Inspiratory muscle training for cystic fibrosis (Review)

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Inspiratory muscle training for cystic fibrosis

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A B S T R A C T

Background

Cystic fibrosis is the most common life-limiting genetic condition in Caucasians and the life-expectancy of those newly diagnosed is increasing. Inspiratory muscle training may be a way of improving the lung function and quality of life of people with cystic fibrosis. Hence there is a need to establish whether this intervention is beneficial.

Objectives

To determine the effect of inspiratory muscle training on health-related quality of life, pulmonary function and exercise tolerance.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials register comprising of references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings.

Date of most recent search: 28 June 2011.

Selection criteria

Randomised or quasi-randomised clinical controlled trials comparing different inspiratory muscle training regimens with each other or a control in people with cystic fibrosis.

Data collection and analysis

Three review authors independently applied the inclusion and exclusion criteria to publications and assessed the quality of the included studies.

Main results

Eleven studies were identified. Of these eight studies with 180 participants met the review inclusion criteria. There was wide variation in the quality of the included studies. Data were not published in sufficient detail or with sufficiently similar outcome measures in these studies to perform meta-analyses.

Authors' conclusions

We have not found any evidence to suggest that this treatment is either beneficial or not. We would advise that practitioners evaluate on a case-by-case basis whether or not to employ this therapy. We recommend that future studies make more use of health-related quality of life and exercise tolerance measures; and that there is an agreement upon a single standard measure of classifying the clinical status of the participants.

PLAIN LANGUAGE SUMMARY

The training of muscles that cause the chest to expand in order to take air into the lungs for people with cystic fibrosis

Cystic fibrosis is the most common life-limiting genetic condition in Caucasians. The life-expectancy of newly diagnosed patients is increasing. Inspiratory muscle training may improve quality of life, lung function and exercise tolerance in people with cystic fibrosis so that these are closer to the levels found in people who do not have cystic fibrosis. It may also boost the clearance of mucus. Inspiratory muscle training can be performed without the help of a carer and wherever the individual feels appropriate. We searched for randomised or quasi-randomised clinical controlled trials. We aimed to determine the effects of inspiratory muscle training in the treatment of people with cystic fibrosis. We were able to include eight studies with 180 participants in the review. We were not able to combine results from these studies to answer our questions, because the studies either did not publish enough detail or did not use the same standard measurements. Given this, we cannot recommend the use, or not, of this intervention. We do recommend that future studies make more use of health-related quality of life and exercise tolerance measures. We also suggest there should be agreement upon standard measurements to be used.

BACKGROUND

Description of the condition

Cystic fibrosis (CF) is the result of a genetic mutation that directly affects ion transport within cells by altering the function of the cystic fibrosis transmembrane conductance regulator (CFTR). In the case of secretory cells, this results in the production of dehydrated, viscous and ultimately dysfunctional secretions (WHO 2005). Two main sites of secretory cells are the digestive and respiratory systems. Both of these systems have a major influence on health and development. The adverse effect on the respiratory system in people with CF contributes to it being the most common, life-limiting autosomal recessive genetic disorder in Caucasians (Kosorok 1996); and in the UK it currently affects over 7500 people (CF Trust 2005). With advancement in the medical management of the condition, the life-expectancy of babies newly diagnosed is now into their fifties (Dodge 2007). This brings with it a responsibility for all clinicians working with people with CF, and in particular physiotherapists, to consider ways of enhancing quality of life.

Description of the intervention

Inspiratory muscle training (IMT) involves the training of muscles that act to expand the chest in order to take in air into the lungs. The specific loads applied to the inspiratory muscles for the purpose of training are flow, threshold or resistive in nature (*see* Table 1 for explanations of these terms: threshold load, resistive loading). Training regimens vary in terms of intensity and duration of session or programme or both (McConnell 2002). It is possible to develop a training regimen that combines a method of stressing the inspiratory muscles with a specific training approach, e.g. continuous or interval training (*see* Table 1). IMT is a technique that can be performed independently and wherever the individual feels appropriate. While the initial provider and setting for initiating IMT will usually involve a therapist in a clinical setting, generally the user of IMT will be left to implement their own training, with or without supervision from another person, such as a carer.

How the intervention might work

A Cochrane Systematic Review has found some limited evidence that general conditioning exercise (physical training) can improve the function of the lungs, the exercise tolerance and health-related quality of life of people who have CF closer to that of healthy people (Bradley 2008). More specifically, IMT may also have these benefits (de Jong 2001). In addition, it has been suggested that

IMT may also enhance the clearance of mucus, which is fundamental to management of the condition (Chatham 2004).

Why it is important to do this review

At present there is no systematic review of the currently available evidence from randomised controlled trials (RCTs) or quasi-randomised controlled trials as to whether IMT is beneficial, nor on the optimal IMT programme (i.e. the nature of the training load and specifics of the training protocol), for people with CF.

OBJECTIVES

1. To determine the effects of IMT in the management of people with CF. Specifically, we plan to examine the effects of IMT in people with CF on:

    i) health-related quality of life;

    ii) pulmonary function;

    iii) exercise tolerance;

2. To report any adverse effects reported in the included trials.

3. To compare the effects of IMT performed using resistive devices, threshold-loading devices and isocapnic hyperpnoea (*see* Table 1) on the above outcomes and adherence.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised or quasi-randomised clinical controlled trials.

Types of participants

People with CF, of any age, diagnosed by clinical criteria, sweat test or genotyping or both.

Types of interventions

Inspiratory muscle training (as achieved by voluntary isocapnic hyperpnoea, resistive loading or threshold loading: *see* Table 1) compared with each other or with no or sham IMT (device or procedure that appears to be IMT but does not have its training properties).

