Singing as an adjunct therapy for children and adults with cystic fibrosis

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[Intervention Review]

Singing as an adjunct therapy for children and adults with cystic fibrosis

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ABSTRACT

Background

Cystic fibrosis is a genetically inherited, life-threatening condition that affects major organs. The management of cystic fibrosis involves a multi-faceted daily treatment regimen that includes airway clearance techniques, pancreatic enzymes and other medications. Previous studies have found that compliance with this intensive treatment is poor, especially among adolescents. Because of both the nature and consequences of the illness and the relentless demands of the treatment, many individuals with cystic fibrosis have a poor quality of life. Anecdotal reports suggest that singing may provide both appropriate exercise for the whole respiratory system and a means of emotional expression which may enhance quality of life.

Objectives

To evaluate the effects of singing as an adjunct therapy to standard treatment on the quality of life, morbidity, respiratory muscle strength and pulmonary function of children and adults with cystic fibrosis.

Search methods

We searched the Group's Cystic Fibrosis Trials Register and the Cochrane Central Register of Controlled Trials. Date of latest search: 31 March 2014.

We also searched major allied complementary data bases, and clinical trial registers. Additionally, we handsearched relevant conference proceedings and journals. Date of latest search: 24 May 2012.

Selection criteria

Randomised controlled trials in which singing (as an adjunct intervention) is compared with either a control intervention (for example, playing computer games or doing craft activities) or no singing in people with cystic fibrosis.

Data collection and analysis

Results of searches were reviewed against pre-determined criteria for inclusion. Only one eligible trial was available for analysis.

Main results

Since only one small study was included, no meta-analysis could be performed. The included study was a parallel, randomised controlled trial undertaken at two paediatric hospitals in Australia. The study evaluated the effects of a singing program on the quality of life and respiratory muscle strength of hospitalised children with cystic fibrosis (mean age 11.6 years, 35% male). While the singing group received eight individual singing sessions, the control group participated in preferred recreational activities, such as playing computer games or watching movies. This study was limited by a small sample size (51 participants) and a high drop-out rate (21%).

There were no significant differences between the groups at either post-intervention or follow up; although by the end of treatment there were some within-group statistically significant increases for both singing and control groups in some of the domains of the quality of life questionnaire Cystic Fibrosis Questionnaire-Revised (e.g. emotional, social and vitality domains). For the respiratory muscle strength indices, maximal expiratory pressure at follow up (six to eight weeks post-intervention) was higher in the singing group, mean difference 25.80 (95% confidence interval 5.94 to 45.66). There was no significant difference between groups for any of the other respiratory function parameters (maximal inspiratory pressure, spirometry) at either post-intervention or follow up.

Authors' conclusions

There is insufficient evidence to determine the effects of singing on quality of life or on the respiratory parameters in people with cystic fibrosis. However, there is growing interest in non-medical treatments for cystic fibrosis and researchers may wish to investigate the impact of this inexpensive therapy on respiratory function and psychosocial well-being further in the future.

PLAIN LANGUAGE SUMMARY

The effects of singing on lung function and quality of life in children and adults with cystic fibrosis

People with cystic fibrosis are at risk of chest infections due to abnormally thick mucus in their airways. Airway clearance is therefore an important part of cystic fibrosis management. Increasing anecdotal reports suggests that singing may support lung function and enhance quality of life in people with cystic fibrosis. We searched for trials using the standard search methods of the Cochrane Cystic Fibrosis and Genetic Disorders Group, and conducted extensive searches in other relevant databases and publications.

One small study evaluated the effects of singing on the quality of life and lung function of children with cystic fibrosis who are in hospital. This study compared singing with other non-physical leisure activities, such as playing computer games or watching movies. The included study was limited by the small number of participants (only 51 participants) and a high drop-out rate (21%). The study assessed the impacts of singing on respiratory muscle strength, quality of life and lung function tests. It found a statistically significant difference in maximal expiratory pressure (a substitute measure of respiratory muscle strength) in favour of singing at one time point. However, both the singing and control groups showed improvements in some quality of life measurements; and no differences were reported in other lung function measures. There is currently not enough evidence to show that singing can improve clinical outcomes in people with cystic fibrosis. Future studies using robust methods are needed to assess the possible effects of singing for people with cystic fibrosis.

BACKGROUND

Description of the condition

Cystic fibrosis (CF) is a genetically inherited life-threatening condition that affects major organs, such as the lungs, pancreas, liver and kidneys. Individuals with CF produce abnormally excessive thick mucus in the airways, which makes them more susceptible to lung diseases. Repeated infections in the airways lead to irreversible lung damage (Phelan 1994).

The management of CF involves a multifaceted daily treatment regimen that usually includes airway clearance techniques, physical exercise, pancreatic enzymes and other medications, as well as hospital admissions. Such an intensive treatment regimen may have a negative psychosocial impact on children and adolescents

(Glasscoe 2008), particularly on adolescents (D'Auria 2000). Previous studies have found that individuals with CF may have poor quality of life (QoL) (Quittner 2008).

Description of the intervention

For individuals with CF, the respiratory muscles play an important role in maintaining lung health (Reid 2008; Sawyer 1993). Respiratory muscle strength is vital for airway clearance techniques, as it helps to generate effective cough to expectorate secretion (Chang 2006; Widdicombe 2006). Respiratory muscle function also affects exercise capacity in people with CF (Enright 2004), and greater levels of exercise capacity are correlated with lower levels of mortality (Nixon 1992). To improve respiratory muscle function in CF, conventional treatment uses inspiratory muscle training (IMT) devices. Some research has shown that an IMT program can improve respiratory muscle function in children (Sawyer 1993); however, a recent systematic review detected only weak evidence that conventional IMT devices were beneficial (Reid 2008). Using an IMT device can also be seen as another chore for individuals with CF, given the complexity of the daily treatment regimen. In contrast, a singing intervention may provide an enjoyable activity which would also have therapeutic benefits.

The dome-shaped diaphragm is a primary inspiratory muscle, and separates the thorax from the abdomen (Titze 1994). The diaphragm flattens as it contracts, and expands the thorax, thus increasing air intake by increasing lung volume (Leanderson 1987; Leanderson 1988). Sundberg found that singing requires greater use of vital lung capacity than normal speech, due to the longer phrases contained in songs (Sundberg 1987). Singers, therefore, need to use their lung capacity efficiently in order to sustain long phrases while singing. Classical singers use almost 100% of their vital lung capacity at the beginning of long phrases, so that extra breaths are not necessary (Sundberg 1987). Although not all trained singers use identical breathing behaviours, opera singers have been found to have highly consistent breathing strategy and greater movement of the rib cage and abdomen while singing (Thomasson 1999).

Anecdotal reports suggest that singing may be beneficial for people with chronic respiratory diseases (Elliott 2009; NHS Choices 2011; Stacy 2002).

Current literature suggests that singing interventions based on diaphragmatic breathing can improve or maintain the respiratory muscle functions in people with chronic obstructive pulmonary disease (COPD) (Bonilha 2009), multiple sclerosis (Wiens 1999) and Parkinson's disease (Di Benedetto 2009). In these studies, the respiratory muscle strength (using maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP)) were measured as the indicators reflecting changes in the respiratory muscle strength attributed to the singing intervention.

Singing can also reduce fear, anxiety and pain perception and improve mood (Kenny 2004; Unwin 2002). Further, singing can provide not only health benefits but also enjoyment. Studies found that when singing or music were part of a breathing exercise, participants with asthma demonstrated better treatment compliance due to greater enjoyment, which enhanced their motivation (Fukuda 2000; Lipawen 2000).

