physiotherapy in other populations. For example, two systematic reviews suggest that, given the unique and multidimensional nature of adherence and non-adherence, combination approaches

that are tailored to needs of individuals are more likely to be effective (McLean 2010; Peek 2016).

Quality of the evidence

We judged the certainty of the evidence to be very low across all outcomes. Small sample sizes and often unclear or high risk of bias were evident in both studies. The nature of the interventions limited the ability of investigators to blind participants and clinicians in both studies, although one study used a blinded non-clinical assessor (Montero-Ruiz 2020). The review authors note that self-reported levels of exercise practice may be biased. Additionally, self-reported physical activity practice across the wide age range of study participants may be inconsistent and should be interpreted with caution.

We graded the outcomes reported in the trial of adherence to ACT as very low-certainty evidence across all comparisons (Summary of findings 1; Summary of findings 2; Summary of findings 3). Reasons for downgrading the certainty of the evidence included risk of bias across several domains (lack of blinding, allocation concealment, selective reporting, and incomplete outcome data) as well as imprecision (small participant numbers), and indirectness (only children and adolescents included). Furthermore, while the Montero-Ruiz 2020 study reported improvements in adherence (a primary outcome of this review), the outcome measure used (Morisky-Green Questionnaire) had not been identified in our list of predetermined methods of measuring adherence (Jones 2020). Additionally, it was not clear which version of the questionnaire was used, or if the tool had been validated for use in this population.

All review outcomes for the adherence to exercise study were identified as very low-certainty evidence due to risk of bias (lack of blinding and allocation concealment), indirectness (only children and adolescents included and the study only measured one type of ACT - exercise), and imprecision (small participant numbers); study numbers were not identified by power calculation, but were based on the difference of the physical score in a quality of life questionnaire from a previous study (Klijn 2004) (Summary of findings 4). The study provided no data on the primary outcomes of interest to this review and, to date, obtaining additional data from this group of authors has not been possible (Hommerding 2015).

Potential biases in the review process

The authors have no conflict of interest regarding the undertaking of this systematic review. The range of comprehensive searches is not likely to have left any relevant studies unidentified.

Agreements and disagreements with other studies or reviews

This is the first systematic review or review paper to assess the effects of interventions to enhance adherence to ACT and exercise therapy in people with CF and their effects on health outcomes.

There is one systematic review, however, which explored interventions to promote adherence to physiotherapist-prescribed self-management in a range of conditions, including musculoskeletal conditions, urinary incontinence, haemophilia, postoperative surgery and chronic obstructive pulmonary disease (Peek 2016). The authors concluded that approaches such as activity monitor use (plus feedback system), written exercise instructions, behavioural exercise programmes (with booster sessions) and goal setting strategies may be effective in promoting adherence to exercise. Both the Peek 2016 review and a systematic review of interventions for enhancing adherence with physiotherapy by McLean 2010 suggest that, given the unique and multidimensional nature of adherence and non-adherence, combination approaches that are tailored to needs of individuals are more likely to be effective (McLean 2010; Peek 2016).

A recent multicentre RCT (CF HealthHub) evaluated whether a multicomponent self-management intervention to promote adherence to inhaled mucoactive agents and antibiotics (conjunctive prescribed therapy to ACT), would reduce the number of exacerbation over a 12-month period in individuals with CF (aged 16 years and over) (Wildman 2022). The intervention group used data-logging nebulisers on a digital platform combined with behavioural change sessions with trained clinical interventionists compared to usual care (data-logging nebulisers). The intervention did not achieve a statistical difference in pulmonary exacerbations or FEV_1, but the authors reported increased objectively measured adherence in this group.

The ongoing Fizzyo Project is a longitudinal observational cohort multicentre trial which will analyse longitudinal data from innovative technology (feedback from ACT-gaming) used in daily physiotherapy treatments in 45 children and young people with CF aged 6 to 16 years over a 16-month period (Raywood 2020). The primary aim is to measure adherence and, secondarily, prospectively evaluate spirometry, exercise capacity, QoL and longitudinal clinical outcomes. While not eligible for inclusion in this review due to the study design, its findings may add context to the current review.

AUTHORS' CONCLUSIONS

Implications for practice

The papers included in this review provide very limited and very low-certainty evidence; however, results suggest improved adherence to airway clearance techniques (ACTs) and physical activity, no evidence of a difference in the frequency of hospitalisation due to respiratory infection where educational (written handbook) or motivational (custom composed music) strategies are used, which may or may not be due to the intervention. The data are currently very limited, and methodological issues mean that findings should be interpreted with a high degree of caution. Given these limitations, it is not currently possible to make robust recommendations for practice. In the absence of relevant data, clinicians should adopt strategies to promote adherence to ACTs and exercise or physical activity based on local guidance and clinical practice guidelines and standards such as those published by the Association of Chartered Physiotherapists in Cystic Fibrosis, (CF Trust 2020). These strategies may involve psycho-educational, psychotherapeutic, motivational or organisational approaches, but should always be underpinned by an understanding of the individual's adherence patterns (CF Trust 2020). People with cystic fibrosis (CF), and their families, should be actively involved in the design of the physiotherapy treatment regimen to ensure a person-centred prescription that is underpinned by the individual's beliefs and personal experiences (Ward 2019).

Implications for research

This review has highlighted the ongoing need for high-quality studies, such as randomised controlled trials (RCTs) and quasi-RCTs, that evaluate the effectiveness of interventions designed to improve long-term adherence to ACTs and exercise or physical activity in people with CF. Robust measurement of treatment adherence should be a key consideration. Objective measures of adherence should be reported, including electronically captured data using activity monitors or modified ACT devices (or both), or exercise games (Bingham 2012; Ward 2020). Adherence measurement tools should also be validated for use with people with CF. These approaches mitigate the risk of social desirability or recall bias which are known to be significant using self-report tools and diary data (Adams 2005; Hoo 2014). Self-report tools may be considered in conjunction with objective measures, but researchers should consider real time options such as patient report apps, or psychometrically validated tools (del Corral 2020).

Whilst this review considered only two eligible studies, it is evident there is increasing interest in evaluating strategies to improve adherence to airway clearance and exercise in people with CF, as demonstrated by the identification of four ongoing trials (Curran 2020; Lang 2019; NCT04249999; NCT05239611).

Future RCTs may draw on studies of adherence to physiotherapy in other populations. For example, a systematic review explored interventions to promote adherence to physiotherapist-prescribed self-management in a range of conditions, including musculoskeletal conditions, urinary incontinence, haemophilia, postoperative surgery and chronic obstructive pulmonary disease (Peek 2016). The authors concluded that approaches such as activity monitoring (plus feedback system), written exercise instructions, behavioural exercise programmes (with booster sessions) and goal setting strategies may be effective in promoting adherence to exercise. The authors noted, however, that all studies used exercise adherence as an outcome, rather than considering other aspects of physiotherapy self-management.

Given the progressive nature of CF, researchers should also consider secondary outcome measures such as frequency of respiratory infection, lung function, quality of life (QoL) measures and exercise capacity. Follow-up periods should be scheduled to ensure that longer-term adherence (beyond six months) is reported.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Hommerding 2015

Study characteristics	
Methods	RCT Design: parallel Duration: 3 months Location: single centre, CF outpatient clinic, Hospital Sao Lucas, Rio Grande do Sul, Brazil
Participants	34 participants: CF adolescents aged 7 to 20 years with no infective exacerbation in the last 15 days. There were no significant difference in characteristics at baseline. Intervention group (n = 17) Age, mean (SD): 13.4 (2.8) years Sex, 58.8% male $FEV_{1,}$ mean(SD): 95.5 (17.9) % predicted Weight, mean (SD): 46.1 (14.0) kg Regular physical activity, n (%): 6 (35.2) Peak VO_2, mean (SD): 34.9 (9.0) mL/kg/min Control group (n = 17) Age, mean (SD): 12.7 (3.3) years Sex, 58.8% male $FEV_{1,}$ mean (SD): 100.1 (21.2) % predicted Weight, mean (SD): 45.0 (16.6) kg Regular physical activity, n (%): 4 (23.5) Peak VO_2, mean (SD): 33.2 (8.2) mL/kg/min
Interventions	**Intervention group:** exercise prescription plus manual with aerobic physical activity guidelines such as jogging, swimming, walking, plus instructions for stretching upper and lower extremities and the trunk. There were no recommendations for exercise intensity. Participants were told to practice the exercise modality they preferred at a minimum frequency of 2 times/week for at least 20 minutes, and to record the frequency, duration and type of physical activity performed. 2-weekly follow-up phone calls were made to reinforce exercise practice. **Control group:** verbal instruction regarding aerobic exercise in line with CF centre protocol on day of study inclusion.
Outcomes	Measurements were taken at baseline and 3 months Physical activity: regularity (%), frequency (3 x a week) and duration (at least 40 mins) Spirometry: FEV_1 (% predicted) FVC (% predicted) FEV1/FVC%, $FEF_{25-75\%}$ Anthropometric evaluation: BMI z-score, triceps skin fold thickness QoL: the CF questionnaire for QoL