Types of outcome measures

Primary outcomes

1. Health-related quality of life
2. Pulmonary function tests (performed at rest):
    i) forced expiratory volume at one second (FEV_1)
    ii) forced vital capacity (FVC)
3. Exercise tolerance:
    i) field-based tests
    ii) laboratory-based tests

Secondary outcomes

1. Pulmonary function tests (performed at rest):
    i) maximal inspiratory pressure (PI_{max})
    ii) inspiratory capacity (IC)
2. Respiratory muscle function (strength and endurance)
3. Frequency and duration of respiratory infections, hospitalisations
4. Adherence to the IMT regimen
5. Death or survival
6. Adverse effects (pneumothorax, musculoskeletal pains or injuries, others)
7. Costs

Search methods for identification of studies

Electronic searches

We identified relevant studies from the Group's Cystic Fibrosis Trials Register using the term 'inspiratory muscle training'.

The Group's Cystic Fibrosis Trials Register, which is compiled from electronic searches of the Cochrane Central Register of Controlled Trials (Clinical Trials) (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 four major cystic fibrosis conferences: the International Cystic Fibrosis Conference; the European Cystic Fibrosis Conference, the North American Cystic Fibrosis Conference and the Australia and New Zealand 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.

We also performed separate searches of the following databases: MEDLINE, EMBASE, CINAHL, AMED (Allied and Complementary Medicine), PEDro (The Physiotherapy Evidence Database), BIOSIS Previews, Science Direct and SCOPUS to 2005, using both the Cochrane RCT and Cystic Fibrosis search

filters; and terms specific to the intervention (Appendix 1; Appendix 2; Appendix 3; Appendix 4). We also searched Current Controlled Trials and the UK National Research Register for ongoing and recently completed studies. These searches were updated and run again on the 08 August 2011 (Appendix 3; Appendix 4; Appendix 5).

Date of the last search of the Group's Cystic Fibrosis Trials Register: 28 June 2011.

Searching other resources

For the original review, we also contacted manufacturers and study investigators and checked reference lists of relevant literature.

Data collection and analysis

Selection of studies

All three authors screened the output of electronic searches (title and abstract) to identify potentially eligible studies. From the full reports, all three authors independently selected studies for inclusion into the review. We planned to resolve any disagreements by discussion and if necessary by arbitration from a third person (Helen Handoll); however, this was not necessary.

Data extraction and management

All three authors independently collected data using standardised forms made available by the Cystic Fibrosis and Genetic Disorders Group. The authors did not need to resolve any disagreements.

Assessment of risk of bias in included studies

In order to assess the risk of bias, using a standardised form, all three authors independently assessed study quality according to the following criteria from the Cochrane risk of bias tool (Higgins 2011a): sequence generation; allocation concealment; the degree of blinding; whether incomplete data was included in the analysis (i.e. the intention-to-treat principle); whether there was selective reporting of results and any other identified sources of bias. We also commented on aspects of external validity, in particular the description of study participants and study interventions (e.g. in resistive IMT, has inspiratory flow rate been specifically controlled or not?), and the reliability of outcome assessment (including any reporting of the participants' 'familiarity' with the intended method of assessment), especially length of follow up. We reported on whether the included studies used systematic methods to record adverse events. We planned to resolve any disagreements by discussion and if necessary by arbitration from a third person (Helen Handoll); however, this was not necessary.

Measures of treatment effect

We have graphically presented quantitative data for the outcomes listed in the inclusion criteria. For each study, we planned to calculate risk ratios (RR) and 95% confidence intervals (CIs) for dichotomous outcomes, and mean differences (MD) and 95% CIs for continuous outcomes.

Unit of analysis issues

Ideally when conducting a meta-analysis combining results from cross-over studies, we will use the inverse variance methods that are recommended by Elbourne (Elbourne 2002). However, if there are limited data available we planned to either use first arm data only or treat the cross-over trial as if it was a parallel trial (assuming a correlation of zero as the most conservative estimate). Elbourne says that this approach produces conservative results as it does not take into account within-patient correlation (Elbourne 2002). Also each participant appears in both the treatment and control group, so the two groups are not independent. There was one cross-over trial included in the review. Currently we have reported results from this trial narratively but for the first update of this review we plan to analyse this using the generic inverse variance (GIV) method. At which point, if we need to combine data from cross-over studies in a meta-analysis with data from parallel studies, we will use the methods discussed by Curtin (Curtin 2002a; Curtin 2002b; Curtin 2002c).

Where studies measured data longitudinally, the authors based the analysis on the final time point results. Methods are not yet available to carry out a meta-analysis of aggregate longitudinal data, where individual patient data (IPD) is not available.

Dealing with missing data

We contacted the authors of some of the studies in order to obtain more specific data to that presented; e.g. means and standard deviations; however, we have received no response to date.

Assessment of heterogeneity

If sufficient studies (at least four) had been included which we were able to combine in a meta-analysis, we planned to test for heterogeneity between comparable studies using a standard chi² test and to consider this statistically significant at P < 0.1. In addition we planned to use the value of the I² statistic to assist in determining levels of heterogeneity (Higgins 2003). We planned to base our judgements on the convention that 0 to 40% is unlikely to be important, 30 to 60% could be indicative of moderate heterogeneity, 50 to 90% may indicate important levels of heterogeneity and 75 to 100% suggests considerable heterogeneity (Higgins 2011b).

Assessment of reporting biases

If sufficient data were available, we planned to attempt to assess publication bias by preparing a funnel plot.

Data synthesis

We planned to pool the results of comparable groups of studies using the fixed-effect model and calculate 95% CIs.

Subgroup analysis and investigation of heterogeneity

We would not perform meta-analysis if we considered it would be misleading to quote an average value for the treatment effect, such as where there is substantial and statistically significant heterogeneity. As pooling of data from the included studies is inappropriate or not possible due variations in the level of IMT employed, we have provided appropriate narrative descriptions of the results. However, we have included graphical representation of some of the extracted data, which may be added to in the future (*see* Data and analyses).

Should there have been significant heterogeneity and if there had been a sufficient number of included studies, we would have explored the possible causes of the heterogeneity using subgroup analysis in terms of the following parameters:

1. type of IMT (e.g. low level versus high level);
2. regimen of IMT (e.g. daily versus three times per week);
3. characteristics of study participants
   i) age (up to 16 years versus older than 16 years);
   ii) gender of study participants;
   iii) genotype;
   iv) participants with 'weak' inspiratory muscles strength compared to those with preserved strength (as determined by PI_{max});
   v) participants with mild hyperinflation to those with severe hyperinflation (as determined by their total lung capacity (TLC)) or mixed populations with comparable interventions.
4. definition of outcome measures.