Additionally, a number of anecdotal reports attest to the benefits of singing in enhancing the quality of life (QoL) of people with chronic lung diseases (Stacy 2002). Studies investigating the effects of a singing or music program on the lung health and QoL of people with COPD (Bonilha 2009; Lord 2010), emphysema (Engen 2005) and asthma (Wade 2002) indicate that singing can be an enjoyable, low-cost and low-risk intervention, which supports lung health and enhances QoL.

How the intervention might work

Studies show that singing requires a regulation of exhaled air flow and promotes the use of vital capacity to the fullest possible extent (Collyer 2009; Sundberg 1987). Similar to other airway clearance techniques, such as the active cycle of breathing technique (Robinson 2010), singing promotes good posture (relaxed neck and shoulders), control of breathing, and thoracic expansion. Furthermore, singing does not require a device or an assistant, and can provide some necessary enjoyment to reduce treatment burden and reinforce further training (Raskin 2009).

A singing intervention can be carried out in a one-to-one or in a group setting, and should be conducted in a non-judgmental and supportive environment. The program needs to be of sufficient length and intensity to allow participants to master the diaphragmatic breathing technique. This can vary from individual to individual, depending on their age, background, illness severity, past experience with singing and music as well as the relationship between the singing facilitator and the patient. A study of people with emphysema (over 60 years of age) indicated that at least two half-hour sessions are necessary for participants to learn the diaphragmatic breathing method correctly (Engen 2005).

Why it is important to do this review

A recent Cochrane systematic review identified very few research studies on non-medical interventions in the field of CF (Glasscoe 2008). Despite progress in medical treatment for CF, psychological therapies to improve emotional well-being have been limited (Elgudin 2004). To date, CF treatment has been dominated by rigorous medical treatments. Although essential, this may also reflect a disease-oriented view, in which only the physical symptoms are treated. A single medical treatment may be unable to provide the care and management required to improve all aspects of QoL in people living with CF. A multidisciplinary treatment regimen may be effective in meeting the complex needs of individuals with CF. Research in health psychology supports this view and provides

strong evidence that numerous factors influence both illness and well-being (Bernard 1994; Knight 1998). These should be taken into account when providing a health service which aims to optimise both medical and psycho-social health outcomes.

Singing is a relatively inexpensive adjunct intervention which can potentially enhance QoL and provide enjoyable and effective exercise for the respiratory system of people with CF.

This is an update of a previous version of this review (Irons 2010).

OBJECTIVES

To evaluate the effects of singing as an adjunct therapy to standard treatment on QoL, respiratory muscle strength, pulmonary function and morbidity of children and adults with CF.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised or quasi-randomised controlled trials.

Types of participants

People with CF, of any age, diagnosed on the basis of sweat testing or genotype analysis.

Types of interventions

All types of singing intervention that included diaphragmatic breathing, which were carried out in a group or one-to-one setting, facilitated by singing instructors or teachers, voice coaches or trainers, or music therapists, for a minimum of two half-hour sessions. Studies comparing singing with a control group that did not involve the activation of the respiratory muscles were to be considered (for example, playing computer games or doing craft activities). Studies using non face-to-face delivery format, such as DVD or CD were not considered as these formats could not address some important issues such as how to use the voice in a healthy way while singing, and to obtain immediate feedback on singing practice, posture and breathing technique. Further, individual or group singing sessions can also be adjusted to the levels of singers, which is hard to achieve through media, such as DVD or CD.

Types of outcome measures

Primary outcomes

1. QoL measured by validated instruments, e.g. Cystic Fibrosis Questionnaire-Revised (CFQ-R) (Quittner 2009), St. George's Respiratory Questionnaire (Jones 1991), Pediatric Quality of Life Inventory^{TM} (PedsQL^{TM}) (Varni 1999)
2. Respiratory muscle function
   i) maximal inspiratory pressure (MIP)
   ii) maximal expiratory pressure (MEP)
   iii) cough peak flow (Table 1)

Secondary outcomes

1. Other subjective scores (e.g. cough diary using Likert scales or visual analogue scales (Table 1) measuring subjective assessment of interference of cough)
2. Spirometry
   i) forced expiratory volume in one second (FEV_1)
   ii) forced vital capacity (FVC)
   iii) forced mid-expiratory flow rate ($FEF_{25-75\%}$)
3. Number of participants experiencing adverse effects (e.g. coughing up blood and difficulty in breathing)
4. Respiratory exacerbations
   i) total number of hospitalised days
   ii) total number of symptomatic days
   iii) number of participants with respiratory exacerbations
5. Adherence to other CF treatments (e.g. measured by a diary, self-evaluation checklist)
6. Psychological assessments measuring self-efficacy, depression and anxiety

Search methods for identification of studies

There were no language or publication restrictions.

Electronic searches

We searched the Group's Cystic Fibrosis Trials Register for relevant trials using the terms: 'cystic fibrosis' AND 'singing'.

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*), quarterly 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 sections of the Cystic Fibrosis and Genetic Disorders Group Module.
Date of search: 31 March 2014.
We also searched the following sources; please see the appendices for details of search terms and dates:

- Allied and Complementary Database AMED (1985 to 2012) (Appendix 1);
- PsycINFO (1872 to 2012) (Appendix 2);
- CINAHL (all years to present) (Appendix 3);
- Dissertation Abstracts International (late 1960 to 2012) (Appendix 4);
- www.clinicaltrials.gov (all years to 2012) (Appendix 5);
- Music therapy research database (all years to 24/09/2009) (Appendix 6);
- National Research Register (NRR) Archive (2000 to 2012) (Appendix 7).

Note: the Music Therapy Research Database has been inactive so there was no new search for the 2012 update.

Searching other resources

We searched other relevant publications, including hand searching of music or singing or music therapy journals.

Journal	Date searched
Nordic Journal of Music Therapy (2003 - 2012; Vol 21 (Issue 1))	24/05/2012
Australian Journal of Music Therapy (1996 - 2011; Vol 22)	24/05/2012
The New Zealand Journal of Music Therapy (1987 - 2012)	24/05/2012
The British Journal of Music therapy (1987 - 2011)	24/05/2012
Musiktherapeutische Umschau (German Music Therapy Journal) (2000 - 2011)	24/05/2012

Further, we have contacted experts (singing or music therapy-related researchers and singing facilitators or teachers) in this area and on receipt of written communication from the authors of trials, would have included these in the review as necessary.

Data collection and analysis

Selection of studies

Two authors (JYI, AC) independently assessed studies for inclusion in the review based on the inclusion criteria stated above. If there was any disagreement in this process, they would have consulted with the third author (DK) and resolved by discussion.

Data extraction and management

Two authors (JYI, AC) independently extracted data from the eligible study on to a standard data extraction form. One author (JYI) entered the data into RevMan for analysis (RevMan 2011) and AC checked the entered data.
The authors reviewed the study that satisfied the inclusion criteria and recorded the following information: study setting, year of study, source of funding, participants recruitment details (including number of eligible people), inclusion and exclusion criteria, other symptoms, randomisation and allocation concealment method, numbers of participants randomised, blinding (masking) of participants, care providers and outcome assessors, duration of intervention, previous singing training, co-interventions, numbers of participants not followed up, reasons for withdrawals from study protocol (clinical, side-effects, refusal and other), details on side-effects of therapy, and whether intention-to-treat analyses were conducted. The authors extracted data on the outcomes described previously at three points: short term (at less than one month), medium term (over one month and up to six months), and longer term (over six months and up to one year and annually thereafter). If in future updates of this review, the authors include further studies and if necessary, they planned to contact the study authors for any missing information.
In a *post hoc* change, the authors considered that reporting the differences (change scores) from baseline to post-intervention or follow up, or both, in the outcome measures to be appropriate in this review.

