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Self-management for non-cystic fibrosis bronchiectasis (Protocol)

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[Intervention Protocol]

Self-management for non-cystic fibrosis bronchiectasis

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the efficacy and cost-effectiveness of self-management interventions for adults and children with non-cystic fibrosis bronchiectasis.

BACKGROUND

Description of the condition

Bronchiectasis, also referred to as non-cystic fibrosis (non-CF) bronchiectasis, is a persistent respiratory condition characterised by abnormal dilation of the airways (Pasteur 2010; Chang 2015). Pathological processes include weakness and destruction of the structural components of the bronchial wall, which together with the loss of ciliated epithelium, and increase in number and hypertrophy of mucus-secreting glands, causes mucus to accumulate, which in turn creates a conducive environment for bacteria and leads to a 'vicious cycle' of bacterial infection (Cole 1986), inflammatory mediator release, airway damage and further infection (Welsh 2015). Chronic infection is associated with a variety of pathogens (Martinez-García 2007; Murray 2011; Chalmers 2012; Tunney 2013), contributing to persistent symptoms and repeated exacerbations (Murray 2011).

Causes of bronchiectasis include a wide range of factors such as damage by serious infection (including mycobacterium tuberculosis), immune deficiency, allergic bronchopulmonary aspergillosis, and recurrent aspiration, although the majority of cases are idiopathic (Pasteur 2000; Goeminne 2012). Diagnosis is based on clinico-radiographic assessments, requiring identification of one or more abnormally dilated bronchi using high-resolution computerised tomography (HRCT) scanning and appropriate symptoms, including chronic productive or wet cough and recurrent lower respiratory tract infections, together with a range of other symptoms such as breathlessness, wheeze, chest pains (related to inflammatory burden) and lethargy (Pasteur 2010; Chang 2015). Factors associated with disease severity include frequency of hospital admissions and mortality, poor lung function, bacterial colonisation, high Medical Research Council (MRC) dyspnoea score and frequency of exacerbations (Chalmers 2014; Martinez-García 2014). The impact on people's quality of life is significant and health status is poor with progressive deterioration. Severity may be assessed with tools such as the Bronchiectasis Severity Index (Chalmers 2014), or FACED (**F**EV1, **A**ge, **C**hronic colonisation, **E**xtension (number of lobes), **D**yspnoea) (Martinez-García 2014), to identify high-risk individuals, though they have limited value as

outcome measures because of the non-modifiable nature of components such as lung function.

Estimates of the prevalence of bronchiectasis vary considerably. Although it has previously been considered a relatively rare disease (Kolbe 1996), more recent studies have suggested an increasing prevalence, particularly in those over 75 years (Weycker 2005), and higher prevalence rates in low-income and middle-income countries (Habesoglu 2011). Co-morbidity may also influence detection and prevalence, with one UK study showing that 29% of people with COPD scanned by HRCT had bronchiectasis (O'Brien 2000). Prevalence rates per 100,000 were estimated at 0.5 in Finland and 3.7 in New Zealand though these data are more than 10 years old (European Lung White Book 2013). Higher prevalence rates have been observed in ethnic populations such as amongst indigenous Australians (up to 14 per 1000) and Native Alaskan children (up to 20.5 per 1000) (Singleton 2000; Twiss 2005). Higher prevalence rates are also observed in women and people aged over 60 years (Chang 2003; Seitz 2012). Recent data suggest that incidence and prevalence in the UK may be higher than previously estimated (Quint 2016). Over a nine-year period to 2013, point prevalence rates per 100,000 rose from 350.5 to 566.1 in women and from 301.2 to 485.5 in men. This reflects an increase of more than 60% with approximately 263,000 adults living with bronchiectasis in 2013. Similarly, the incidence rates per 100,000 person-years rose from 21.2 to 35.2 in women and from 18.2 to 26.9 in men, a 63% increase in new cases to over 15,000 in 2013. However, these increases may be due to improved diagnosis resulting from easier access to high quality CT scanners, rather than a true rise in prevalence (Goeminne 2016).

