

Cochrane Database of Systematic Reviews - - Cochrane Review

# Comparative efficacy and safety of CFTR modulators for people with cystic fibrosis with phe508del mutation: a systematic review and bayesian network meta-analysis.

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Author: Safer V S M

## Study design (if review, criteria of inclusion for studies)

Randomised controlled trials (RCTs) comparing different types of psychological interventions for improving adherence to inhaled therapies in people with CF of any age, or comparing psychological interventions with usual care. Quasi-RCTs included if one could reasonably assume that the baseline characteristics were similar in both groups

## Participants

People with cystic fibrosis (CF).

## Interventions

Psychological interventions. A secondary objective is to establish the most effective components, or behaviour change techniques (BCTs), of interventions for improving adherence to inhaled therapies in people with CF, using the BCT Taxonomy version 1 (Michie 2013).

## Outcome measures

Adherence to inhaled therapies in people with cystic fibrosis (CF).

## Main results

We included 10 trials (1642 participants) in the review (children and adolescents in four trials; adults in five trials; and children and adults in one trial). Nine trials compared a psychological intervention with usual care; we could combine data from some of these in a number of quantitative analyses. One trial compared a psychological intervention with an active comparator (education plus problem-solving (EPS)). We identified five ongoing trials. Psychological interventions were generally multi-component and complex, containing an average of 9.6 BCTs (range 1 to 28). The two most commonly used BCTs included 'problem-solving' and 'instruction on how to perform the behaviour'. Interventions varied in their type, content and mode of delivery. They included a problem-solving intervention; a paper-based self-management workbook; a telehealth intervention; a group training programme; a digital intervention comprising medication reminders and lung function self-monitoring; a life-coaching intervention; a motivational interviewing (MI) intervention; a brief MI intervention (behaviour change counselling); and a digital intervention combined with behaviour change sessions. Intervention duration ranged from 10 weeks to 12 months. Assessment time points ranged from six to eight weeks up to 23 months. Psychological interventions compared with usual care We report data here for the 'over six months and up to 12 months' time point. We found that psychological interventions probably improve adherence to inhaled therapies (primary outcome) in people with CF compared with usual care (mean difference (MD) 9.5, 95% confidence interval (CI) 8.60 to 10.40; 1 study, 588 participants; moderate-certainty evidence). There was no evidence of a difference between groups in our second primary outcome, treatment-related adverse events: anxiety (MD 0.30, 95% CI -0.40 to 1.00; 1 study, 535 participants), or depression (MD -0.10, 95% CI -0.80 to 0.60; 1 study, 534 participants), although this was low-certainty evidence. For our secondary outcomes, there was no evidence of a difference between groups in terms of lung function (forced expiratory volume in one second (FEV1) % predicted MD 1.40, 95% CI -0.20 to 3.00; 1 study, 556 participants; moderate-certainty evidence); number of pulmonary exacerbations (adjusted rate ratio 0.96, 95% CI 0.83 to 1.11; 1 study, 607 participants; moderate-certainty evidence); or respiratory symptoms (MD 0.70, 95% CI -2.40 to 3.80; 1 study, 534 participants; low-certainty evidence). However, psychological interventions may improve treatment burden (MD 3.90, 95% CI 1.20 to 6.60; 1 study, 539 participants; low-certainty evidence). The overall certainty of the evidence ranged from low to moderate across these outcomes. Reasons for downgrading included indirectness (current evidence included adults only whereas our review question was broader and focused on people of any age) and lack of blinding of outcome assessors. Psychological interventions compared with an active comparator For this comparison the overall certainty of evidence was very low, based on one trial (n = 128) comparing an MI intervention to EPS for 12 months. We are uncertain whether an MI intervention, compared with EPS, improves adherence to inhaled therapies, lung function, or quality of life in people with CF, or whether there is an effect on pulmonary exacerbations. The included trial for this comparison did not report on treatment-related adverse events (anxiety and depression). We downgraded all reported outcomes due to small participant numbers, indirectness (trials included only adults), and unclear risk of bias (e.g. selection and attrition bias).

## Authors' conclusions

Due to the limited quantity of trials included in this review, as well as the clinical and methodological heterogeneity, it was not possible to identify an overall intervention effect using meta-analysis. Some moderate-certainty evidence suggests that psychological interventions (compared with usual care) probably improve adherence to inhaled therapies in people with CF, without increasing treatment-related adverse events, anxiety and depression (low-certainty evidence). In future review updates (with ongoing trial results included), we hope to be able to establish the most effective BCTs (or 'active ingredients') of interventions for improving adherence to inhaled therapies in people with CF. Wherever possible, investigators should make use of the most objective measures of adherence available (e.g. data-logging nebulisers) to accurately determine intervention effects. Outcome reporting needs to be improved to enable combining or separation of measures as appropriate. Likewise, trial reporting needs to include details of intervention content (e.g. BCTs used); duration; intensity; and fidelity. Large trials with a longer follow-up period (e.g. 12 months) are needed in children with CF. Additionally, more research is needed to determine how to support adherence in 'underserved' CF populations.

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### See also

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### Keywords

Adult; Caregivers; Child; non pharmacological intervention - psycho-soc-edu-org; Psychoeducation; training; Self-Management; Systemic interventions; Behavioural interventions; Cognitive analytic therapy; information; Acapella; Active Cycle of Breathing Technique -ACBT-; Adolescent; Aerobic training; Airway clearance drugs -expectorants- mucolytic- mucociliary-; Airway clearance technique; Autogenic drainage; Chest physiotherapy; Chest Wall Oscillation; Combined Modality Therapy; Drainage; exercise; flutter; forced expiration technique; High Frequency Chest Wall Oscillation -HFCWO-; Inhalation OR nebulised; inspiratory muscle training; Intrapulmonary Percussive Ventilation; non pharmacological intervention - devices OR physiotherapy; oscillating devices; Percussion; pharmacological\_intervention; Positive-Pressure Respiration- PEP- pep mask; Postural Drainage; Respiratory Tract Diseases; strength training; VEST Airway Clearance System; Vibration;