Hommerding 2015 *(Continued)*

	Ergo-spirometry: HR, SaO_2, peak VO_2, treadmill time, treadmill speed
Notes	No mention of funding source, but authors stated no interests to declare.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computer-based program was used for randomisation (Random Allocation Software 1.0, developed by M. Saghaei MD, Department of Anesthesia, University of Medical Sciences, Isfahan, Iran) in blocks of 6 participants, who were assigned to either the intervention (group 1) or the control (group 2).
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Self-reported record of frequency, duration and type of physical activity performed kept by intervention group. Authors acknowledge risk of bias with levels of physical activity practice as intervention group had to confirm their aerobic exercise practice during follow-up phone calls.
Blinding (performance bias and detection bias) Patients	High risk	Authors acknowledge risk of bias with levels of physical activity practice as intervention group had to confirm regular aerobic exercise practice during follow-up phone calls. It was not possible to blind participants to which group they were in due to the differing interventions, and while a lack of blinding is unlikely to affect objective outcomes such as respiratory infections, it may affect subjective outcomes of which there are several in this review.
Blinding (performance bias and detection bias) Personnel	Unclear risk	Not reported.
Blinding (performance bias and detection bias) Outcome Assessors	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	34 participants started and completed the study. All participants' data included in analysis.
Selective reporting (reporting bias)	High risk	Only dara for self-reported physical exercise practice were collected. Unclear what unit was self-reported or how investigators evaluated these data. Percentage change in between-group physical activity reported.
Other bias	Low risk	No other risks of bias noted.

Montero-Ruiz 2020

Study characteristics

Methods	RCT Design: parallel Duration: 3 months Location: single centre, Paediatric Pulmonology Centre, Malaga Regional Hospital, Spain

Montero-Ruiz 2020 *(Continued)*

Participants	There were no significant differences in characteristics at baseline. 43 adolescents with CF, age range 2 to 17 years Treatment group (n = 15) Age, mean (SD): 7.93 (4.7) years Sex male, N (%): 10 (66.7) Bhalla score, median (SD), range: 18.9 (4.7), 9 to 24 BMI, median (SD), range: 16.9 (2.2), 12.8 to 19.6 ACT frequency per day, median (SD), range: 1.4 (0.5), to 1 to 2 ACT duration, median (SD), range: 27.3 (3.4), 10 to 60 min Placebo group (n = 13) Age, mean (SD): 8.13 (5.6) years Sex male, N (%): 9 (69.2) Bhalla score, median (SD), range: 18.5 (4.7), 10 to 25 BMI, median (SD), range: 16.3 (2.2), 12.1 to 19.1 ACT frequency per day, median (SD), range: 1.4 (0.5), 1 to 2 ACT duration, median (SD), range: 22.4 (3.7), 10 to 45 min Control group (n = 15) Age, mean (SD): 7.2 (4.3) years Sex male, N (%): 8 (53.3) Bhalla score, median (SD), range: 19.4 (3.8), 13 to 25 BMI, median (SD), range: 16.6 (1.7), 13.7 to 19.4 ACT frequency per day, median (SD), range: 1.3 (0.5), 1 to 2 ACT duration, median (SD), range: 26.0 (3.4), 10 to 60 min
Interventions	**Treatment group:** use of music specifically composed for the treatment group used as an adjunct to ACT routine **Placebo group:** use of self-selected music enjoyed by the participant as an adjunct to ACT routine **Control group:** standard practice of ACT routine (no music) ACT defined as comprising 3 sections: nebuliser inhalation treatment, ACTs and relaxation or antibiotic nebuliser treatment, if necessary
Outcomes	Measurements taken at baseline (face to face), 6 weeks and 12 weeks (telephone) Enjoyment and perception of time using validated questionnaires (Likert scale and choice of 3/12 descriptive words) Perception of time measured as the difference between actual time to complete ACT versus subjective perception of time to complete ACT Respiratory infection requiring hospitalisation measured by frequency and days of hospitalisation for the 3 months before the trial and the 3 months during the trial Time to complete ACT routine in minutes* Morisky-Green questionnaire of medication adherence* *results from these outcome measures received on request from authors
Notes	This research was funded by the project PIN-0342-2016 from Consejeria de Salud de la Junta de Andalucia and Plan Propio de Investigacion de la Universidad de Malaga. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Risk of bias

Bias	Authors' judgement	Support for judgement

Montero-Ruiz 2020 *(Continued)*

Random sequence generation (selection bias)	Low risk	The participants were randomly allocated using the 'Subjects assignment to treatment' module of the software for the epidemiologic analysis of tabulated data Epidat.
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded to study objective.
Blinding (performance bias and detection bias) Patients	High risk	Participants not blinded.
Blinding (performance bias and detection bias) Personnel	High risk	Personnel not blinded.
Blinding (performance bias and detection bias) Outcome Assessors	Low risk	Outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	11 participants withdrawn before trial completion: n = 3 unable to be contacted by telephone; n = 2 rejected consent; n = 6 failed to comply with the study protocol for their group. Whilst the authors reported the reasons for withdrawal, it is unclear how these were distributed across the 3 groups.
Selective reporting (reporting bias)	Unclear risk	Study registry indicated adherence to ACT would be measured, but these data were not included in the published paper and had to be requested. Also, authors did not report which version of the Morisky-Green questionnaire was used, or if it had been validated for use in this population.
Other bias	Unclear risk	Not all participants met the inclusion criteria of aged 7 years or more. No details provided regarding the number of participants who were aged less than 7 years. Mean age of participants was, however, over 7 years old.

ACT: airway clearance techniques
BMI: body mass index
CF: cystic fibrosis
$FEF_{25-75\%}$: forced expiratory flow from 25% to 75% of vital capacity
FEV_1: forced expiratory volume at 1 second
FVC: forced vital capacity
HR: heart rate
QoL: quality of life
RCT: randomised controlled trial
SaO_2: oxygen saturation
SD: standard deviation
VO_2: oxygen consumption
vs: versus

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

Study	Reason for exclusion
Bingham 2012	A cross-over RCT
del Corral 2018	This study compared different physical activity interventions and not different interventions or strategies to increase adherence (the intervention to promote adherence was the weekly telephone check, which was given to both groups). Additionally, it excluded participants who were not able to attend at least 80% of the intervention sessions.

RCT: randomised controlled trial

Characteristics of studies awaiting classification *[ordered by study ID]*

De Marchis 2017

Methods	RCT In hospital Duration: 14 days
Participants	30 children with CF (diagnosis confirmed using sweat test), aged 6 to 18 years and hospitalised for a pulmonary exacerbation.
Interventions	Intervention: psychomotor intervention ("animal games" (jumping like a rabbit, then like a kangaroo…), circuit routes with different materials, traditional games (cherry picking, cops and robbers…)). Control: exercise programme.
Outcomes	6MWT, FEV_1, CFQ-R, preference via Likert scale. All measurements were performed at admission and at discharge.
Notes	

6MWT: 6-minute walk test
CF: cystic fibrosis
CFQ-R: Cystic Fibrosis Questionnaire - Revised
FEV_1: forced expiratory volume in 1 second
RCT: randomised controlled trial

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

Curran 2020

Study name	Steps Ahead: optimising physical activity and health in adults with CF
Methods	RCT Parallel design Duration: 6 months Single centre: Limerick, Ireland
Participants	60 clinically stable adults (over 18 years) of both sexes with CF and access to a smartphone/tablet to access and upload to Fitbit Application.

Curran 2020 *(Continued)*

Interventions	Intervention: goal setting via fitness tracker and text message. Control: fitness tracker only.
Outcomes	**Primary outcomes**: change in FEV_1 (% predicted), change oxygen uptake (% predicted), change in daily step count. All measured at baseline, 3 months and 6 months. **Secondary outcomes**: change in maximal aerobic power (% predicted), change in FVC (% predicted), change in grip strength, change in BMI (kg/m^2), change in muscle mass (kg), change in % body fat, change in CFQ-R (domains: physical, role/school, vitality, emotion, social, body image, eating, treatment burden, health perceptions; symptom scales: weight, respiratory, and digestion), change in self-reported physical activity (International Physical Activity Questionnaire Short Form), Pittsburgh Sleep Quality Index, University of California San Diego Shortness of Breath Questionnaire, change in wellbeing (Alfred Wellness Score), change in number of minutes spent in moderate to vigorous physical activity. All measured at baseline, 3 months and 6 months. **Other outcomes**: time to exacerbation (measured at baseline to 3 months and baseline to 6 months), semi-structured interviews (measured at 6 months).
Starting date	1 October 2018.
Contact information	Principal Investigators: Roisin Cahalan, PhD (University of Limerick) and Audrey Tierney, PhD (University of Limerick) Contact: Roisin Cahalan, PhD; +353 61 202959 ext +35361202959; roisin.cahalan@ul.ie Contact: Maire Curran, BSc; +353 61 482151 ext +35361202959; maire.curran@ul.ie
Notes	Estimated completion date: 28 June 2020. Currently, website states still recruiting.