Assessment of risk of bias in included studies

Two review authors independently assessed the risk of bias of the included study using the 'Risk of Bias' tool as described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Generation of the allocation sequence

The authors assessed the study for the generation of allocation sequence as follows:

1. low risk of bias, if methods of randomisation include using a random number table, computer-generated lists or similar methods;
2. unclear risk of bias, if the trial was described as randomised, but no description of the methods used to allocate participants to treatment group was described;
3. high risk of bias, if methods of randomisation include alternation, the use of case record numbers, dates of birth or day of the week, and any procedure that was entirely transparent before allocation.

Allocation concealment

The authors assessed whether allocation was adequately concealed, to prevent both participants and investigators from foreseeing assignment:

1. low risk of bias, if the allocation of participants involved a central independent unit, on-site locked computer, identically appearing numbered drug bottles or containers prepared by an independent pharmacist or investigator, or sealed opaque envelopes;
2. unclear risk of bias, if the method used to conceal the allocation was not described;
3. high risk of bias, if the allocation sequence was known to the investigators who assigned participants, for example it was based on day of admission or case record number.

Blinding (or masking)

Due to the nature of the intervention, it is impossible to blind participants. The authors assessed the included study as to whether the outcome assessors were blinded to treatment allocation (low risk of bias); unclear whether they were blinded (unclear risk of bias); or not blinded to treatment (high risk of bias).

Follow up

The authors graded the study as to whether numbers of and reasons for dropouts and withdrawals in all intervention groups were described; or whether it was specified that there were no dropouts or withdrawals:

1. low risk of bias, if reasons for dropouts and withdrawals described;
2. unclear risk of bias, if insufficient or selective reporting of dropouts and withdrawals;
3. high risk of bias, if not reporting reasons for dropouts and withdrawals likely to be related to true outcome.

Selective outcome reporting

The authors tried to identify and report on any selective reporting in the included study, by comparing the study protocol with the final published paper. If in future the authors include further studies, for which the protocols are not available, the authors will compare the 'Methods' and 'Results' sections of the published study. Authors will make risk of bias judgements as follows:

1. low risk of bias, if all outcomes reported as being measured were reported;
2. unclear risk of bias, if it was unclear whether all measured outcomes were reported;
3. high risk of bias, if not all outcomes that were measured were reported.

Other potential sources of bias

The authors tried to identify any other sources of bias not reported elsewhere in the review and assessed their potential for putting the study results at risk of bias.

Measures of treatment effect

If the authors had identified more than one study, they would have undertaken an initial qualitative comparison of all the individually analysed studies to examine whether pooling of results (meta-analysis) was reasonable. This would have taken into account differences in study populations, inclusion and exclusion criteria, interventions and outcome assessment. The results from studies that met the inclusion criteria and that report any of the outcomes of interest would have been included in the subsequent meta-analyses.

For the dichotomous outcome variables of each individual study, the authors planned to calculate the odds ratio (OR) and 95% confidence intervals (CIs) using intention to treat analysis. The authors used the Cochrane statistical package RevMan 5.1 (RevMan 2011). If the authors include more studies in future, they will calculate the numbers needed to treat (NNT) from the pooled OR and its 95% CI applied to a specified baseline risk (from the control group) using an online calculator (Cates 2003).

For continuous outcomes, the authors calculated the mean difference (MD) and 95% CIs using RevMan 5.1 (RevMan 2011) using 'as treated' approach. If, in future, studies report outcomes using different measurement scales, the authors will calculate the standardised mean difference.

Unit of analysis issues

Cross-over trials are not appropriate for this intervention and thus the authors planned to only include data from the first arm of any cross-over studies.

Dealing with missing data

The authors would have requested further information from the primary investigators where appropriate.

Assessment of heterogeneity

If more than one study were available, the authors planned to describe heterogeneity between the study results and test this to see if it reached statistical significance using the chi^2 test. The authors would have considered heterogeneity to be significant if the P value was less than 0.10 (Higgins 2011). The authors also planned to present the I^2 statistic, which quantifies the inconsistency of the results of the studies as described in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), and would have defined heterogeneity as low if less than 25%, moderate if the value was between 25% and 75%, and high if the value was over 75% (Higgins 2003).

Assessment of reporting biases

If the combination of data and a meta-analysis (with at least 10 studies) had been possible, the authors would have assessed publication bias using a funnel plot.

Data synthesis

The authors calculated the summary OR and mean differences with 95% CIs using a fixed-effect model. They would have used a random-effects model if they had concerns about statistical heterogeneity, i.e. when there was at least moderate heterogeneity as defined above using the I^2 statistic, where I^2 is at least 50%.
The authors planned only to combine 'Other subjective scores' (see Secondary outcomes), if they deemed it clinically appropriate.

Subgroup analysis and investigation of heterogeneity

If the authors had been able to include sufficient studies in the review and it was appropriate, they planned the following *a priori* sub-group analyses:

1. children (under 18 years old) versus adults;
2. severity of CF (based on FEV_1% predicted, where over 80% is classified as mild; 50% to 79% is classified as moderate; 30% to 49% is classified as severe; and less than 30% is classified as very severe);
3. type of singing intervention (e.g. individual or group singing, length of follow up);
4. intervention conducted during an acute exacerbation versus stable state.

Sensitivity analysis

The authors also planned sensitivity analyses to assess the impact of the potentially important factors on the overall outcomes, if there were sufficient studies (n = 10):

1. variation in the inclusion criteria (e.g. studies conducted during exacerbations versus stable state, duration of intervention);
2. risk of bias in the included studies (selection, performance, detection, attrition and reporting bias);
3. analysis using random-effects model (to assess heterogeneity).