Sensitivity analysis

If sufficient studies had been included, we planned to perform sensitivity analyses exploring the effects of published and unpublished studies, allocation concealment, assessor blinding and loss to follow up. We planned to conduct best-case and worst-case scenario plots to investigate the potential effects of loss to follow up.

R E S U L T S

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The results of the first stage of the search are given below.

- The Cystic Fibrosis and Genetic Disorders Group's CF Trials Register provided nine citations for five studies all of which were considered as potentially eligible for inclusion. When this review was updated in September 2011 an additional three studies were considered for inclusion.
- A search of EBSCOhost databases (OVID for the original review), MEDLINE, EMBASE, CINAHL, BIOSIS Previews and AMED (Allied and Complementary Medicine) returned 184 potential studies, of which, 10 were considered as eligible for potential inclusion.
- A search of PEDro (The Physiotherapy Evidence Database) returned 73 potential studies, of which, 12 were considered for potential inclusion.
- A search of Science Direct and SCOPUS did not produce any studies not already identified by the above searches.

All three authors reviewed the abstracts of the returned studies and selected those relevant to the scope of this review. This process left us with a final pool of 11 studies. From these 11, eight studies with a total of 180 participants were included (Albinni 2004; Amelina 2006; Asher 1983; Chatham 1997; de Jong 2001; Enright 2004; Heward 2000; Sawyer 1993) and three were excluded (Howard 2000; Keens 1977; Sartori 2008). Of the eight included studies, four were published as abstracts only (Albinni 2004; Amelina 2006; Chatham 1997; Heward 2000).

Included studies

A full comparison of the included studies can be found in the table Characteristics of included studies.

Of the eight included studies, seven were of a parallel design; i.e. a control and an experimental group participating in the study concurrently (Albinni 2004; Amelina 2006; Chatham 1997; de Jong 2001; Enright 2004; Heward 2000; Sawyer 1993) with one of these having three arms to the study, i.e. a control and two levels of training (Enright 2004). One was of a cross-over design; i.e. the participants were randomly allocated to receive the training first or second (Asher 1983); we appreciate that these data would best be analysed in RevMan using the generic inverse variance (GIV) method; however, the trial authors did not supply the parameters required for this analysis. The mean age of participants was not consistently reported. There was great variation as to the method and level of training employed by the included studies; e.g. IMT as a percentage of maximum effort or by threshold loading. Three studies used 80% compared to 20% of maximal effort (Chatham 1997; Enright 2004; Heward 2000); one study used 60% of maximal effort (Sawyer 1993); one study used 40% of

maximal effort (de Jong 2001); one study used 30% of maximal effort (Amelina 2006) and two studies did not specify the level of resistance (Albinni 2004; Asher 1983). The duration of the intervention ranged from four to twelve weeks and all outcomes were recorded at the end of the trial period in each case. Finally, the outcome measures selected by the studies also varied greatly, as did the countries in which the studies were run; the USA (Heward 2000; Sawyer 1993), the UK (Chatham 1997; Enright 2004), the Netherlands (de Jong 2001), Canada (Asher 1983); Russia (Amelina 2006); and Austria (Albinni 2004).

Excluded studies

One study was excluded from the original search as the allocation was not randomised (Keens 1977); likewise a study identified in the 2011 update was excluded as the allocation was not randomised (observational study) (Sartori 2008). A further study was identified and excluded from the 2011 update as the intervention was not appropriate (Howard 2000) (*see* Characteristics of excluded studies).

Risk of bias in included studies

Allocation

Generation of allocation sequence

Although eight of the studies state that they randomised their participants to the treatment groups, only one study offers any indication of the methods of allocation by stating that they employed the minimisation method (de Jong 2001). We graded this study as having a low risk of bias, but the remaining seven studies were graded as having an unclear risk of bias.

Concealment of allocation sequence

None of the included studies made specific reference as to how, or even whether, this was addressed. All studies were assessed as having an unclear risk of bias in relation to this criteria.

Blinding

Performance bias

We have scored all the included studies as having a high risk of bias in this parameter. In all studies there was clear difference between the experimental and control training; ranging from no details being provided for the control group (Asher 1983) and "no IMT training" (Albinni 2004; Enright 2004; Heward 2000) through to

minimal training and "sham" training (Amelina 2006; Chatham 1997; de Jong 2001; Sawyer 1993). Although we acknowledge the methodological difficulties of blinding the participants to this type of intervention, it would have been straight forward to survey the participants at the end of data collection to establish whether they could tell if they received the training dose or not.

Dectection bias

Two studies blinded the outcome assessors at the final data collection session, although they did not state whether this was the case at the initial assessment or even if the same assessors carried out all the assessments (Enright 2004; Sawyer 1993). Another study reports that the observers were blinded, although it does not expand on the level of this (Asher 1983). The other five studies make no overt reference to any blinding (Albinni 2004; Amelina 2006; Chatham 1997; de Jong 2001; Heward 2000).

Incomplete outcome data

No study explicitly refers to intention-to-treat. However, five studies do report withdrawals. In the de Jong study, one participant in the intervention group withdrew after experiencing earache at 40% PI_{max} training intensity (de Jong 2001). In the Asher study, two participants did not perform one of the post-treatment outcome measures, namely PI_{Max}, due to expiration up to residual volume resulting in coughing (Asher 1983). In the Sawyer study two participants did not complete their pulmonary function tests: one was due to an oversight on the part of the researchers; and the other did not complete the test (Sawyer 1993). There is no indication as to which group these participants are from (Sawyer 1993). We consider that, for all three studies, these withdrawals relate to the true outcome and therefore introduce a high risk of bias.