Lang 2019

Study name	CyFiT telehealth: protocol for RCT of an online outpatient physiotherapy service for children with CF
Methods	RCT Parallel design (non-inferiority trial) Duration: 12-month intervention and further follow-up at 6 months Single centre in Australia
Participants	110 children (boys and girls) medically diagnosed with CF, aged 8 to 18 years.
Interventions	Intervention: enhanced interactive telehealth rehabilitation plus activity tracker. Control: face-to-face, telephone or standard telehealth. All participants will partake in 4 1-hour assessment sessions taking place on a 6-monthly basis from the commencement of the study: initial (0 months), 6 months, 12 months, and 6 months follow-up (i.e. 18 months after initial commencement).
Outcomes	**Primary outcome**: CFQ-R (measured every 6 months for 18 months) **Secondary outcomes**: modified SWT, medical record information, self-reported cough and CAPE and PAC activity questionnaires, adherence to exercise therapy, clinical consultation visits (at 12

Lang 2019 *(Continued)*

	months), CAPE-PAC assessment of participation in activities of daily living (every 6 months for 18 months), economic feasibility (using medical records and information such as time off work/school for clinical visit, travel costs, cost of equipment/connection costs to determine an overall cost of service; this will then be analysed in context of all other outcome measures such as quality of life (CFQ-R), physical function (modified SWT), and participation (CAPE-PAC and Life-H Assessment) to enable the calculation of quality-adjusted life years and enable cost-utility and/or cost-benefit statistical analysis), hospitalisation rate (number of inpatient days during the 12 months period of intervention), MPOC assessment (quality of the health service from a participant perspective; measured every 6 months), modified SWT (measured every 6 months), self-reported activity and cough questionnaire (measured weekly across 12 months).
Starting date	5 February 2018
Contact information	Mr Ray Lang School of Health and Rehabilitation Sciences Building 84A The University of Queensland St Lucia, Queensland, 4072 Australia Telephone: +614 22 193 168 Email: lei.lang@uqconnect.edu.au
Notes	Monetary support from Health Practitioner Research Scheme 2017 Funding Round - Department of Health Allied Health Professions' Office of Queensland (Queensland Health).

NCT04249999

Study name	ActivOnline: physical activity in CF trial UK (ActiOnPACTUK)
Methods	RCT Parallel design Duration: 3 months intervention with additional 3-month follow-up Single centre: Exeter, UK
Participants	94 people of both sexes with CF, aged 12 to 35 years. Need access to the internet via computer or mobile device.
Interventions	Intervention: behavioural intervention (access to online physical activity platform (www.activonline.com.au)) in addition to usual care. Control: usual care.
Outcomes	**Primary outcome**: change in physical activity objectively measures using ActiGrpah GT9X Link accelerometer, change in physical activity subjectively measured using the Habitual Activity Estimation Scale. All measured at baseline, 3 months and 3 months postintervention. **Secondary outcomes**: change in FEV_1 (L), change in FVC (L), change in FEV_1 (% predicted), change in FVC (% predicted), change in exercise attitudes measured using the Behavioural Regulation in Exercise Questionnaire, change in quality of life measured using age-specific CFQ-R, change in anxiety measured using Hospital Anxiety and Depression Scale, change in depression measured using Hospital Anxiety and Depression Scale, change in depression measured using Center for Epidemiological Studies-Depression Scale, change in sleep quality measured using Pittsburgh Sleep Quality Index. All measured at baseline, 3 months and 3 months postintervention. **Other outcomes**: qualitative assessment of barriers and facilitators to physical activity (measured at 3 months postintervention), qualitative assessment of Activ Online programme (measured at 3 months postintervention), usage of Activ Online programme (measured at 3 months), changes in physical activity, measured by Sport England Short Active Lives Survey (measured at 3 months and

NCT04249999 *(Continued)*

	3 months postintervention), changes in physical activity, measured by Sport England Engagement in Sport Questions (measured at 3 months and 3 months postintervention).
Starting date	7 May 2020
Contact information	Contact: Owen W Tomlinson, PhD; +44(0)1392727049; o.w.tomlinson@exeter.ac.uk. Principal Investigator: Craig A Williams, PhD; University of Exeter.
Notes	UPDATE JUNE 2021: Due to ongoing restrictions placed upon research by the global COVID-19 pandemic, modifications to the protocol are necessary. Recruitment and consenting will now take place online, and testing procedures will be completed by participants in their own homes. The nature, and length, of intervention remains unchanged.

NCT05239611

Study name	Feasibility of home-based exercise program for adults with cystic fibrosis
Methods	Feasibility RCT. Parallel design. Duration: 3 months. Single centre: Kansas, USA.
Participants	30 adults with CF aged 18 years and older; both sexes. Stable clinical condition and with access to internet. Not involved in an exercise intervention in the previous 6 months, and not performing structured exercise > 150 minutes per week.
Interventions	Intervention: weekly exercise coaching sessions via telehealth platform, an app and phone, text or email support. Control: usual care.
Outcomes	**Primary outcomes**: modified SWT (at 3 months), ventilation defect percentage as detected by 129Xenon MRI (at 3 months). **Secondary outcomes**: FEV_1 (measured at baseline and 3 months), CFQ-R (measured at 3 months), weekly adherence to prescribed exercise as % prescribed exercise time completed.
Starting date	14 February 2022
Contact information	Contact: Joel Mermis MD, +9135886045, jmermis@kumc.edu; Dave Burnett PhD, 913-588-9499, dburnett@kumc.edu. Principal Investigator: Dave Burnett
Notes	

BMI: body mass index
CAPE: Children's Assessment of Participation and Enjoyment
CF: cystic fibrosis
CFQ-R: Cystic Fibrosis Questionnaire - Revised
FEV_1: forced expiratory volume at 1 second
FVC: forced vital capacity
MPOC: Measure of Processes of Care

MRI: magnetic resonance imaging
PAC: Preferences for Activity of Children
RCT: randomised controlled trial
SWT: shuttle walk test

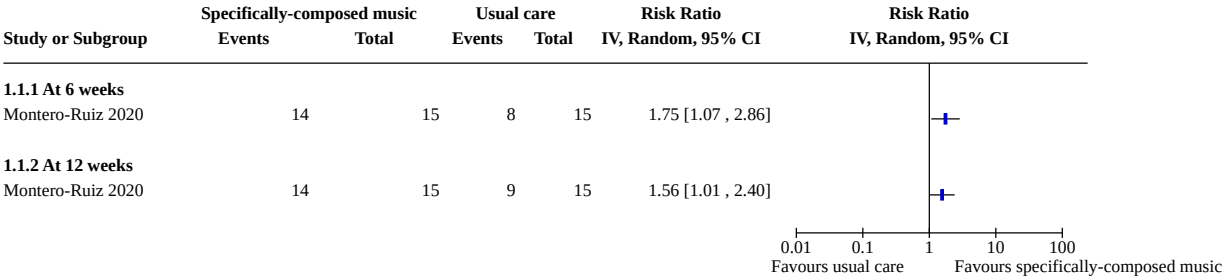
DATA AND ANALYSES

Comparison 1. Adherence to ACT

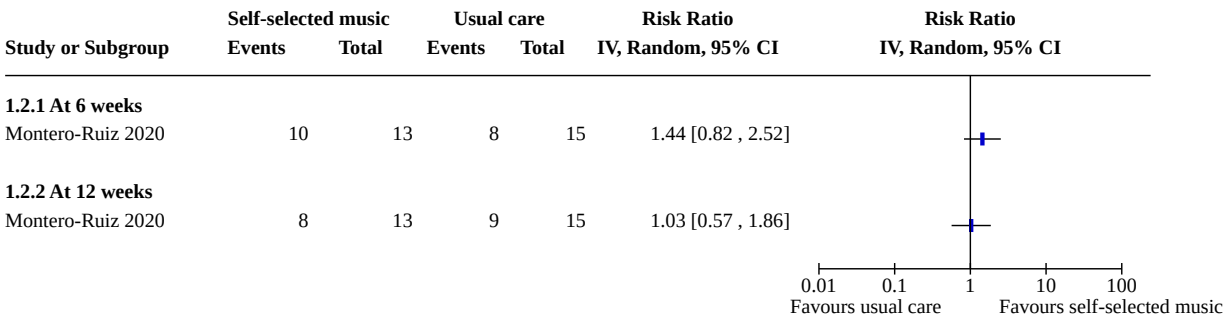
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Morisky-Green questionnaire - specifically-composed music versus usual care	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.1.1 At 6 weeks	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.1.2 At 12 weeks	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.2 Morisky-Green questionnaire - self-selected music versus usual care	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.2.1 At 6 weeks	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.2.2 At 12 weeks	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.3 Morisky-Green questionnaire - specifically-composed music versus self-selected music	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.3.1 At 6 weeks	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.3.2 At 12 weeks	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.4 Hospitalisation - specifically-composed music versus usual care	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.4.1 Medium term	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.5 Hospitalisation - self-selected music versus usual care	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.5.1 Medium term	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.6 Hospitalisation - specifically-composed music vs self-selected music	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.6.1 Medium term	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected

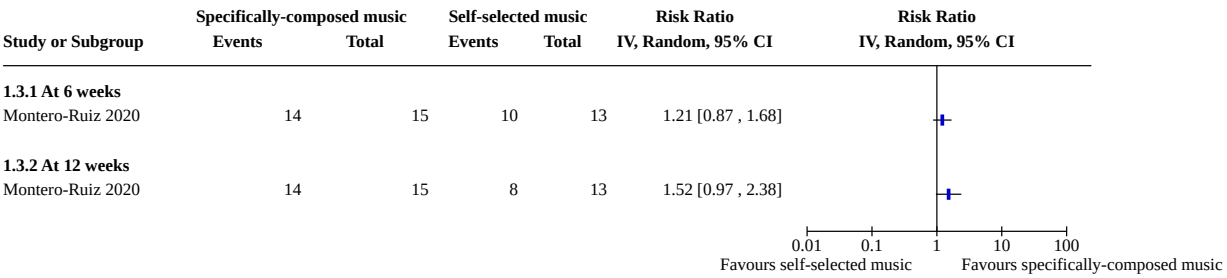
Analysis 1.1. Comparison 1: Adherence to ACT, Outcome 1: Morisky-Green questionnaire - specifically-composed music versus usual care



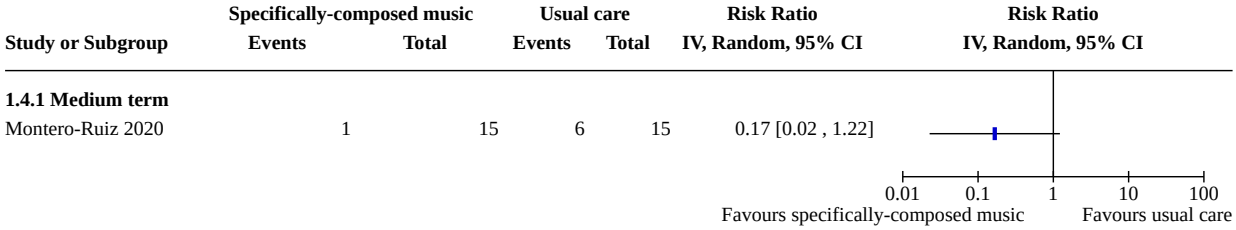
Analysis 1.2. Comparison 1: Adherence to ACT, Outcome 2: Morisky-Green questionnaire - self-selected music versus usual care



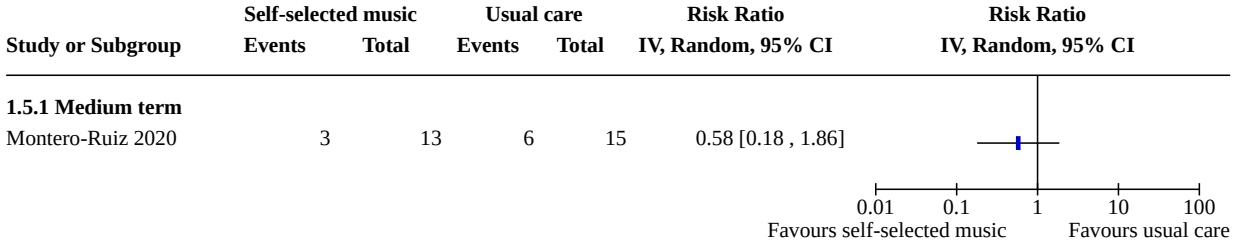
Analysis 1.3. Comparison 1: Adherence to ACT, Outcome 3: Morisky-Green questionnaire - specifically-composed music versus self-selected music



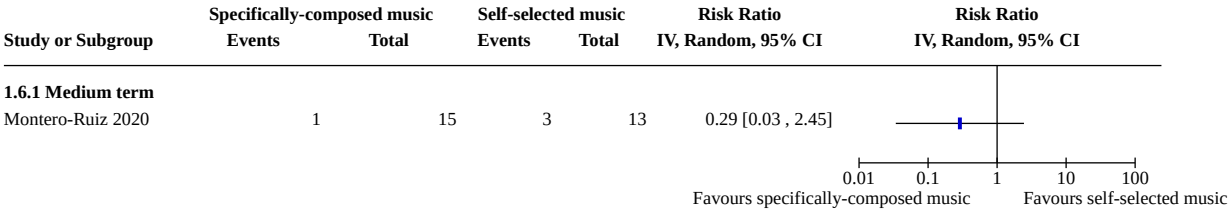
Analysis 1.4. Comparison 1: Adherence to ACT, Outcome 4: Hospitalisation - specifically-composed music versus usual care



Analysis 1.5. Comparison 1: Adherence to ACT, Outcome 5: Hospitalisation - self-selected music versus usual care



Analysis 1.6. Comparison 1: Adherence to ACT, Outcome 6: Hospitalisation - specifically-composed music vs self-selected music

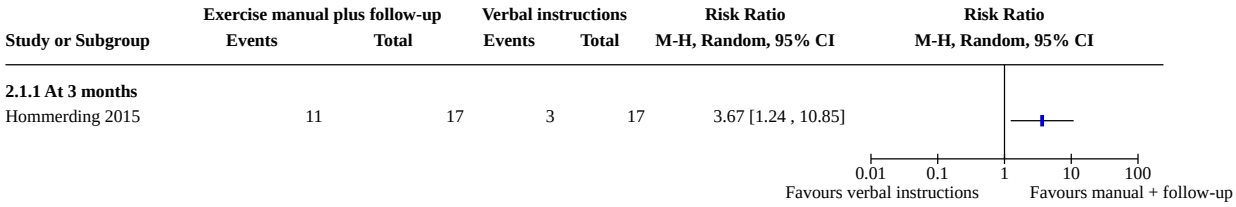


Comparison 2. Adherence to exercise

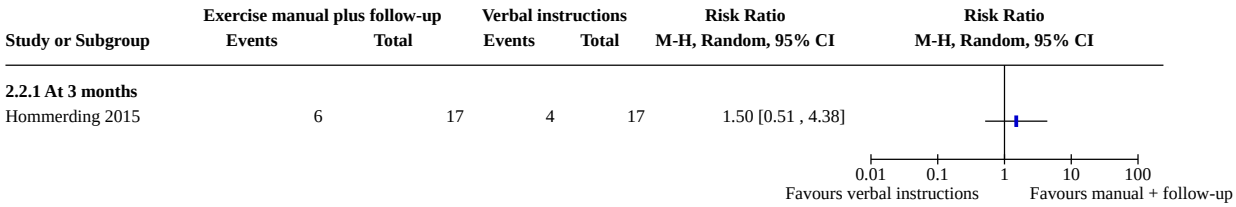
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Participants undertaking physical activity	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1.1 At 3 months	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.2 Participants undertaking activity 3x per week	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.2.1 At 3 months	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.3 Participants undertaking at least 40 mins exercise/week	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.3.1 At three months	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4 FEV_1 % predicted (change from baseline)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.4.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5 FVC % predicted (change from baseline)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.6 FEV_1/FVC % (change from baseline)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.6.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.7 VO_2 peak (change from baseline)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.7.1 At 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 2.1. Comparison 2: Adherence to exercise, Outcome 1: Participants undertaking physical activity

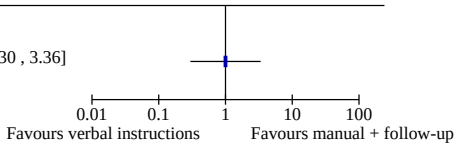


Analysis 2.2. Comparison 2: Adherence to exercise, Outcome 2: Participants undertaking activity 3x per week



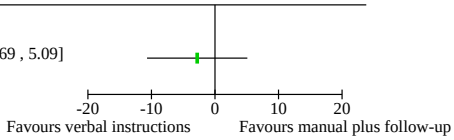
Analysis 2.3. Comparison 2: Adherence to exercise, Outcome 3: Participants undertaking at least 40 mins exercise/week

Study or Subgroup	Exercise manual plus follow-up Events	Total	Verbal instructions Events	Total	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
2.3.1 At three months						
Hommerding 2015	4	17	4	17	1.00 [0.30 , 3.36]	



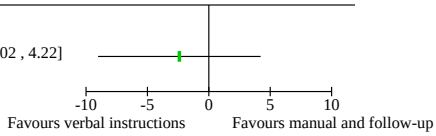
Analysis 2.4. Comparison 2: Adherence to exercise, Outcome 4: FEV_1 % predicted (change from baseline)