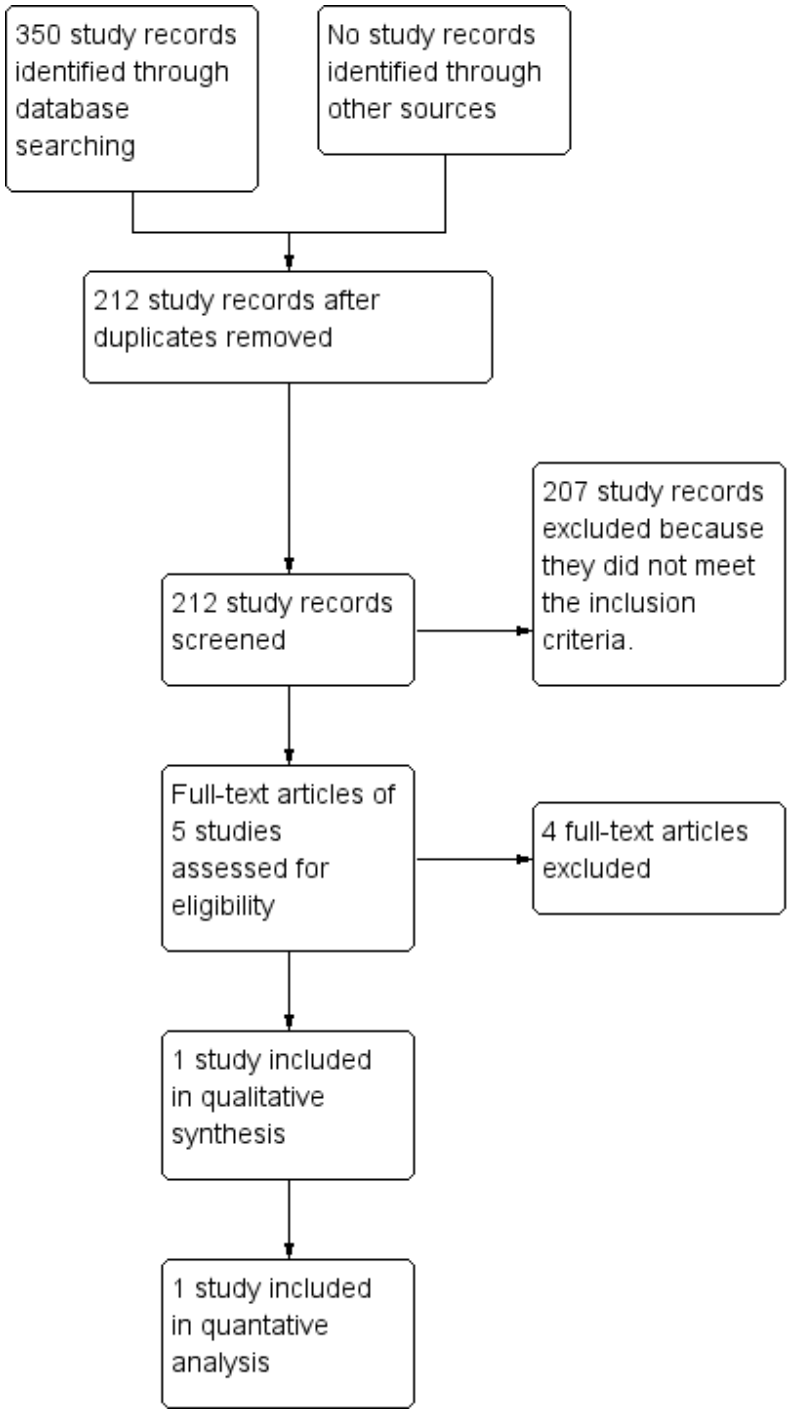
RESULTS

Description of studies

Results of the search

Two authors (JYI and AC) undertook initial screening of the abstracts of these studies. Since the 2009 review, an additional 156 potential studies were identified; a total of 17 papers were reviewed for detailed assessment. Of these, none fulfilled the inclusion criteria; hence in the current review four studies are listed in the Characteristics of excluded studies table. The Irons study, previously listed as ongoing in the original review, has since been completed, and been added as the sole included study (Irons 2012). A study flow diagram is shown in the figures (Figure 1).

Figure 1. Study flow diagram.



Included studies

The included study was a dual-centre (both in Australia), parallel, randomised controlled study, which included hospitalised children and adolescents (aged 7 to 17 years) with a pulmonary exacerbation (Irons 2012). A total of 51 young people were randomly assigned to either a singing group or a control group participating in non-physical recreational activities. The singing group participated in eight individual singing lessons during hospitalisation over a period of approximately two weeks; these lessons consisted of:

1. exercises to develop the desired posture for singing;
2. diaphragmatic breathing exercises;
3. vocal warm-ups; and
4. singing using the diaphragmatic technique.

Children in the control group participated in their preferred non-physical recreational activities (e.g. playing computer games or watching movies) for the same period of time. Outcome measures included CFQ-R (QoL), MIP, MEP and spirometry (FEV_1, FVC, $FEF_{25-75\%}$). These were reported at post-intervention (approximately two weeks from baseline) and follow up (six to eight weeks post-intervention). In addition, for the post-intervention period a singing diary, which consisted of six simple daily tasks for six weeks, was given to the participants in the singing group only in order to encourage their singing activities at home. The participants of the control group were encouraged to perform their usual CF management at home.

Only 40 participants (20 for each group) were included in analysis at post-intervention and 30 (15 for each group) at follow up.

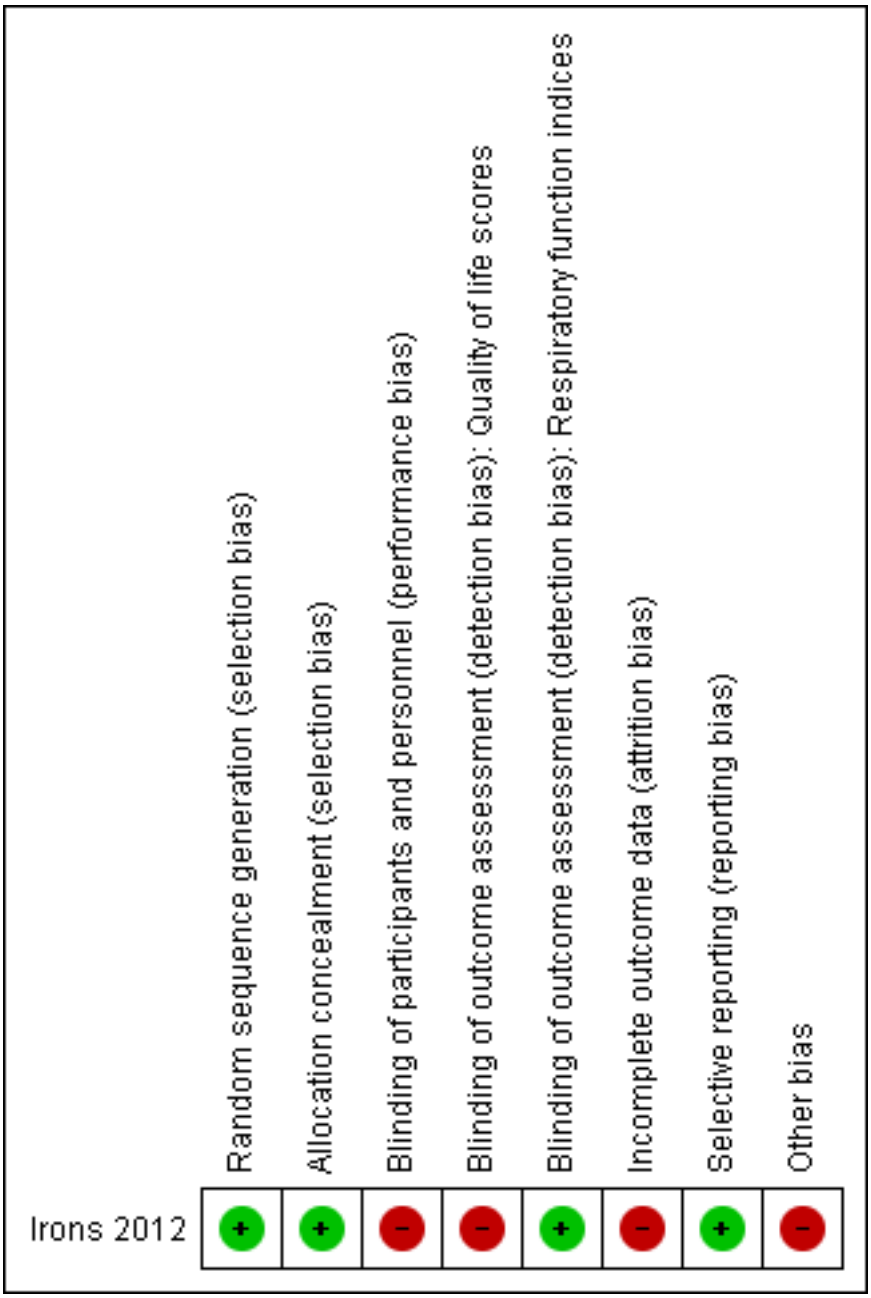
Excluded studies

A total of four studies were excluded (Grasso 2000; Kaak 2011; Reichardt 2011; Roux 2007). One music therapy study used pre-recorded music as an adjunct to regular chest physiotherapy for toddlers with CF (under 24 months old) and their caregivers; however, singing was not explored in this study (Grasso 2000). Another study investigated the effects of listening to Bach's *Magnificat* (a religious choral work) on 40 adults with pneumonia or acute bronchitis; again singing (as opposed to listening to music) was not part of the intervention in this study (Roux 2007). Two further studies, both in German, were excluded: one investigated the effects of playing the didgeridoo (as opposed to singing) with people with CF (Kaak 2011); and the remaining study reported the benefits of a singing program (Hustifex® - Brummer®) based on observations; however the program was designed for patients with chronic obstructive pulmonary disease and not CF (Reichardt 2011).