In the Chatham study, three participants in the control group did not complete the trial (Chatham 1997); and in the Amelina study, one participant in the intervention group did not complete the trial (Amelina 2006). Neither of these last two studies offered any explanation for these withdrawals. As they are both abstracts we have graded them as 'unclear' on the grounds that they had limited space in which to explain the omissions. The two trials added during the update to this review did not provide statistical data on their control groups, merely stating that there was no change in their outcomes (Amelina 2006; Chatham 1997). We do acknowledge, however, that these were both abstracts published in conference proceedings and that there are likely to be editorial constraints responsible for this. Therefore, they are regarded as having an 'unclear' risk of bias.

The remaining three trials do not provide any information with regards to participant withdrawals, so we judge these to have an unclear risk of bias (Albinni 2004; Enright 2004; Heward 2000).

Selective reporting

One study mentions that the investigators carried out post-training measures of pulmonary function but do not report the results (Heward 2000). It is acknowledged that this study is only published as an abstract; however, there is a potential risk of bias due to the limited reporting of their outcomes. Likewise for the study by Amelina, two outcomes (respiratory muscle strength and dyspnoea) are mentioned as having been analysed, but no data are provided for them (Amelina 2006).

There was insufficient information provided by the other publications to make a judgement on the risk of bias due to selective reporting from six trials and we judge these to have an unclear risk of bias (Albinni 2004; Asher 1983; Chatham 1997; de Jong 2001; Enright 2004; Sawyer 1993).

Other potential sources of bias

We have given all the included studies a grading of 'unclear' risk of bias as none provided sufficient information to arrive at a definitive conclusion.

Effects of interventions

Due to the lack of studies using identical intensities of IMT or outcome measures, or both, it continues to be impossible, at this time, to pool any of the data; we have deemed it inappropriate to combine the data from the included trials. Please note that all outcomes were recorded at the end of the study period in each study.

Primary outcomes

1. Health-related quality of life

Two of the studies included in the review reported having used an outcome measure of this type. Both used the Chronic Respiratory Disease Questionnaire (CRDQ), which evaluates four domains considered important to individuals with chronic airflow obstruction; dyspnoea, mastery, fatigue and emotion (Enright 2004; Chatham 1997).

i. 80% of maximal effort

One study reported significant improvement in the two parameters of mastery and emotion ($P < 0.01$) (Chatham 1997). No statistically significant change was reported in the other paper for any of the four categories (Enright 2004).

ii. 60% of maximal effort

The Sawyer study did not report on this outcome (Sawyer 1993).

iii. 40% of maximal effort

The de Jong study did not report on this outcome (de Jong 2001).

iv. 20% of maximal effort

No statistically significant change was reported in the paper for any of these four categories (Enright 2004).

v. unspecified level of maximal effort

The Asher and Albinni studies did not report on this outcome (Albinni 2004; Asher 1983).

2. Pulmonary function tests (performed at rest)

a. Forced expiratory volume at one second (FEV_1)

Data for FEV_1 were reported in six of the included studies (Albinni 2004; Amelina 2006; Asher 1983; de Jong 2001; Enright 2004; Sawyer 1993). One study stated that post-training measures of pulmonary function were determined, but did not report any further details (Heward 2000); and the remaining study did not mention this outcome (Chatham 1997).

i. 80% of maximal effort

Enright reported mean and SD data for all groups and reported no significant difference between all three of their groups (two intensities of IMT (see also 20% of maximal effort below) and a control) (Enright 2004).

ii. 60% of maximal effort

The Sawyer study presented FEV_1 in litres and reported a P value indicating no difference between IMT and control ($P = 0.10$) (Sawyer 1993).

iii. 40% of maximal effort

The de Jong study presents FEV_1 in litres and reports a P value indicating no difference between IMT and control (P = 0.82) (de Jong 2001).

iv. 30% of maximal effort

The Amelina study presented FEV_1 in per cent predicted and reports a mean improvement within the training group from 48% to 51% with a P value of 0.014 (Amelina 2006).

v. 20% of maximal effort

Enright reported mean and SD data for this group, but did not report any significant difference between IMT and control (Enright 2004).

vi. unspecified level of maximal effort

The Asher and Albinni studies did not report any data, but state that there was no change in FEV_1 in either the IMT or the control group (Albinni 2004; Asher 1983).

b. Forced vital capacity (FVC)

This outcome is reported in three studies (Albinni 2004; de Jong 2001; Enright 2004); all using the same unit of measurement (litres).

i. 80% of maximal effort

Enright presented mean and standard deviations for all groups, pre- and post-IMT and these figures have been presented in the graphs. There were no reported statistically significant changes following the training (Enright 2004). Chatham did not report on this outcome (Chatham 1997).

ii. 60% of maximal effort

This outcome was not reported by Sawyer (Sawyer 1993).

iii. 40% of maximal effort

The de Jong study quoted mean and standard deviations for all groups, pre- and post-IMT and these figures have been presented in the graphs. There were no reported statistically significant changes following the training, but de Jong did report the actual level of significance (P = 0.99) (de Jong 2001).

iv. 30% of maximal effort

The Amelina study presented FVC in per cent predicted and reports a mean improvement within the training group from 65% to 68% with a P value of 0.049 (Amelina 2006).

v. 20% of maximal effort

Enright presented mean and standard deviations for all groups, pre- and post-IMT and these figures have been presented in the graphs. There were no reported statistically significant changes following the training (Enright 2004).

vi. unspecified level of maximal effort

Albini stated there was no change in FVC in either group, but gave no further details (Albinni 2004). This outcome was not reported by Asher (Albinni 2004; Asher 1983).

3. Exercise tolerance

a. Field-based tests

No studies reported this outcome.

b. Laboratory-based tests

Three studies reported VO_2max (Albinni 2004; Asher 1983; de Jong 2001).

i. 80% of maximal effort

Neither study reported on this outcome (Chatham 1997; Enright 2004).

ii. 60% of maximal effort

This outcome was not reported by Sawyer (Sawyer 1993).

iii. 40% of maximal effort

The de Jong study reported no statistically significant change in VO_2 max (P = 0.99) (de Jong 2001).

iv. 20% of maximal effort

Enright did not report this outcome (Enright 2004).

v. unspecified level of maximal effort

One study reported a significant improvement in VO_2max within the IMT group (P = 0.01) (Albinni 2004); although no data were reported to allow inclusion in our analysis. A second study reported pre- and post-intervention mean scores but no statistical analysis, although they did state that no difference was detected between the groups (Asher 1983).