Study or Subgroup	Exercise manual plus follow-up Mean	SD	Total	Verbal instructions Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
2.4.1 At 3 months								
Hommerding 2015	-1.8	8.6	17	1	14.2	17	-2.80 [-10.69 , 5.09]	



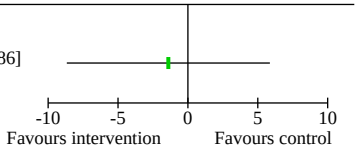
Analysis 2.5. Comparison 2: Adherence to exercise, Outcome 5: FVC % predicted (change from baseline)

Study or Subgroup	Exercise manual plus follow-up Mean [%]	SD [%]	Total	Verbal instructions Mean [%]	SD [%]	Total	Mean Difference IV, Random, 95% CI [%]	Mean Difference IV, Random, 95% CI [%]
2.5.1 At 3 months								
Hommerding 2015	-0.4	6.7	17	2	12.2	17	-2.40 [-9.02 , 4.22]	



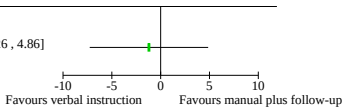
Analysis 2.6. Comparison 2: Adherence to exercise, Outcome 6: FEV_1/FVC % (change from baseline)

Study or Subgroup	Exercise manual plus follow-up Mean	SD	Total	Verbal instructions Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
2.6.1 At 3 months								
Hommerding 2015	-0.4	7.7	17	1	13.2	17	-1.40 [-8.66 , 5.86]	



Analysis 2.7. Comparison 2: Adherence to exercise, Outcome 7: VO_2 peak (change from baseline)

Study or Subgroup	Exercise manual plus follow-up Mean [mL/kg/min]	SD [mL/kg/min]	Total	Verbal instructions Mean [mL/kg/min]	SD [mL/kg/min]	Total	Mean Difference IV, Random, 95% CI [mL/kg/min]	Mean Difference IV, Random, 95% CI [mL/kg/min]
2.7.1 At 3 months								
Hommerding 2015	1.1	4.6	17	2.3	11.9	17	-1.20 [-7.26 , 4.86]	



APPENDICES

Appendix 1. Additional electronic search strategies

Database	Date(s) searched	Search strategy
Cochrane Cystic Fibrosis and Genetic Disorders Review Group's Cystic Fibrosis Trials Register	1 March 2023	(physiotherapies & exercising AND treatment adherence):kw
Scopus Elsevier	1823 to 28 February 2023	[Advanced Document Search] (TITLE-ABS-KEY (cystic AND fibrosis OR mucoviscidosis OR mucoviscidose)) AND (TITLE-ABS-KEY (((physical PRE/0 (therap* OR activit*)) OR exercis* OR "airway clearance" OR act OR sport* OR train* OR retrain* OR condition* OR strength* OR fitness OR danc* OR aerobic OR treadmill OR walk* OR running OR cycl* OR bicyc* OR swim* OR trampolin OR yoga OR pilates OR tai AND chi OR taichi OR stretch* OR physiotherap* OR physio OR vibrat* OR percussi* OR acapella OR oscillat* OR {positive expiratory pressure} OR pep OR {active cycle breathing technique} OR act OR drainage OR "bilevel positive airway pressure" OR bipap OR {expiratory positive airway pressure} OR epap OR cornet OR expiration OR huff OR hydro-acoustic OR hydroacoustic OR massag* OR manoeuvr*))) AND (TITLE-ABS-KEY (adhere OR adherence OR adhered OR nonadherence OR persist OR persistance OR persisted OR compliance OR comply OR complied OR noncompliance OR concordance OR nonconcordance OR cooperative OR cooperation OR cooperate OR cooperated OR uncooperative OR conform*))
Medline Ovid	1946 to 24 February 2023	[Advanced Search] 1 (cystic fibrosis or mucoviscidosis or mucoviscidose).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 2 Cystic Fibrosis/ 3 1 or 2 4 ((physical adj (therap* or activit*)) or exercis* or "airway clearance" or ACT or sport* or train* or retrain* or condition* or strength* or fitness or danc* or aerobic or treadmill or walk* or running or cycl* or bicyc* or swim* or trampolin or yoga or pilates or Tai chi or Taichi or stretch* or physiotherap* or physio or vibrat* or percussi* or acapella or oscillat* or "positive expiratory pressure" or PEP or "active cycle breathing technique" or ACT or drainage or "bilevel positive airway pressure" or bipap or "expiratory positive airway pressure" or epap or cornet or expiration or huff or Hydro-acoustic or Hydroacoustic or massag* or manoeuvr*).ti,ab,kf. 5 exp physical therapy modalities/ or exp Respiratory Therapy/ or exp exercise movement techniques/ or exp exercise therapy/ or exp Exercise/ 6 4 or 5 7 (adhere or adherence or adhered or nonadherence or persist or persistance or persisted or compliance or comply or complied or noncompliance or concordance or nonconcordance or cooperative or cooperation or cooperate or cooperated or uncooperative or conform*).ti,ab,kf. 8 exp "Treatment Adherence and Compliance"/ 9 (engag* or encourag* or reinforc* or motivat* or train* or reward* or condition or remind* or monitor* or instruct* or educat* or knowledge or supervis* or communicat* or counsel* or self-regulat* or self-manage*).ti,ab,kf.

(Continued)

		10 (positive or enjoy* or perception or perceive* or attitude* or feedback or accept or cope or coping or coped or problem* or emotion* or social* or socio* or psycho* or behavio* or cognitive or mental* or verbal* or knowledge or personal or construct or crisis or aversion or assertiv* or accept* or commit* or mind* or mood* or support* or well* or habit* or talk* or depress*).ti,ab,kf. 11 (team* or diar* or famil* or parent*).ti,ab,kw. 12 (technology or app or apps or application* or telehealth or telecare or telemedicine or interactive or mobile or web or internet or online or game or games or gaming or text or messag* or telemonitor* or chip or chipped or track* or digital or Bluetooth or video* or teleconferen* or smartphone* or iphone or ipad or electronic or computer* or schedul* or telerehab*).ti,ab,kf. 13 Telemedicine/ 14 Internet-Based Intervention/ 15 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 16 3 and 6 and 15 7021 17 randomized controlled trial.pt. 18 controlled clinical trial.pt. 19 randomized.ab. 20 placebo.ab. 21 drug therapy.fs. 22 randomly.ab. 23 trial.ab. 24 groups.ab. 25 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 26 exp animals/ not humans.sh. 27 25 not 26 28 16 and 27 NOTE: Lines 17-27 are the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version (2008 revision); Ovid format. Available: https://training.cochrane.org/handbook/version-6/chapter-4-tech-suppl (Accessed 28/02/2023)
PsychINFO APA Publishing	1806 to 28 February 2023	[Advanced Search] S1 TX "cystic fibrosis" OR mucoviscidosis OR mucoviscidose S2 DE "Cystic Fibrosis" S3 S1 OR S2 S4 (((TI physical OR AB physical OR SU physical) W1 ((TI therap* OR AB therap* OR SU therap*) OR (TI activit* OR AB activit* OR SU activit*))) OR (TI exercis* OR AB exercis* OR SU exercis*) OR (TI "airway clearance" OR AB "airway clearance" OR SU "airway clearance") OR (TI ACT OR AB ACT OR SU ACT) OR (TI sport* OR AB sport* OR SU sport*) OR (TI train* OR AB train* OR SU train*) OR (TI retrain* OR AB retrain* OR SU retrain*) OR (TI condition* OR AB condition* OR SU condition*) OR (TI strength* OR AB strength* OR SU strength*) OR (TI fitness OR AB fitness OR SU fitness) OR (TI danc* OR AB danc* OR SU danc*) OR (TI aerobic OR AB aerobic OR SU aerobic) OR (TI treadmill OR AB treadmill OR SU treadmill) OR (TI walk* OR AB walk* OR SU walk*) OR (TI running OR AB running OR SU running) OR (TI cycl* OR AB cycl* OR SU cycl*) OR (TI bicyc* OR AB bicyc* OR SU bicyc*) OR (TI swim* OR AB swim* OR SU swim*) OR (TI trampolin OR AB trampolin OR SU trampolin) OR (TI yoga OR AB yoga OR SU yoga) OR (TI pilates OR AB pilates OR SU pilates) OR (TI "Tai chi" OR AB "Tai chi" OR SU "Tai chi") OR (TI Taichi OR AB Taichi OR SU Taichi) OR (TI stretch* OR AB stretch* OR SU stretch*) OR (TI physiotherap* OR AB physiotherap* OR SU physiotherap*) OR (TI physio OR AB physio OR SU physio) OR (TI vibrat* OR AB vibrat* OR SU vibrat*) OR (TI percussi* OR AB percussi* OR SU percussi*) OR (TI acapella OR AB acapella OR SU acapella) OR (TI oscillat* OR AB oscillat* OR SU oscillat*) OR (TI "positive expiratory pressure" OR AB "positive expiratory pressure" OR SU "positive expiratory pressure") OR (TI PEP OR AB PEP OR SU PEP) OR (TI "active cycle breathing technique" OR AB "active cycle breathing technique" OR SU "active cycle breathing technique") OR (TI ACT OR AB ACT OR SU ACT) OR