Risk of bias in included studies

An overview of our judgement of the risk of bias in the included study is presented in the figures (Figure 2).

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



Allocation

The randomisation sequence was computer-generated by a person external to the study; thus there is a low risk of bias (Irons 2012). Allocation was concealed by using opaque stickers on a randomisation list, and again the risk of bias is low (Irons 2012).

Blinding

Due to the nature of intervention, blinding was not possible for either patients or clinicians, leading to a high risk of bias. In addition, the researcher who collected the QoL data was not blinded to the intervention allocation, leading to a high risk of bias for these outcomes. However, the respiratory scientists who collected data for all lung function tests were blinded to participants' allocation. This factor gave a low risk of bias due to blinding for outcome assessors for these outcomes (Irons 2012).

Incomplete outcome data

The attrition rate was high, which may represent a bias; however, there were similar dropout rates in both groups (Irons 2012). The authors judged there to be an high risk of bias for this domain.

Selective reporting

The study was considered at low risk of bias for reporting bias. The study reported all outcomes according to their protocol in line with the record on the Australian New Zealand Clinical Trials Registry. The authors also reported all time-points (baseline, post-intervention, follow up) as planned (Irons 2012).

Other potential sources of bias

There may have been a selection bias, as people with a previous positive experience of singing may have been more likely to agree to enrol in a singing study (high risk of bias).

The paper did not report the sample size calculation. Study authors reported that the calculation was based on power of 90% (at 5% significance) for a MD (standard deviation (SD)) of 10 (10) cm H_2O in MIP between groups (Irons 2012). This estimated a required sample size of 23 participants per group.

Effects of interventions

Primary outcomes

1. QoL

There were no significant differences between the two groups at either post-intervention or follow up. Although there were some within-group statistically significant increases in some domains for treatment and control groups (e.g. emotional, social and vitality) between baseline and post-intervention assessment, as presented in the additional tables (Table 2).

Investigators assessed QoL using the CFQ-R questionnaire which has 12 different domains, some of which apply only for adolescents (from 14 years of age) (Quittner 2009). The data from 40 participants in these 12 domains were partially skewed, and thus non-parametric tests (Wilcoxon signed-rank) were performed for the original analysis. We present medians and IQR at baseline, post-intervention and follow up in the additional tables (Table 2), since it would be inappropriate to analyse the means and SD of the QoL data from the included study (Irons 2012). Post-intervention assessment took place after eight sessions (i.e. on average, between 10 and 14 days from baseline). Follow-up assessment took place six to eight weeks after the post-intervention time-point. There were 40 participants included in the analysis from baseline to post-intervention, while 30 were included for follow-up analysis. Four domains (vitality, health perception, role and weight) apply only for adolescents (between14 and 17 years of age). For these domains, data from six adolescents from each group were included for the post-intervention analysis and from five adolescents for the follow-up analysis.

2. Respiratory muscle function

a. MIP

There were no statistically significant differences between the singing and control groups at either post-intervention, MD 6.00 (95% CI -1.67 to 13.67); or follow up, MD 4.40 (95% CI -9.36 to 18.16) (Analysis 1.1).

b. MEP

There were no statistically significant differences between the singing and control groups at post-intervention, MD 3.05 (95% CI -12.43 to 18.53). However, statistical significance in the mean difference was detected at follow up favouring the singing group, MD 25.80 (95% CI 5.94 to 45.66) (Analysis 1.2).

c. Cough peak flow

This outcome was not reported.

Secondary outcomes

1. Other subjective scores

Other subjective scores (e.g. cough diary using Likert scales or visual analogue scales measuring subjective assessment of interference of cough) were not reported.

2. Spirometry

a. FEV_1

There were no statistically significant differences between the two groups at either post-intervention, MD -0.04 (95% CI -0.20 to 0.11); or follow up, MD -0.15 (95% CI -0.36 to 0.06) (Analysis 2.1).

b. FVC

There were no statistically significant differences between the two groups at either post-intervention, MD -0.10 (95% CI -0.25 to 0.06); or follow up, MD -0.11 (95% CI -0.29 to 0.07) (Analysis 2.2).

c. $FEF_{25-75\%}$

There were no statistically significant differences between the two groups at either post-intervention, MD -0.03 (95% CI -0.39 to 0.33); or follow up, MD -0.29 (95% CI -0.81 to 0.24) (Analysis 2.3).

3. Number of participants experiencing adverse effects

Irons reported that no adverse effects were observed in the singing group; adverse events for the control group were not reported in the paper.

4. Respiratory exacerbations

a. total number of hospitalised days

This outcome was not reported.

b. total number of symptomatic days

This outcome was not reported.

c. number of participants with respiratory exacerbations

This outcome was not reported.

6. Adherence to other CF treatments

This outcome was not reported.

7. Psychological assessments measuring self-efficacy, depression and anxiety

This outcome was not reported.

DISCUSSION

Summary of main results

In this update, only one small study conducted by three of the review authors has been included (Irons 2012). At follow up, a statistically significant improvement in MEP favouring the singing group was found, MD 25.80 (95% CI 5.94 to 45.66); however there were no differences in other lung function parameters and both groups experienced improvements in a number of QoL domains. At follow up, only the singing group continued with any form of the intervention; although singing sessions did not continue as they had in the hospital, participants were asked to keep a diary of six simple singing tasks for six to eight weeks following hospital discharge.

Overall completeness and applicability of evidence

There is insufficient evidence to make a judgement on the efficacy of singing for people with CF. The single included study was limited by the small sample size, high attrition rate and the limited applicability of MIP and MEP (Irons 2012). There is no guideline on the minimal clinically important difference in MIP and MEP for children and adolescents with CF; and the normal range of MIP and MEP is reported to be wide (Domenech-Clar 2003). Therefore, the result should be interpreted with caution.

Quality of the evidence

The quality of the evidence is currently low due to the small sample size, high attrition rate of participants and the non-blinded assessment of QoL measures.

Potential biases in the review process

The authors sought to limit potential biases through extensive searches and attempts to identify all relevant studies. As already declared in the protocol, authors of the included study are also authors of this review.

Agreements and disagreements with other studies or reviews

The results of the included study (Irons 2012) were similar to those of previous singing studies in other chronic respiratory conditions (Bonilha 2009; Lord 2010), in multiple sclerosis (MS) (Wiens 1999) and in Parkinson's Disease (Di Benedetto 2009). While CF is a different condition to these other chronic illnesses, there are similarities with regard to the disease impact on QoL, the characteristics of the obstructive lung disease, the respiratory symptoms (difficulty in breathing, breathlessness), and the nature of the chronic conditions. For example, patients with chronic obstructive pulmonary disorder (COPD) demonstrated increased respiratory muscle strength measured by MEP (mean change from baseline to post-intervention 3.0 H_2O cm; P = 0.05) after 24 weekly singing sessions (Bonilha 2009). Another study in patients with COPD found that 12 bi-weekly group singing sessions reduced anxiety and depression and enhanced general well-being (Lord 2010). Also, a 12-week singing intervention in patients with MS improved MEP (mean change from baseline to post-intervention 2.8 H_2O cm; P > 0.05) (Wiens 1999), and a 13-week singing program in people with Parkinson's Disease helped to improve MIP (mean change from baseline to post-intervention 7.4 H_2O cm; P = 0.02) and MEP (mean change from baseline to post-intervention 21 H_2O cm; P = 0.01) (Di Benedetto 2009).