One study reported on "exercise capacity" although no units were provided not was there any explanation as to the method of assessment; they reported no improvement in this outcome (Amelina 2006).

Secondary outcomes

1. Pulmonary function tests (performed at rest)

a. Maximal inspiratory pressure (PI_{max})

i. 80% of maximal effort

Neither study reported on this outcome (Chatham 1997; Enright 2004).

ii. 60% of maximal effort

When the data for this outcome from the Sawyer study are entered into the analysis there is a significant difference in favour of the treatment group, MD 26.00 (95% CI 8.63 to 43.47) (Sawyer 1993) (Analysis 2.2).

iii. 40% of maximal effort

The de Jong study did not report on this outcome (de Jong 2001).
iv. 30% of maximal effort
The Amelina study presented PI_{max} in per cent predicted and reports a mean improvement within the training group from 77% to 91% with a P value of 0.023 (Amelina 2006).

v. 20% of maximal effort

The Enright study did not report on this outcome (Enright 2004).

vi. unspecified level of maximal effort

Asher utilised two inspiratory measures (Pim-FRC and PI_{max}) suggesting that one measurement technique was used but at two different lung volumes (Asher 1983). The study reported significant changes in both measures in the IMT group (P < 0.025 and P < 0.05 respectively). The investigators also reported that, for the Pim-FRC measure, only three participants registered an increase that was more than two standard deviations (2SD) from the control group; and for the PI_{max} measure, two participants had an increase greater than two SD from the control values.

b. Inspiratory capacity (IC)

This outcome was not reported by any study.

2. Respiratory muscle function (strength and endurance)

Inspiratory muscle endurance (IME) was reported in two studies (Albinni 2004; de Jong 2001).

i. 80% of maximal effort

The Chatham study reported figures for mean (SD) and a P value for the training group only; therefore, they have not been included in our analysis. There was a mean improvement within the training group from 118 (31.5) to 149 (24.7) mmH_2O with a P value of less than 0.04 (Chatham 1997). Enright did not report this outcome (Enright 2004).

ii. 60% of maximal effort

This outcome was not reported by Sawyer (Sawyer 1993).

iii. 40% of maximal effort

The de Jong study quoted figures for mean, standard deviation and P value and has therefore been included in our analysis. There was a statistically significant difference in favour of the IMT group, MD 12.00 (95% CI 0.55 to 23.45) (de Jong 2001) (Analysis 3.5).
iv. 30% of maximal effort
The Amelina study reported this outcome in joules (J) and reports a mean improvement within the training group from 89J to 150J with a P value of 0.002 (Amelina 2006).

v. 20% of maximal effort

Enright did not report this outcome (Enright 2004).

vi. unspecified level of maximal effort

Albinni reported that IME improved significantly in the training group (P = 0.0002) (Albinni 2004).

3. Frequency and duration of respiratory infections, hospitalisations

This outcome was not reported by any study.

4. Adherence to the IMT regimen

This outcome was not reported by any study.

5. Death or survival

No deaths were reported and survival was not analysed in any study.

6. Adverse effects (pneumothorax, musculoskeletal pains or injuries, others)

One study, using 40% of maximal effort, reported that one participant experienced earache whilst performing IMT (de Jong 2001).

7. Costs

This outcome was not reported by any study.

DISCUSSION

Overall the quality of the included studies was inconsistent and none addressed all aspects completely. The execution of the included studies (randomisation and blinding) ranged from being fully acknowledged, considered and reported to either being merely stated as "randomised to the two groups" or not being mentioned. The external validity (with particular regard to the participant demographics) was explicit in only three of the studies (de Jong 2001; Enright 2004; Sawyer 1993). This aspect is of particular significance given that people who have CF are the target population. The nature of the disease means that two people of similar age, height and weight may have been affected by the condition in drastically different ways and therefore may not "match" as far as clinical status goes. Adverse events were poorly covered by the studies, with only one making specific reference to this (de Jong 2001). Two studies report withdrawals but offer no explanation for these (Amelina 2006; Chatham 1997). We acknowledge that the nature of the intervention (IMT) makes it very difficult to blind the participants to which arm they are in, although five studies made use of "sham" interventions for controls (Amelina 2006; Chatham 1997; de Jong 2001; Enright 2004; Sawyer 1993).

There is currently insufficient evidence to either support or refute the use of IMT for people with CF (Altman 1995). There are several factors that may have contributed to this conclusion. Firstly, four out of the eight studies have only been published as abstracts within conference proceedings. This format limits the amount of detailed data that are presented and, therefore, that can be extracted from the studies. This is particularly true in this case. Without that detail a full meta-analysis cannot be performed and this subsequently detracts from the rigour of the process. Another, more generic, factor relates to the execution of studies examining the effects of a rehabilitation technique for people with CF. A systematic review requires homogeneity between the included studies to allow firm conclusions to be drawn. Despite only finding eight studies which met the inclusion criteria of this review, the variation in their methodologies and outcomes (type and units) was such that no combined analyses could be made. These differences occurred in all the major aspects of the studies, i.e. the outcomes employed, the selected units of measurement for certain of these outcomes and the method and extent to which the clinical status of the participants was established or reported.

Two pulmonary function measures, FEV_1 and FVC, are both routinely used in general clinical practice to monitor the pulmonary function and (due to the nature of the condition) the disease severity within people with CF. It could be argued that expiratory measures such as these would not be altered by an inspiratory intervention. We, however, support the studies' use of expiratory measures, primarily, because of their routine clinical usage and relevance in monitoring the progression of the disease. In selecting task specific measures some studies are opting for ones that specifically assess changes within the muscles of ventilation, e.g. diaphragm thickness. The problem with this is that they are not measures with which people with CF, or even the average professional working in the field, would be sufficiently familiar in order to be able to draw any meaningful conclusions. It would appear, even from this small sample, that this dilemma continues and needs resolving. Descriptive analysis of the studies considered suggests that the measures that can best detect the effects of an IMT programme are PI_{max} exercise tests such as inspiratory muscle endurance and, to a lesser extent, VO_2max. Although it is acknowledged that this is not supported by a meta-analysis of trials, they are the measures the included studies report as showing significant improvement within their IMT groups. Also, these are measures that are of particular relevance to professionals involved in the rehabilitation of people with CF and ones that are most likely to influence quality of life.