(Continued)

(TI drainage OR AB drainage OR SU drainage) OR (TI "bilevel positive airway pressure" OR AB "bilevel positive airway pressure" OR SU "bilevel positive airway pressure") OR (TI bipap OR AB bipap OR SU bipap) OR (TI "expiratory positive airway pressure" OR AB "expiratory positive airway pressure" OR SU "expiratory positive airway pressure") OR (TI epap OR AB epap OR SU epap) OR (TI cornet OR AB cornet OR SU cornet) OR (TI expiration OR AB expiration OR SU expiration) OR (TI huff OR AB huff OR SU huff) OR (TI Hydro-acoustic OR AB Hydro-acoustic OR SU Hydro-acoustic) OR (TI Hydroacoustic OR AB Hydroacoustic OR SU Hydroacoustic) OR (TI massag* OR AB massag* OR SU massag*) OR (TI manoeuvr* OR AB manoeuvr* OR SU manoeuvr*))
S5 DE "Physical Therapy" OR DE "Movement Therapy"
S6 DE "Exercise" OR DE "Aerobic Exercise"
S7 S4 OR S5 OR S6
S8 ((TI adhere OR AB adhere OR SU adhere) OR (TI adherence OR AB adherence OR SU adherence) OR (TI adhered OR AB adhered OR SU adhered) OR (TI nonadherence OR AB nonadherence OR SU nonadherence) OR (TI persist OR AB persist OR SU persist) OR (TI persistance OR AB persistance OR SU persistance) OR (TI persisted OR AB persisted OR SU persisted) OR (TI compliance OR AB compliance OR SU compliance) OR (TI comply OR AB comply OR SU comply) OR (TI complied OR AB complied OR SU complied) OR (TI noncompliance OR AB noncompliance OR SU noncompliance) OR (TI concordance OR AB concordance OR SU concordance) OR (TI nonconcordance OR AB nonconcordance OR SU nonconcordance) OR (TI cooperative OR AB cooperative OR SU cooperative) OR (TI cooperation OR AB cooperation OR SU cooperation) OR (TI cooperate OR AB cooperate OR SU cooperate) OR (TI cooperated OR AB cooperated OR SU cooperated) OR (TI uncooperative OR AB uncooperative OR SU uncooperative) OR (TI conform* OR AB conform* OR SU conform*))
S9 DE "Treatment Compliance"
S10 ((TI engag* OR AB engag* OR SU engag*) OR (TI encourag* OR AB encourag* OR SU encourag*) OR (TI reinforc* OR AB reinforc* OR SU reinforc*) OR (TI motivat* OR AB motivat* OR SU motivat*) OR (TI train* OR AB train* OR SU train*) OR (TI reward* OR AB reward* OR SU reward*) OR (TI condition OR AB condition OR SU condition) OR (TI remind* OR AB remind* OR SU remind*) OR (TI monitor* OR AB monitor* OR SU monitor*) OR (TI instruct* OR AB instruct* OR SU instruct*) OR (TI educat* OR AB educat* OR SU educat*) OR (TI knowledge OR AB knowledge OR SU knowledge) OR (TI supervis* OR AB supervis* OR SU supervis*) OR (TI communicat* OR AB communicat* OR SU communicat*) OR (TI counsel* OR AB counsel* OR SU counsel*) OR (TI self-regulat* OR AB self-regulat* OR SU self-regulat*) OR (TI self-manage* OR AB self-manage* OR SU self-manage*))
S11 ((TI positive OR AB positive OR SU positive) OR (TI enjoy* OR AB enjoy* OR SU enjoy*) OR (TI perception OR AB perception OR SU perception) OR (TI perceive* OR AB perceive* OR SU perceive*) OR (TI attitude* OR AB attitude* OR SU attitude*) OR (TI feedback OR AB feedback OR SU feedback) OR (TI accept OR AB accept OR SU accept) OR (TI cope OR AB cope OR SU cope) OR (TI coping OR AB coping OR SU coping) OR (TI coped OR AB coped OR SU coped) OR (TI problem* OR AB problem* OR SU problem*) OR (TI emotion* OR AB emotion* OR SU emotion*) OR (TI social* OR AB social* OR SU social*) OR (TI socio* OR AB socio* OR SU socio*) OR (TI psycho* OR AB psycho* OR SU psycho*) OR (TI behavio* OR AB behavio* OR SU behavio*) OR (TI cognitive OR AB cognitive OR SU cognitive) OR (TI mental* OR AB mental* OR SU mental*) OR (TI verbal* OR AB verbal* OR SU verbal*) OR (TI knowledge OR AB knowledge OR SU knowledge) OR (TI personal OR AB personal OR SU personal) OR (TI construct OR AB construct OR SU construct) OR (TI crisis OR AB crisis OR SU crisis) OR (TI aversion OR AB aversion OR SU aversion) OR (TI assertiv* OR AB assertiv* OR SU assertiv*) OR (TI accept* OR AB accept* OR SU accept*) OR (TI commit* OR AB commit* OR SU commit*) OR (TI mind* OR AB mind* OR SU mind*) OR (TI mood* OR AB mood* OR SU mood*) OR (TI support* OR AB support* OR SU support*) OR (TI well* OR AB well* OR SU well*) OR (TI habit* OR AB habit* OR SU habit*) OR (TI talk* OR AB talk* OR SU talk*) OR (TI depress* OR AB depress*

(Continued)

		OR SU depress*)) S13 ((TI team* OR AB team*) OR (TI diar* OR AB diar*) OR (TI famil* OR AB famil*) OR (TI parent* OR AB parent*)) S12 ((TI technology OR AB technology OR SU technology) OR (TI app OR AB app OR SU app) OR (TI apps OR AB apps OR SU apps) OR (TI application* OR AB application* OR SU application*) OR (TI telehealth OR AB telehealth OR SU telehealth) OR (TI telecare OR AB telecare OR SU telecare) OR (TI telemedicine OR AB telemedicine OR SU telemedicine) OR (TI interactive OR AB interactive OR SU interactive) OR (TI mobile OR AB mobile OR SU mobile) OR (TI web OR AB web OR SU web) OR (TI internet OR AB internet OR SU internet) OR (TI online OR AB online OR SU online) OR (TI game OR AB game OR SU game) OR (TI games OR AB games OR SU games) OR (TI gaming OR AB gaming OR SU gaming) OR (TI text OR AB text OR SU text) OR (TI messag* OR AB messag* OR SU messag*) OR (TI telemonitor* OR AB telemonitor* OR SU telemonitor*) OR (TI chip OR AB chip OR SU chip) OR (TI chipped OR AB chipped OR SU chipped) OR (TI track* OR AB track* OR SU track*) OR (TI digital OR AB digital OR SU digital) OR (TI Bluetooth OR AB Bluetooth OR SU Bluetooth) OR (TI video* OR AB video* OR SU video*) OR (TI teleconferen* OR AB teleconferen* OR SU teleconferen*) OR (TI smartphone* OR AB smartphone* OR SU smartphone*) OR (TI iphone OR AB iphone OR SU iphone) OR (TI ipad OR AB ipad OR SU ipad) OR (TI electronic OR AB electronic OR SU electronic) OR (TI computer* OR AB computer* OR SU computer*) OR (TI schedul* OR AB schedul* OR SU schedul*) OR (TI telerehab* OR AB telerehab* OR SU telerehab*)) S13 DE "Telemedicine" OR DE "Online Therapy" OR DE "Teleconferencing" OR DE "Teleconsultation" OR DE "Telepsychiatry" OR DE "Telepsychology" OR DE "Telerehabilitation" S14 S8 OR S9 OR S10 OR S11 OR S12 OR S13 S15 S3 AND S7 AND S14
CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature)	1982 to 27 February 2023	[Advanced Search] S1 TX "cystic fibrosis" OR mucoviscidosis OR mucoviscidose S2 (MH "Cystic Fibrosis") S3 S1 OR S2 S4 (((TI physical OR AB physical OR SU physical) W1 ((TI therap* OR AB therap* OR SU therap*) OR (TI activit* OR AB activit* OR SU activit*))) OR (TI exercis* OR AB exercis* OR SU exercis*) OR (TI "airway clearance" OR AB "airway clearance" OR SU "airway clearance") OR (TI ACT OR AB ACT OR SU ACT) OR (TI sport* OR AB sport* OR SU sport*) OR (TI train* OR AB train* OR SU train*) OR (TI retrain* OR AB retrain* OR SU retrain*) OR (TI condition* OR AB condition* OR SU condition*) OR (TI strength* OR AB strength* OR SU strength*) OR (TI fitness OR AB fitness OR SU fitness) OR (TI danc* OR AB danc* OR SU danc*) OR (TI aerobic OR AB aerobic OR SU aerobic) OR (TI treadmill OR AB treadmill OR SU treadmill) OR (TI walk* OR AB walk* OR SU walk*) OR (TI running OR AB running OR SU running) OR (TI cycl* OR AB cycl* OR SU cycl*) OR (TI bicyc* OR AB bicyc* OR SU bicyc*) OR (TI swim* OR AB swim* OR SU swim*) OR (TI trampolin OR AB trampolin OR SU trampolin) OR (TI yoga OR AB yoga OR SU yoga) OR (TI pilates OR AB pilates OR SU pilates) OR (TI "Tai chi" OR AB "Tai chi" OR SU "Tai chi") OR (TI Taichi OR AB Taichi OR SU Taichi) OR (TI stretch* OR AB stretch* OR SU stretch*) OR (TI physiotherap* OR AB physiotherap* OR SU physiotherap*) OR (TI physio OR AB physio OR SU physio) OR (TI vibrat* OR AB vibrat* OR SU vibrat*) OR (TI percussi* OR AB percussi* OR SU percussi*) OR (TI acapella OR AB acapella OR SU acapella) OR (TI oscillat* OR AB oscillat* OR SU oscillat*) OR (TI "positive expiratory pressure" OR AB "positive expiratory pressure" OR SU "positive expiratory pressure") OR (TI PEP OR AB PEP OR SU PEP) OR (TI "active cycle breathing technique" OR AB "active cycle breathing technique" OR SU "active cycle breathing technique") OR (TI ACT OR AB ACT OR SU ACT) OR (TI drainage OR AB drainage OR SU drainage) OR (TI "bilevel positive airway pressure" OR AB "bilevel positive airway pressure" OR SU "bilevel positive airway pressure") OR (TI bipap OR AB bipap OR SU bipap) OR (TI "expiratory positive airway pressure" OR AB "expiratory positive airway pressure" OR SU "expiratory positive airway pressure") OR (TI epap OR AB epap OR SU epap) OR