The included study demonstrated a mean (SD) improvement of 12.1 (7.8) H_2O cm in MIP scores from baseline to post-intervention in the singing group; the mean (SD) increase of 6.1 (14.5) H_2O cm seen in the control arm was less, but the difference between groups was not statistically significant (Irons 2012). Nevertheless, the increase in MIP in the included study was a greater improvement than in other studies on singing as an intervention (Bonilha 2009; Di Benedetto 2009; Wiens 1999), although the numbers cannot be compared directly given the differences between other conditions (COPD, Parkinson's Disease and MS) and CF. The magnitude of the increase in MIP in the Irons study is similar to that seen with a conventional inspiratory muscle training method for 10 weeks during a stable period, a study of which reported an increase in mean MIP post-intervention of 14 H_2O cm (Sawyer 1993).

In relation to the QoL results from the Irons study, participants in both the singing and control groups showed similar improvements in respiratory symptoms and treatment burden domains at post-intervention (Irons 2012). Only the singing group continued to have a reduced treatment burden at follow up as they had continued their singing activities at home after discharge. In addition, the control group improved in the social and vitality domains, and the singing group in the emotional and digestion domains of the CFQ-R. Both groups' improvements in some QoL domains may be due to the standard medical treatment they received as inpatients or the fact that they were discharged from hospital, or a combination of both. It was not possible for this study design to assess the impact of singing independent of this standard treatment. In summary, without sufficient data, the effect of a singing intervention on QoL for people with CF cannot be confirmed and more studies are needed to assess possible health benefits, in light of other studies which have indicated a positive impact of singing on QoL (Bonilha 2009; Engen 2005; Kenny 2004; Lord 2010; Lord 2012; Unwin 2002; Wiens 1999).

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to recommend singing as an effective adjunct treatment in individuals with CF. However, people with CF who enjoy singing should be encouraged to do so. There is growing interest in non-medical treatments for CF, and more research into these treatments, including singing, is needed to inform health practitioners, people with CF and their families (Butler 2012).

Implications for research

Adequately-powered and carefully-designed research studies are needed. The design of future RCTs should take account of CF severity (mild, moderate and severe), and include detailed information about the singing intervention (vocal exercises, song type, pitch and dynamic range); delivery format (individual or group); length and frequency of sessions and prescribed singing practice time. Future studies could also take account of participants' previous experience with singing. Trials evaluating short-term (acute admission, up to one month), medium-term (over one month and up to six months) and longer-term outcomes (over six months and up to one year and annually thereafter) are also required. Future studies could also address the effects of singing for people with advanced CF in relation to QoL.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Irons 2012

Methods	A dual-centre (two paediatric hospitals in Australia), parallel, RCT; singing group versus non-physical recreation group during hospitalisation due to a pulmonary exacerbation; intervention duration approximately 2 weeks. Follow up 6 - 8 weeks post-intervention
Participants	51 inpatients enrolled (singing group n = 26; control group n = 25), analysed 40 at post-intervention (singing group n = 20; control group n = 20) and 30 at follow up (singing group n = 15; control group n = 15) Age range: 7 - 17 years; mean (SD) age: singing group = 12.1 (3.1) years; control group = 11.1 (3.7) years Gender: singing group = 35% male; control group = 50% male. Inclusion criteria: young people with an established diagnosis of CF who were being treated as inpatients for a respiratory exacerbation Exclusion criteria: young people who had undertaken individual singing lessons within the past 5 years, who had an intellectual disability or who, according to their treating physician, were too ill to participate in singing activities
Interventions	Experimental (singing) group: 8 standard individual singing sessions consisting of 4-stage program including posture, diaphragmatic breathing exercise, vocal warm-up and singing favourite songs Control group: 8 individual non-physical recreation sessions (e.g. playing computer games, watching movies) Both groups received intravenous antibiotic treatment and chest physiotherapy as the standard hospital care Singing and recreation session facilitator was a qualified, experienced music therapist Post-intervention only for the singing group: a singing diary of 6 simple singing tasks for 6 - 8 weeks
Outcomes	Changes in MIP, MEP, QoL (CFQ-R), and spirometry (FEV_1, FVC, $FEF_{25-75\%}$) from baseline to post-intervention, and to follow up (6 - 8 weeks post-intervention)
Notes	No adverse events reported. Ethics approvals obtained; informed consent by participants and their parent/caregiver; This study was conducted as a part of the first author's PhD studies and she received a small amount of funding from the University of Sydney for transport and purchasing some equipment through the Post-graduate Research Support Scheme (PRSS) during the data collection period

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sequence was computer-generated by an external person to the study

Allocation concealment (selection bias)	Low risk	Allocation was concealed by opaque stickers on the randomisation list
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and clinicians were not blinded due to the nature of the intervention
Blinding of outcome assessment (detection bias) Quality of life scores	High risk	Person who collected the QoL data was not blinded due to the nature of the intervention
Blinding of outcome assessment (detection bias) Respiratory function indices	Low risk	Respiratory scientists who conducted lung function tests were blinded to the participants' group allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Attrition rate was relatively high (21.6%), but similar drop-out rates in both groups were observed. Reasons for drop-out were stated and similar in both groups
Selective reporting (reporting bias)	Low risk	All planned outcome measures were reported at the planned time-points
Other bias	High risk	Selection bias, as people with a previous positive experience of singing more likely to agree to enrol in the study

CF: cystic fibrosis
CFQ-R: cystic fibrosis questionnaire (revised)
$FEF_{25-75\%}$: mid-expiratory flow
FEV_1: forced expiratory volume at one second
FVC: forced vital capacity
MEP: maximum expiratory pressure
MIP: maximum inspiratory pressure
QoL: quality of life
RCT: randomised controlled trial
SD: standard deviation

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

Study	Reason for exclusion
Grasso 2000	Intervention is not singing, but using pre-recorded music during daily chest percussion routine with toddlers
Kaak 2011	Intervention is not singing, but playing the didgeridoo.
Reichardt 2011	People with CF were not included; a observational study on Hustifex®-Brummer® - a singing method specially developed for patients with COPD
Roux 2007	Intervention is not singing, but listening to music; people with CF were not included

CF: cystic fibrosis
COPD: chronic obstructive pulmonary disorder

DATA AND ANALYSES

Comparison 1. Respiratory muscle strength tests

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in maximal inspiratory pressure (cm H_2O)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 short term (up to 1 month)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 medium term (> 1 month and < 6 months)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Change in maximal expiratory pressure (cm H_2O)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 short term (up to 1 month)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 medium term (> 1 month and < 6 months)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 2. Spirometry

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in FEV_1 (L/sec)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 short term (up to 1 month)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 medium term (> 1 month and < 6 months)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Change in FVC (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 short term (up to 1 month)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 medium term (> 1 month and < 6 months)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Change in $FEF_{25-75\%}$ (L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 short term (up to 1 month)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 medium term (> 1 month and < 6 months)	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

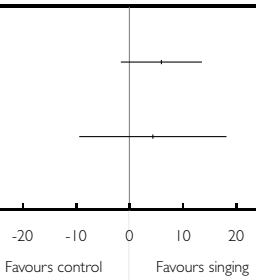
Analysis 1.1. Comparison 1 Respiratory muscle strength tests, Outcome 1 Change in maximal inspiratory pressure (cm H2O).