Only two of the studies included in the review reported having used an outcome measure assessing health-related quality of life (Chatham 1997; Enright 2004). We believe that this is a major omission on the part of the other studies, which severely limits the external validity of the research base. There is an ever growing drive to consider the efficacy of our interventions, as McClarey and Duff summarise, in the UK it is being driven centrally from the

UK National Health Service (UK NHS) (McClarey 1997). What McClarey and Duff fail to fully acknowledge is that efficacy cannot be fully established without thorough assessment of how people with a particular condition perceive the benefits of their treatment (McClarey 1997). This ought to be of particular importance in long-term life-limiting conditions, such as CF. It is acknowledged, however, that certain of the studies may have been undertaken at a time before this became such an important consideration within clinical practice.

Due to the life-limiting nature of CF, the clinical status of the participants recruited to studies in this population is of particular importance. The participants from the included studies have a mean age of approximately 18.5 years. With average life expectancy around 31 years (CF Trust 2007), the participants in these studies are effectively in middle age. It is possible that due to the progressive nature of the condition, the pulmonary function of the participants prevented the benefits shown in healthy populations manifesting in this participant group (Enright 2000).

AUTHORS' CONCLUSIONS

Implications for practice

Given that we have not found any evidence to suggest that this treatment is either beneficial or not. We would advise that practitioners evaluate on a case-by-case basis whether or not to employ this therapy.

Implications for research

We recommend that future studies choose task specific measures such as PI_{max} and inspiratory muscle strength and endurance as well as exercise tests such as VO_2max. Such functional measures ought to dovetail nicely with an assessment of health-related quality of life.

To facilitate such future research and to improve research into the remedial benefits of IMT, it is necessary for the research community to agree upon a single standard measure of classifying the clinical status of the participants.

Finally, there is emerging evidence to suggest that IMT is beneficial to people with other chronic respiratory conditions, such as COPD (O'Brien 2008). It would be prudent to apply this to the clinical population and implement longitudinal studies to assess the role of IMT in maintaining good pulmonary function and exercise tolerance within the CF population.

ACKNOWLEDGEMENTS

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Albinni 2004

Methods	Parallel design over 12 weeks
Participants	n = 27 Age range: 6 - 18 years Gender mix: no information
Interventions	IMT: no details; plus, cycle ergometer training 3 times per week Control: cycle ergometer training 3 times per week
Outcomes	FEV_1, FVC, IMS, IME, MEC, perceived breathlessness, antibiotic use and ease or degree of expectoration
Notes	IME protocol: abstract only, no details given

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as randomised, no details given
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Performance bias: clear difference between the interventions received Dectection bias: No reference to any blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided. Intention to treat: unclear
Selective reporting (reporting bias)	Unclear risk	Insufficient information available to arrive at a conclusion
Other bias	Unclear risk	Insufficient information available to arrive at a conclusion

Amelina 2006

Methods	Parallel design over six weeks
Participants	n = 20 Age range was not stated Gender mix: no information

Interventions	Threshold loading device:
	Intervention group: 30% of PI_{max}
	Control group: 7cm H_2O
	Training regimen: 10 to 15 minutes bd for 6 weeks

Outcomes	FEV_1, FVC, PI_{max}, IC, RMS, RME and exercise capacity

Notes	Abstract only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The authors only state that the allocation was random without explaining the process involved
Allocation concealment (selection bias)	Unclear risk	No details are provided
Blinding (performance bias and detection bias) All outcomes	High risk	Performance bias: The comparison group are referred to only as the "control group" with no mention of the intensity of the training used; i.e. if it was at "sham" or sub-maximal levels Dectection bias: No reference to any blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	No statistical data is presented for the control group. One subject from the intervention group did not complete the trial; it was not stated whether they were included or excluded from the final analysis
Selective reporting (reporting bias)	High risk	Two outcomes (respiratory muscle strength and dyspnoea) are mentioned as having been analysed, but no data are provided for them
Other bias	Unclear risk	Insufficient information available to arrive at a conclusion

Asher 1983

Methods	Consecutive, self-control design over 8 weeks

Participants	n = 11
	Age range: 9 - 24 years
	Gender mix: no information

Interventions	IMT: Inspiratory resistance, 15 minutes bd, no dosage
	Control: no details provided

Asher 1983   (*Continued*)

Outcomes	IMS, W_{max}, VO_2max, VE and heart rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as randomised, no details given
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Performance bias: no details of the control training regimen are provided = high risk Dectection bias: observer blind = low risk
Incomplete outcome data (attrition bias) All outcomes	High risk	Two participants were unable to satisfactorily perform the outcome measure PI_{Max}, due to expiration up to residual volume resulting in coughing. The authors do not stipulate whether this occurred during the intervention or control phase of the trial Intention to treat: unclear
Selective reporting (reporting bias)	Unclear risk	Insufficient information available to arrive at a conclusion
Other bias	Unclear risk	Insufficient information available to arrive at a conclusion

Chatham 1997

Methods	Parallel design over 8 weeks
Participants	Intervention: n = 9 Control: n = 9 No data was provided on the ages of the participants
Interventions	Intervention: Computer-generated through range inspiratory muscle training (TIRE) at 80% of individual capacity Control: Threshold loading device at 30% of peak; the measure used is not named
Outcomes	Chronic Respiratory Disease Questionnaire ('mastery' and 'emotion' elements), RMS and RME
Notes	