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(TI cornet OR AB cornet OR SU cornet) OR (TI expiration OR AB expiration OR SU expiration) OR (TI huff OR AB huff OR SU huff) OR (TI Hydro-acoustic OR AB Hydro-acoustic OR SU Hydro-acoustic) OR (TI Hydroacoustic OR AB Hydroacoustic OR SU Hydroacoustic) OR (TI massag* OR AB massag* OR SU massag*) OR (TI manoeuvr* OR AB manoeuvr* OR SU manoeuvr*))
S5 (MH "Physical Therapy+")
S6 (MH "Respiratory Therapy+")
S7 (MH "Exercise+")
S8 S4 OR S5 OR S6 OR S7
S9 ((TI adhere OR AB adhere OR SU adhere) OR (TI adherence OR AB adherence OR SU adherence) OR (TI adhered OR AB adhered OR SU adhered) OR (TI non-adherence OR AB nonadherence OR SU nonadherence) OR (TI persist OR AB persist OR SU persist) OR (TI persistance OR AB persistance OR SU persistance) OR (TI persisted OR AB persisted OR SU persisted) OR (TI compliance OR AB compliance OR SU compliance) OR (TI comply OR AB comply OR SU comply) OR (TI complied OR AB complied OR SU complied) OR (TI noncompliance OR AB noncompliance OR SU noncompliance) OR (TI concordance OR AB concordance OR SU concordance) OR (TI nonconcordance OR AB nonconcordance OR SU nonconcordance) OR (TI cooperative OR AB cooperative OR SU cooperative) OR (TI cooperation OR AB cooperation OR SU cooperation) OR (TI cooperate OR AB cooperate OR SU cooperate) OR (TI cooperated OR AB cooperated OR SU cooperated) OR (TI uncooperative OR AB uncooperative OR SU uncooperative) OR (TI conform* OR AB conform* OR SU conform*))
S10 (MH "Patient Compliance+"
S11 ((TI engag* OR AB engag* OR SU engag*) OR (TI encourag* OR AB encourag* OR SU encourag*) OR (TI reinforc* OR AB reinforc* OR SU reinforc*) OR (TI motivat* OR AB motivat* OR SU motivat*) OR (TI train* OR AB train* OR SU train*) OR (TI reward* OR AB reward* OR SU reward*) OR (TI condition OR AB condition OR SU condition) OR (TI remind* OR AB remind* OR SU remind*) OR (TI monitor* OR AB monitor* OR SU monitor*) OR (TI instruct* OR AB instruct* OR SU instruct*) OR (TI educat* OR AB educat* OR SU educat*) OR (TI knowledge OR AB knowledge OR SU knowledge) OR (TI supervis* OR AB supervis* OR SU supervis*) OR (TI communicat* OR AB communicat* OR SU communicat*) OR (TI counsel* OR AB counsel* OR SU counsel*) OR (TI self-regulat* OR AB self-regulat* OR SU self-regulat*) OR (TI self-manage* OR AB self-manage* OR SU self-manage*))
S12 ((TI positive OR AB positive OR SU positive) OR (TI enjoy* OR AB enjoy* OR SU enjoy*) OR (TI perception OR AB perception OR SU perception) OR (TI perceive* OR AB perceive* OR SU perceive*) OR (TI attitude* OR AB attitude* OR SU attitude*) OR (TI feedback OR AB feedback OR SU feedback) OR (TI accept OR AB accept OR SU accept) OR (TI cope OR AB cope OR SU cope) OR (TI coping OR AB coping OR SU coping) OR (TI coped OR AB coped OR SU coped) OR (TI problem* OR AB problem* OR SU problem*) OR (TI emotion* OR AB emotion* OR SU emotion*) OR (TI social* OR AB social* OR SU social*) OR (TI socio* OR AB socio* OR SU socio*) OR (TI psycho* OR AB psycho* OR SU psycho*) OR (TI behavio* OR AB behavio* OR SU behavio*) OR (TI cognitive OR AB cognitive OR SU cognitive) OR (TI mental* OR AB mental* OR SU mental*) OR (TI verbal* OR AB verbal* OR SU verbal*) OR (TI knowledge OR AB knowledge OR SU knowledge) OR (TI personal OR AB personal OR SU personal) OR (TI construct OR AB construct OR SU construct) OR (TI crisis OR AB crisis OR SU crisis) OR (TI aversion OR AB aversion OR SU aversion) OR (TI assertiv* OR AB assertiv* OR SU assertiv*) OR (TI accept* OR AB accept* OR SU accept*) OR (TI commit* OR AB commit* OR SU commit*) OR (TI mind* OR AB mind* OR SU mind*) OR (TI mood* OR AB mood* OR SU mood*) OR (TI support* OR AB support* OR SU support*) OR (TI well* OR AB well* OR SU well*) OR (TI habit* OR AB habit* OR SU habit*) OR (TI talk* OR AB talk* OR SU talk*) OR (TI depress* OR AB depress* OR SU depress*))
S13 ((TI team* OR AB team*) OR (TI diar* OR AB diar*) OR (TI famil* OR AB famil*) OR (TI parent* OR AB parent*))
S14 ((TI technology OR AB technology OR SU technology) OR (TI app OR AB app OR SU app) OR (TI apps OR AB apps OR SU apps) OR (TI application* OR