Review: Singing as an adjunct therapy for children and adults with cystic fibrosis

Comparison: 1 Respiratory muscle strength tests

Outcome: 1 Change in maximal inspiratory pressure (cm H_2O)

Study or subgroup	Singing N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 short term (up to 1 month)						
Irons 2012	20	12.1 (9.78)	20	6.1 (14.52)		6.00 [-1.67, 13.67]
2 medium term (> 1 month and < 6 months)						
Irons 2012	15	12.467 (17.683)	15	8.07 (20.662)		4.40 [-9.36, 18.16]



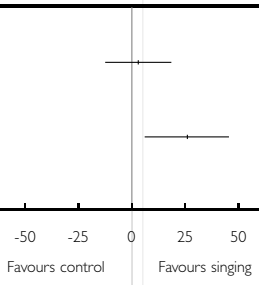
Analysis 1.2. Comparison 1 Respiratory muscle strength tests, Outcome 2 Change in maximal expiratory pressure (cm H2O).

Review: Singing as an adjunct therapy for children and adults with cystic fibrosis

Comparison: 1 Respiratory muscle strength tests

Outcome: 2 Change in maximal expiratory pressure (cm H_2O)

Study or subgroup	Singing N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 short term (up to 1 month)						
Irons 2012	20	9 (17.63)	20	5.95 (30.62)		3.05 [-12.43, 18.53]
2 medium term (> 1 month and < 6 months)						
Irons 2012	15	26.4 (26.532)	15	0.6 (28.908)		25.80 [5.94, 45.66]



Analysis 2.1. Comparison 2 Spirometry, Outcome 1 Change in FEV1 (L/sec).

Review: Singing as an adjunct therapy for children and adults with cystic fibrosis

Comparison: 2 Spirometry

Outcome: 1 Change in FEV_1 (L/sec)

Study or subgroup	Singing N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 short term (up to 1 month)						
Irons 2012	20	0.053 (0.21)	20	0.1 (0.28)		-0.04 [-0.20, 0.11]
2 medium term (> 1 month and < 6 months)						
Irons 2012	15	-0.03 (0.29)	15	0.12 (0.285)		-0.15 [-0.36, 0.06]

Analysis 2.2. Comparison 2 Spirometry, Outcome 2 Change in FVC (L).

Review: Singing as an adjunct therapy for children and adults with cystic fibrosis

Comparison: 2 Spirometry

Outcome: 2 Change in FVC (L)

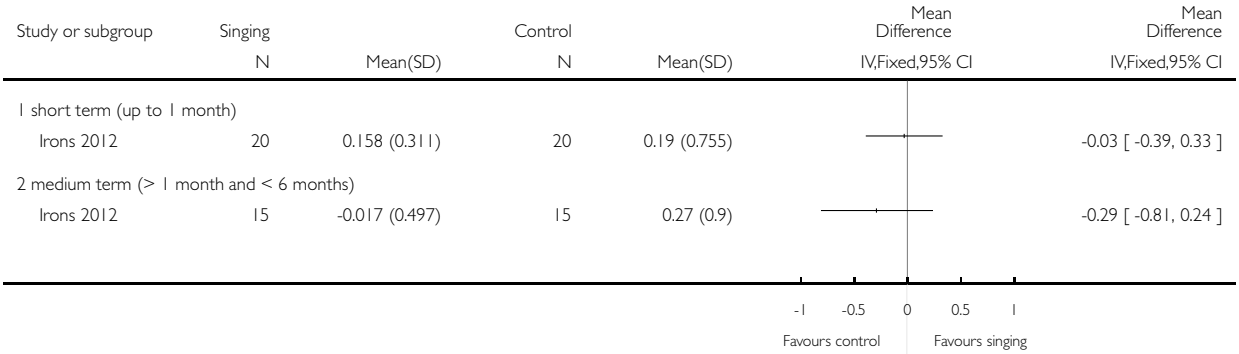
Study or subgroup	Singing N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
1 short term (up to 1 month)						
Irons 2012	20	0.017 (0.239)	20	0.11 (0.258)		-0.10 [-0.25, 0.06]
2 medium term (> 1 month and < 6 months)						
Irons 2012	15	-0.045 (0.265)	15	0.06 (0.236)		-0.11 [-0.29, 0.07]

Analysis 2.3. Comparison 2 Spirometry, Outcome 3 Change in FEF25-75% (L).

Review: Singing as an adjunct therapy for children and adults with cystic fibrosis

Comparison: 2 Spirometry

Outcome: 3 Change in $FEF_{25-75\%}$ (L)



ADDITIONAL TABLES

Table 1. Glossary

Term	Explanation
cough peak flow	highest expiratory flow generated during a forced cough manoeuvre, measured in litre per second
visual analogue scale	a response scale commonly used in questionnaires, to indicate levels of agreement or disagreement to a statement on a continuous line, e.g. strongly disagree, disagree, agree, strongly agree

Table 2. QoL results

Domain	Time	Treatment group medians (IQR)	Statistical significance in change from baseline	Control group medians (IQR)	Statistical significance in change from baseline
Physical	baseline	80.50 (54.1 to 88.88)		72.21 (56.94 to 88.80)	
	post-intervention	83.30 (62.48 to 93.74)		83.30 (51.39 to 95.46)	

Table 2. QoL results (*Continued*)

	follow up	83.30 (70.8 to 95. 83)		91.66 (75.00 to 100. 00)	
Emotional	baseline	81.65 (71.46 to 87. 50)		84.97 (60.63 to 92. 88)	
	post-intervention	83.30 (73.73 to 92. 91)	P = 0.031	80.00 (64.58 to 91. 65)	
	follow up	75.00 (66.60 to 91. 60)		83.30 (66.66 to 100. 00)	
Social	baseline	71.42 (57.10 to 79. 76)		71.80 (61.90 to 85. 70)	
	post-intervention	71.81 (62.48 to 83. 30)		66.60 (54.50 to 76. 17)	P = 0.044
	follow up	71.42 (66.6 to 85. 71)		72.20 (52.38 to 90. 47)	
Body image	baseline	83.29 (66.62 to 100. 00)		77.77 (69.42 to 100. 00)	
	post-intervention	94.44 (66.66 to 100. 00)		83.25 (66.66 to 97. 22)	
	follow up	100.00 (66.60 to 100.00)		88.80 (77.70 to 100. 00)	
Eating	baseline	100.00 (55.55 to 100.00)		100.00 (66.62 to 100.00)	
	post-intervention	88.88 (66.60 to 100. 00)		83.29 (66.62 to 100. 00)	
	follow up	88.88 (66.60 to 100. 00)		100.00 (88.80 to 100.00)	
Treatment burden	baseline	66.63 (55.50 to 77. 77)		61.08 (47.21 to 77. 70)	
	post-intervention	77.74 (66.62 to 97. 20)	P = 0.014	66.60 (44.44 to 94. 44)	P = 0.026
	follow up	77.70 (55.50 to 100. 00)	P = 0.031	66.60 (44.40 to 77. 77)	

Table 2. QoL results (*Continued*)