Chatham 1997 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Described as randomised, no details given
Allocation concealment (selection bias)	Unclear risk	Insufficient information available to arrive at a conclusion
Blinding (performance bias and detection bias) All outcomes	High risk	Perfomance bias: the training intensities employed (80% and "threshold" 30% training) could, potentially, have led the participants to know which group they were in Dectection bias: no reference to any blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information available to arrive at a conclusion; no statistical data is presented for the control group Intention to treat: 3 from 18 (17%)
Selective reporting (reporting bias)	Unclear risk	As this study (to date) is only published in abstract form it is unclear whether the reported outcomes are all that were analysed
Other bias	Unclear risk	Insufficient information available to arrive at a conclusion

de Jong 2001

Methods	Parallel design over 6 weeks
Participants	Intervention: n = 8; mean (SD) age = 17 (5.2) years Control: n = 8; mean (SD) age = 19 (5.5) years
Interventions	IMT: Threshold loading; 20 minutes a day, 5 days per week. At 40% of PI_{max} Control: Threshold loading; 20 minutes a day, 5 days per week. At 10% of PI_{max}
Outcomes	FEV_1, FVC, W_{max}, VO_2max, VE_{max}, IME, perceived breathlessness, general fatigue, physical fatigue, reduced activity score, reduced motivation score, mental fatigue and dyspnoea
Notes	IME protocol: a commercially-available threshold-loading device (Threshold, Healthscan Products, Inc. U.S.A.) was used during an incremental loading procedure. In order to obtain pressures over 41 cm H_2O an additional spring was inserted with a double-spring constant. Participants started inspiring from a threshold-loading device set at 30% of PI_{max} for 2 min. The threshold load was then increased every 2 min in increments of 10% of Pimax. The maximal load was defined as the highest load which could be reached and maintained for at least 1 min as a percentage of PI_{max}. The breathing pattern was not regulated.

de Jong 2001 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Minimisation
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Performance bias: both training intensities were low; however, no attempt was made to ascertain whether the participants knew if the received the training intensity Detection bias: no reference to any blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	One participant in the intervention group was withdrawn due to earache experienced whilst training at 40% of PI_{max} Intention to treat: 1 from 15 (6%)
Selective reporting (reporting bias)	Unclear risk	Insufficient information available to arrive at a conclusion
Other bias	Unclear risk	Insufficient information available to arrive at a conclusion

Enright 2004

Methods	Parallel design over 8 weeks
Participants	All participants: n = 29, mean (SD) age = 22 (4.2) years Intervention 1: n = 9, mean (SD) age = 24.8 (5.5) years Intervention 2: n = 10, mean (SD) age = 20 (4.7) years Control: n = 6, mean (SD) age = 21.3 (2.7) years
Interventions	Intervention 1: IMT at 80% of "maximal inspiratory effort" Intrevention 2: IMT at 20% of "maximal inspiratory effort" IMT: Incremental maximal effort with progressively shorter rest periods, 3 times a week Control: "No Training"
Outcomes	FEV_1 (% predicted), FVC (% predicted), PI_{max}, SPI_{max}, heart rate, perceived exertion, dyspnoea and Chronic Respiratory Disease Questionnaire
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Enright 2004   (*Continued*)

Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding (performance bias and detection bias) All outcomes	High risk	Performance bias: the comparison was "no training" making it clear to the participants which arm they were in Dectection bias: outcome assessors at the final data collection session, although they did not state whether this was the case at the initial assessment or even if the same assessors carried out all the assessments
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention is made of whether all subjects completed the trial or not. Nor are there any statistical indications Intention to treat: unclear
Selective reporting (reporting bias)	Unclear risk	Insufficient information available to arrive at a conclusion
Other bias	Unclear risk	Insufficient information available to arrive at a conclusion

Heward 2000

Methods	Parallel design over 8 weeks
Participants	Experimental: n = 19, mean (SD) age = 22.5 (3.5) years Control: n = 20, mean (SD) age = 21.5 (3.5) years Gender matched groups
Interventions	IMT: IMT at 80% of "maximal effort". No dosage stated 3 control groups: healthy participants: IMT at 80% of "maximal effort"; healthy participants: "No Training" and CF participants: "No Training"
Outcomes	VC, TLC
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as randomised, no details given
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Performance bias: the comparison was "no training" making it clear to the participants which arm they were in Detection bias: no reference to any blinding

Heward 2000 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided Intention to treat: unclear
Selective reporting (reporting bias)	High risk	The post-training pulmonary function results were not presented
Other bias	Unclear risk	Insufficient information available to arrive at a conclusion

Sawyer 1993

Methods	Parallel design over 10 weeks
Participants	Experimental: n = 10, mean (SD) age = 11.46 (2.45) Sham: n = 10, mean (SD) age = 9.76 (2.57)
Interventions	IMT: IMT at 60% PI_{max} Control: IMT at 10% PI_{max}
Outcomes	FEV_1, VC, FRC, IC, RV, TLC, RV/TLC, FEV_1/FVC, MVV, exercise time
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as randomised, no details given
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Performance bias: there was a clear difference in the intensity of training although no attempt was made to ascertain whether the participants in the training groups knew if they received the training intensity Dectection bias: outcome assessors at the final data collection session, although they did not state whether this was the case at the initial assessment or even if the same assessors carried out all the assessments
Incomplete outcome data (attrition bias) All outcomes	High risk	2 participants removed from analysis and the reasons for this were explained; however, it is unclear which group (s) they were in Intention to treat: unclear
Selective reporting (reporting bias)	Unclear risk	Insufficient information available to arrive at a conclusion

Sawyer 1993 (*Continued*)

Other bias	Unclear risk	Insufficient information available to arrive at a conclusion

% predicted: the volume of air exhaled expressed as a percentage of the expected volume based on the physical attributes of the individual

bd: twice a day

FEV_1: volume of air exhaled over the first second of a forced exhalation

FEV_1/FVC = the ratio of FEV_1 to FVC

FRC: functional residual capacity

FVC: total volume of air forcibly exhaled

FEF 25-75%: forced expiratory flow 25-75%

IC: inspiratory capacity

IME: inspiratory muscle endurance

IMF: inspiratory muscle function

IMS: inspiratory muscle strength

IMT: inspiratory muscle training

MEC: maximal exercise capacity

MVV: maximum voluntary ventilation

RME: respiratory muscle endurance

RMS: respiratory muscle strength

n: number of participants

PI_{max}: maximal inspiratory pressure

RV: residual volume; i.e. the volume of air retained in the lungs following a maximal, voluntary exhalation (FVC)