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		AB application* OR SU application*) OR (TI telehealth OR AB telehealth OR SU telehealth) OR (TI telecare OR AB telecare OR SU telecare) OR (TI telemedicine OR AB telemedicine OR SU telemedicine) OR (TI interactive OR AB interactive OR SU interactive) OR (TI mobile OR AB mobile OR SU mobile) OR (TI web OR AB web OR SU web) OR (TI internet OR AB internet OR SU internet) OR (TI online OR AB online OR SU online) OR (TI game OR AB game OR SU game) OR (TI games OR AB games OR SU games) OR (TI gaming OR AB gaming OR SU gaming) OR (TI text OR AB text OR SU text) OR (TI messag* OR AB messag* OR SU messag*) OR (TI telemonitor* OR AB telemonitor* OR SU telemonitor*) OR (TI chip OR AB chip OR SU chip) OR (TI chipped OR AB chipped OR SU chipped) OR (TI track* OR AB track* OR SU track*) OR (TI digital OR AB digital OR SU digital) OR (TI Bluetooth OR AB Bluetooth OR SU Bluetooth) OR (TI video* OR AB video* OR SU video*) OR (TI teleconferen* OR AB teleconferen* OR SU teleconferen*) OR (TI smartphone* OR AB smartphone* OR SU smartphone*) OR (TI iphone OR AB iphone OR SU iphone) OR (TI ipad OR AB ipad OR SU ipad) OR (TI electronic OR AB electronic OR SU electronic) OR (TI computer* OR AB computer* OR SU computer*) OR (TI schedul* OR AB schedul* OR SU schedul*) OR (TI telerehab* OR AB telerehab* OR SU telerehab*)) S15 (MH "Telehealth+") S16 S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 S17 S3 AND S8 AND S16 S18 MH randomized controlled trials S19 MH double-blind studies S20 MH single-blind studies S21 MH random assignment S22 MH pretest-posttest design S23 MH cluster sample S24 TI (randomised OR randomized) S25 AB (random*) S26 TI (trial) S27 MH (sample size) AND AB (assigned OR allocated OR control) S28 MH (placebos) S29 PT (randomized controlled trial) S30 AB (control W5 group) S31 MH (crossover design) OR MH (comparative studies) S32 AB (cluster W3 RCT) S33 MH animals+ S34 MH (animal studies) S35 TI (animal model*) S36 S33 OR S34 OR S35 S37 MH (human) S38 S36 NOT S37 S39 S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 S40 S39 NOT S38 S41 S17 AND S40 NOTE: Lines S18-S40 are the Cochrane CINAHL Plus filter. Available: https://training.cochrane.org/handbook/version-6/chapter-4-tech-suppl (accessed 27/02/2023)
AMED EBSCO (Allied and Complementary Medicine)	1985 to 27 February 2023	S1 TX "cystic fibrosis" OR mucoviscidosis OR mucoviscidose S2 (ZU "cystic fibrosis") S3 S1 OR S2 S4 (((TI physical OR AB physical OR SU physical) W1 ((TI therap* OR AB therap* OR SU therap*) OR (TI activit* OR AB activit* OR SU activit*))) OR (TI exercis* OR AB exercis* OR SU exercis*) OR (TI "airway clearance" OR AB "airway clearance" OR SU "airway clearance") OR (TI ACT OR AB ACT OR SU ACT) OR (TI sport* OR AB sport* OR SU sport*) OR (TI train* OR AB train* OR SU train*) OR (TI retrain* OR AB retrain* OR SU retrain*) OR (TI condition* OR AB condition* OR SU condition*) OR (TI strength* OR AB strength* OR SU strength*) OR (TI fit-

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ness OR AB fitness OR SU fitness) OR (TI danc* OR AB danc* OR SU danc*) OR (TI aerobic OR AB aerobic OR SU aerobic) OR (TI treadmill OR AB treadmill OR SU treadmill) OR (TI walk* OR AB walk* OR SU walk*) OR (TI running OR AB running OR SU running) OR (TI cycl* OR AB cycl* OR SU cycl*) OR (TI bicyc* OR AB bicyc* OR SU bicyc*) OR (TI swim* OR AB swim* OR SU swim*) OR (TI trampolin OR AB trampolin OR SU trampolin) OR (TI yoga OR AB yoga OR SU yoga) OR (TI pilates OR AB pilates OR SU pilates) OR (TI "Tai chi" OR AB "Tai chi" OR SU "Tai chi") OR (TI Taichi OR AB Taichi OR SU Taichi) OR (TI stretch* OR AB stretch* OR SU stretch*) OR (TI physiotherap* OR AB physiotherap* OR SU physiotherap*) OR (TI physio OR AB physio OR SU physio) OR (TI vibrat* OR AB vibrat* OR SU vibrat*) OR (TI percussi* OR AB percussi* OR SU percussi*) OR (TI acapella OR AB acapella OR SU acapella) OR (TI oscillat* OR AB oscillat* OR SU oscillat*) OR (TI "positive expiratory pressure" OR AB "positive expiratory pressure" OR SU "positive expiratory pressure") OR (TI PEP OR AB PEP OR SU PEP) OR (TI "active cycle breathing technique" OR AB "active cycle breathing technique" OR SU "active cycle breathing technique") OR (TI ACT OR AB ACT OR SU ACT) OR (TI drainage OR AB drainage OR SU drainage) OR (TI "bilevel positive airway pressure" OR AB "bilevel positive airway pressure" OR SU "bilevel positive airway pressure") OR (TI bipap OR AB bipap OR SU bipap) OR (TI "expiratory positive airway pressure" OR AB "expiratory positive airway pressure" OR SU "expiratory positive airway pressure") OR (TI epap OR AB epap OR SU epap) OR (TI cornet OR AB cornet OR SU cornet) OR (TI expiration OR AB expiration OR SU expiration) OR (TI huff OR AB huff OR SU huff) OR (TI Hydro-acoustic OR AB Hydro-acoustic OR SU Hydro-acoustic) OR (TI Hydroacoustic OR AB Hydroacoustic OR SU Hydroacoustic) OR (TI massag* OR AB massag* OR SU massag*) OR (TI manoeuvr* OR AB manoeuvr* OR SU manoeuvr*))
S5 (ZU "physical therapy modalities") or (ZU "physical therapy speciality") or (ZU "physical therapy techniques")
S6 (ZU "respiratory therapy")
S7 (ZU "exercise") or (ZU "exercise aerobic") or (ZU "exercise movement techniques") or (ZU "exercise therapy")
S8 S4 OR S5 OR S6 OR S7
S9 ((TI adhere OR AB adhere OR SU adhere) OR (TI adherence OR AB adherence OR SU adherence) OR (TI adhered OR AB adhered OR SU adhered) OR (TI nonadherence OR AB nonadherence OR SU nonadherence) OR (TI persist OR AB persist OR SU persist) OR (TI persistance OR AB persistance OR SU persistance) OR (TI persisted OR AB persisted OR SU persisted) OR (TI compliance OR AB compliance OR SU compliance) OR (TI comply OR AB comply OR SU comply) OR (TI complied OR AB complied OR SU complied) OR (TI noncompliance OR AB noncompliance OR SU noncompliance) OR (TI concordance OR AB concordance OR SU concordance) OR (TI nonconcordance OR AB nonconcordance OR SU nonconcordance) OR (TI cooperative OR AB cooperative OR SU cooperative) OR (TI cooperation OR AB cooperation OR SU cooperation) OR (TI cooperate OR AB cooperate OR SU cooperate) OR (TI cooperated OR AB cooperated OR SU cooperated) OR (TI uncooperative OR AB uncooperative OR SU uncooperative) OR (TI conform* OR AB conform* OR SU conform*))
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WHO International Clinical Trials Registration Platform (ICTRP) (trialsearch.who.int/)	28 March 2023	[Basic Search] (cystic fibrosis OR mucoviscidosis OR mucoviscidose) AND (physical therapy OR airway clearance OR physiotherapy OR physiotherapies OR exercise OR exercises OR exercising) AND (adherence OR adhere OR nonadherence OR compliance OR noncompliance)
US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov)	28 March 2023	[Advanced Search] Condition or disease: cystic fibrosis OR mucoviscidosis OR mucoviscidose Other terms: (physical therapy OR airway clearance OR physiotherapy OR physiotherapies OR exercise OR exercises OR exercising) AND (adherence OR adhere OR nonadherence OR compliance OR noncompliance) Study type: Interventional Studies (Clinical Trials)

(Continued)

ISRCTN registry (www.isrctn.com)	28 March 2023	[Basic Search] (cystic fibrosis OR mucoviscidosis OR mucoviscidose) AND ("physical therapy" OR "physical therapies" OR “airway clearance” OR physiotherapy OR physiotherapies OR exercise OR exercises OR exercising) AND (adherence OR adhere OR nonadherence OR compliance OR noncompliance)

HISTORY

Protocol first published: Issue 5, 2020

CONTRIBUTIONS OF AUTHORS

Roles and responsibilities

Task	Author
Protocol stage: draft the protocol	MJ, FM
Review stage: select which trials to include (2 + 1 arbiter)	MJ, FM with AH as third author when needed
Review stage: extract data from trials (2 people)	MJ, FM with AH as third author when needed
Review stage: enter data into RevMan	MJ, FM
Review stage: carry out the analysis	JR, MJ, FM with statistical help
Review stage: interpret the analysis	MJ, FM, JR with statistical help
Review stage: draft the final review	MJ, FM
Update stage: update the review	MJ, FM

DECLARATIONS OF INTEREST

MJ: none known.

FM: none known.

AH: none known.

JR: none known.

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Internal sources

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- School of Health Sciences, University of Nottingham, UK

  This Cochrane Review was supported by the School of Health Sciences.

External sources

- National Institute for Health & Care Research, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The lower limit of seven years for participants was a post hoc protocol change given that we became aware that specialist units anticipate that children with CF are likely to manage their physiotherapy independently from the age of seven rather than eight (with potential supervision, but not active involvement, from parents) (Jones 2020).

NOTES

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

INDEX TERMS

Medical Subject Headings (MeSH)

*Cystic Fibrosis [complications]; Exercise; Physical Therapy Modalities; Quality of Life; Respiratory Therapy

MeSH check words

Adolescent; Adult; Child; Child, Preschool; Female; Humans; Male; Young Adult