Respiratory symptoms	baseline	66.60 (52.08 to 77.03)		58.30 (50.00 to 2.92)	
	post-intervention	80.54 (75.00 to 88.80)	P = 0.001	79.15 (60.38 to 87.43)	P = 0.002
	follow up	83.30 (72.20 to 91.66)	P = 0.016	83.30 (66.60 to 88.80)	P = 0.013
Digestion	baseline	83.33 (66.62 to 100.00)		94.40 (66.60 to 100.00)	
	post-intervention	100.00 (88.88 to 100.00)	P = 0.024	100.00 (66.62 to 100.00)	
	follow up	100.00 (88.80 to 100.00)		100.00 (66.66 to 100.00)	
Vitality	baseline	45.80 (33.32 to 54.17)		49.95 (33.32 to 64.55)	
	post-intervention	41.63 (33.30 to 66.62)		66.65 (45.83 to 91.60)	P = 0.043
	follow up	50.00 (41.67 to 58.33)		75.00 (49.95 to 85.40)	
Health perception	baseline	61.05 (38.86 to 80.50)		44.42 (30.53 to 80.48)	
	post-intervention	61.05 (47.18 to 83.28)		77.70 (61.06 to 100.00)	
	follow up	55.50 (33.31 to 83.29)		88.80 (58.32 to 94.40)	
Role	baseline	58.33 (47.90 to 77.08)		62.47 (54.13 to 87.48)	
	post-intervention	58.30 (39.53 to 66.62)		66.63 (58.30 to 77.08)	
	follow up	75.00 (58.33 to 75.00)		83.30 (49.95 to 95.83)	
Weight	baseline	100.00 (0.00 to 100.00)		33.30 (24.98 to 50.00)	

Table 2. QoL results (*Continued*)

	post-intervention	100.00 (24.98 to 100.00)		66.60 (33.32 to 100.00)	
	follow up	100.00 (0.00 to 100.00)		66.60 (33.31 to 100.00)	

IQR: inter-quartile range

APPENDICES

Appendix 1. AMED Search Strategy (searched on 24/05/2012)

AMED Search Strategy
1. exp Cystic Fibrosis/
2. Cystic Fibrosis.tw
3. CF.tw
4. Mucoviscidosis.tw
5. 1 or 2 or 3 or 4
6. Sing or Singing or Singer* or Song*.tw
7. (Vocal* or breath*) adj2 exercis*.tw
8. Choir*.tw
9. Diaphragm* adj2 breath*.tw
10. 6 or 7 or 8 or 9
11. Exp Clinical trials/
12. Clinical trial.pt
13. Random*.tw
14. Placebo.tw
15. Crossover or Cross-over.tw
16. 11 or 12 or 13 or 14 or 15
16. 5 and 10 and 16

Key
tw: textword
Exp/: exploded AMED Thesaurus term
pt: publication type

Appendix 2. PsychINFO Search Strategy (searched on 24/05/2012)

PsycINFO Search Strategy via OvidSP

1. Cystic Fibrosis/ [PsyINFO Thesaurus Descriptor]
2. Cystic Fibrosis [keyword]
3. CF [keyword]
4. Mucoviscidosis [keyword]
5. 1 or 2 or 3 or 4
6. Sing or Singing or Singer* or Song* [keyword]
7. (Vocal* or breath*) adj2 exercis*[keyword]
8. Choir*[keyword]
9. Diaphragm* adj2 breath* [keyword]
10. 6 or 7 or 8 or 9
11. Clinical trials [PsychINFO Thesaurus Descriptor]
12. Random* [keyword]
13. Placebo.tw [keyword]
14. Crossover or Cross-over [keyword]
15. 11 or 12 or 13 or 14
16. 5 and 10 and 15

Appendix 3. CINAHL Search Strategy (searched on 24/05/2012)

CINAHL Search Strategy via EBSCO

1. (MH "Cystic Fibrosis") [CINAHL Subject Heading]
2. Cystic Fibrosis [all text]
3. CF [all text]
4. Mucoviscidosis [all text]
5. 1 or 2 or 3 or 4
6. Sing or Singing or Singers or Song* [all text]
7. (Vocal* or breath*) adj2 exercis* [all text]
8. Choir* [all text]
9. Diaphragm* adj2 breath* [all text]
10. 6 or 7 or 8 or 9
11. (MH "Clinical Trials+") [Exploded CINAHL Subject heading]
12. Clinical trial [publication type]
13. Random* [all text]
14. Placebo [all text]
15. Crossover or Cross-over [all text]
16. 11 or 12 or 13 or 15
17. 5 and 10 and 16

Appendix 4. ProQuest Search Strategy: Dissertation Abstracts International (late 1960 to present) (searched on 25/05/2012)

ProQuest Search Strategy: Dissertation Abstracts International (late 1960 to present)
1. [as key words in citation and abstract] Cystic fibrosis
2. [as key words in citation and abstract] Cystic fibrosis AND Breathing
3. [as key words in citation and abstract] Cystic fibrosis AND Voice
4. [as key words in citation and abstract] Cystic fibrosis AND music
5. [as key words in citation and abstract] Cystic fibrosis AND singing
6. [as key words in citation and abstract] Music therapy AND breathing
7. [as key words in citation and abstract] Singing AND breathing
8. [as key words in citation and abstract] singing OR breathing exercise AND respiratory
9. [as key words in citation and abstract] choir AND effect

Appendix 5. Clinicaltrials.gov Search Strategy (searched on 25/5/2012)

Clinicaltrials.gov Search Strategy
Advanced Search
Condition: Cystic Fibrosis
Interventions: sing/singing/singer/song/diaphragmatic/vocal/choir

Appendix 6. Music therapy research database (www.musictherapyworld.de) Search Strategy (searched on 24/09/2009)

Music therapy research database (www.musictherapyworld.de) **Search Strategy**
No electronic search was possible using search terms. Thus, all abstracts were reviewed
1. Dissertations on Music Therapy (1994 - 2006)
2. Conference Reports Archive (1993 - 2001)

Appendix 7. National Research Register Archive Search Strategy (2000 - 2012)

National Research Register Archive Search Strategy
cystic fibrosis AND sing OR singing OR breathing OR choir OR vocal

WHAT'S NEW

Last assessed as up-to-date: 31 March 2014.

Date	Event	Description
31 March 2014	New citation required and conclusions have changed	The previously ongoing study has been completed and results have been added to this review (Irons 2012). While no meta-analysis was possible since there is only one study included, we have presented results in forest plots where available
31 March 2014	New search has been performed	A search of the Group's Cystic Fibrosis Trials Register identified no new reference potentially eligible for inclusion in this review. New searches including hand searching identified no new eligible studies to be included for this review

CONTRIBUTIONS OF AUTHORS

Protocol stage: draft the protocol	JY Irons, AB Chang, DT Kenny
Review stage: select which trials to include (2 + 1 arbiter)	JY Irons, AB Chang + DT Kenny
Review stage: draft the final review	JY Irons, AB Chang, DT Kenny
Update stage: update the review	JY Irons, AB Chang, P Petocz

DECLARATIONS OF INTEREST

The authors of the original review have conducted the only trial included in this review - a randomised controlled trial with inpatients with CF. Clinical trial registration (ACTRN 12609000471280).

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- NHMRC, Australia.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In a *post hoc* change, the authors considered that reporting the differences (change scores) from baseline to post-intervention or follow up, or both, in the outcome measures to be appropriate in this review.

In order to assess possible adverse effects from both treatment and control interventions "Adverse effects of the intervention" has been changed into "Adverse effects".

INDEX TERMS

Medical Subject Headings (MeSH)

*Music Therapy; Cystic Fibrosis [*therapy]

MeSH check words

Adolescent; Adult; Child; Humans