RV/TLC: the ratio of residual volume to total lung capacity

SD: standard deviation

SPI_{max}: sustained maximal inspiratory pressure

TLC: total lung capacity; i.e. the calculated maximum potential volume of an individual's lungs

VC: the total volume of air that can be exhaled in any one breath

VE(max): peak expired ventilation

VO_2max: peak oxygen consumption

W_{max}: maximum work load

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

Study	Reason for exclusion
Howard 2000	Study excluded as the intervention was not inspiratory muscle training
Keens 1977	Study excluded as allocation not randomised
Sartori 2008	Observational study, no randomisation

DATA AND ANALYSES

Comparison 1. IMT (80% of maximal effort) versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Forced expiratory volume at one second (litres)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Two to six months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Forced vital capacity (litres)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Two to six months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Chronic Respiratory Disease Questionnaire (mastery)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4 Chronic Respiratory Disease Questionnaire (emotion)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 2. IMT (60% of maximal effort) versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Forced expiratory volume at one second (litres)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Two to six months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 PImax (cmH2O)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Two to six months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 3. IMT (40% of maximal effort) versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Forced expiratory volume at one second (litres)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Less than two months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Forced expiratory volume at one second (% predicted)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Less than two months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Forced vital capacity (litres)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Less than two months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Forced vital capacity (% predicted)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Less than two months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Inspiratory muscle endurance (%PImax)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 Less than two months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 4. IMT (20% of maximal effort) versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Forced expiratory volume at one second (litres)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Two to six months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Forced expiratory volume at one second (% predicted)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Two to six months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Forced vital capacity (litres)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Two to six months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

ADDITIONAL TABLES

Table 1. Explanation of terms

Term	Explanation
Continuous training	Training at 70% to 80% of maximum effort for 30 to 45 minutes. The percentage of maximal effort and/or the duration of the training may be adjusted depending on the goal of the training
Elastic load	Refers to the load imposed by the stiffness of the lung and chest wall that must be overcome by the inspiratory muscles in order to generate inspiratory flow. Elastic loads are greater when breathing from a higher lung volume as a consequence of the associated decrease in lung and chest wall compliance. Imposing elastic loads has not been used to train the inspiratory muscles most likely due to the need for complicated equipment and poor clinical utility
Forced expiratory volume at 1 second (FEV1)	The volume of air expelled during the 1st second of forced exhalation from total lung capacity
Forced vital capacity (FVC)	The total volume of air expelled during a forced exhalation from total lung capacity
Inspiratory capacity (IC)	The maximum volume of air taken into the lungs during a maximal inhalation from functional residual capacity
Forced expiratory flow 25-75% (FEF 25-75%)	The speed of the air leaving the lungs during the middle section of a forced exhalation

Table 1. Explanation of terms   (*Continued*)

Interval Training	Periods of intense training interspersed with periods of recuperation. As with continuous training, the level of effort required during the training period may be adjusted to suit the individual and the intended goal. The period of recuperation will be adjusted accordingly
Maximal inspiratory pressure [PI_{max}]	The maximum pressure generated by the inspiratory muscles against an occluded airway
Resistive loading	Requires person to breathe through a narrow Inspiratory pathway/aperture. The load imposed is dependent on inspiratory flow, i.e. when using resistive training devices, participants can reduce the load imposed by manipulating their breathing pattern. Breathing pattern, specifically inspiratory flow, should be controlled when using resistive inspiratory muscle training devices
Threshold loading	Requires the person to inspire through a device which imposes a threshold load via either a weighted plunger system or a spring-loaded valve. The person needs to generate a critical inspiratory pressure, prior to the threshold valve opening and allowing inspiratory flow. Once the threshold valve is open, pressure and flow are largely independent and therefore the person is unable to reduce the load imposed by the device by manipulations in breathing pattern
Total lung capacity (TLC)	The maximum amount of air the lungs can hold when they are fully inflated
Voluntary isocapnic (normocapnic) hyperpnoea	Requires the person to maintain a high level of minute ventilation for a specified period. Imposes a high flow, low pressure load on the inspiratory muscles which is analogous to the loads borne by the inspiratory muscles during periods of increased minute ventilation (i.e. during exercise). Requires the use of complex equipment to ensure stable levels of carbon dioxide in the arterial blood (PaCO2), so is rarely used in the clinical setting

WHAT'S NEW

Last assessed as up-to-date: 27 September 2011.

Date	Event	Description
28 September 2011	New search has been performed	A search of the Cystic Fibrosis Trials Register identified three new references which were potentially eligible for inclusion in this review (Amelina 2006; Chatham 1997; Howard 2000). Two studies were eligible for inclusion (Amelina 2006; Chatham 1997); the third study was excluded (Howard 2000). Additional searching undertaken for the updated review identified one study that was potentially eligible for inclusion (Sartori 2008); however this was excluded on closer examination.

HISTORY

Protocol first published: Issue 3, 2006

Review first published: Issue 4, 2008

Date	Event	Description
28 April 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Brian Houston drafted the protocol with comments from Helen Handoll and Cees van der Schans.

Nicola Mills, Arturo Solis-Moya and Brian Houston extracted data and assessed trial quality. Brian Houston drafted the full review with comments from Nicola Mills and Arturo Solis-Moya.

Brian Houston acts as guarantor of the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- University of Teesside, Middlesbrough, UK.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Update 2011

Due to Teesside University (location of the lead author) changing its search engine, some of the search strategies have been re-written. The search strategies in Appendix 5 have superseded those in Appendix 1.

INDEX TERMS

Medical Subject Headings (MeSH)

*Breathing Exercises; Cystic Fibrosis [*therapy]; Inhalation [*physiology]; Randomized Controlled Trials as Topic; Respiratory Muscles [*physiology]

MeSH check words

Humans