Mortality rates in England and Wales rose by 3% per year between 2001 to 2007 (Roberts 2010), and hospitalisations also increased by 3% per year over a nine-year period in the US (Seitz 2010). Average mortality rates per 100,000 general population in Europe are estimated at 0.3 in 27 of the 28 countries in the EU (ranging from 0.01 in Germany to 1.18 in the UK) and 0.2 in nine non-EU countries (ranging from 0.01 in Azerbaijan to 0.67 in Kyrgyzstan), based on 2005 to 2009 data (European Lung White Book 2013). The recent UK study reported higher age-adjusted mortality rates, with estimates 2.26 times higher in women and 2.14 times higher in men compared to the general population (Quint 2016).

The main aims of therapeutic management are: preservation of lung function, reduction of symptoms and exacerbations, minimising complications, and improvement in quality of life (Pasteur 2010; Saleh 2014; Chang 2015).

Description of the intervention

Taylor 2014 describe a taxonomy in which long-term conditions are diagnosed and brought under control by professionals; thereafter the individual self-manages the condition with support, to achieve stable maintenance. Self-management support empowers the person with the condition by enabling them to modify treatment or behaviour, or to seek professional advice and has been defined as "increasing the capacity, confidence, and efficacy of the individual" (Kennedy 2013). Self-management interventions are defined as structured programmes for individuals, designed to improve self-health behaviours and self-management skills (Lorig 2003). Self-management programmes should ideally include training with feedback to improve problem solving, decision making, resource utilisation, formation of patient-provider partnerships, action planning and self-tailoring (Lorig 2003). People become more confident at managing their own health and this in turn supports the development and maintenance of beneficial health behaviours (Lorig 2003; Bourbeau 2004).

Self-management support is delivered in a range of ways, all of which aim to equip the individual with knowledge, ability, and confidence, to take appropriate action. The support can take the form of specific techniques employed to help people choose healthy behaviours, but it can also be a fundamental alteration of the patient-caregiver relationship into a collaborative partnership (de Silva 2011). Interventions can range from individualised support such as the provision of educational material, to larger but localised whole system approaches. An example of a whole system approach involved practitioners trained to offer a range of resources such as a tool to assess the support needs of patients, guidebooks on self-management, and a web-based directory of local self-management resources (Kennedy 2013). There are also extensive generic programmes such as the 'Expert Patients Programme' (Department of Health 2001).

Self-management support increasingly includes a mutually agreed individualised plan which incorporates behavioural elements including goal setting and problem solving. Recent work conducted by the Richmond Group of Charities and The King's Fund suggests that clients and professionals should co-create a personalised self-management plan which could include patient and career education, medicines' management advice and support, use of telecare and telehealth to aid self-monitoring, psychological interventions (e.g. coaching), telephone-based health coaching, symptom management and patient access to their own records (Naylor 2015). Self-management support and interventions can therefore vary significantly. All approaches aim to enable the individual to develop the knowledge and confidence to appropriately manage their long-term condition, and to seek professional support when needed.

The components of self-management programmes may need to be condition specific; for example education may be particularly beneficial for diabetes, but cognitive and behavioural interventions may work well for people with depression (de Silva 2011).

The principal aims of management in bronchiectasis are to maintain and improve pulmonary function and to improve quality of life by reducing symptoms and exacerbations (Pasteur 2010; Chang 2015). British Thoracic Society guidelines recommend a range of therapeutic strategies including physiotherapy for airway clearance, pulmonary rehabilitation for significant dyspnoea,

bronchodilators for reversible airflow obstruction and a range of antibiotic therapy to reduce bacterial load. The latter may include short-term courses for exacerbations, prophylactic therapy for frequent exacerbators (≥ 3 exacerbations requiring antibiotics per year) and combination therapy for people with multiple airway pathogens (Pasteur 2010). Recommendations are often based on a small number of short trials that are insufficient to draw firm conclusions about benefits and harms (Welsh 2015).

Bronchiectasis impacts upon physical and psychosocial well-being and there is the potential to improve self-management through self-regulation of medication, adherence to airway clearance techniques and patient education about management of the condition (Lavery 2007). Current guidelines recommend airway clearance techniques, adherence to medication, action plans, exercise (including pulmonary rehabilitation), and patient education as potential components of self-management interventions for bronchiectasis (Pasteur 2010; Chang 2015). The educational component focuses on understanding the basic principles of disease management and early recognition of an exacerbation to facilitate timely intervention (Pasteur 2010). In COPD, self-management programmes that include action plans have been shown to accelerate appropriate treatment-seeking behaviours (Walters 2010), and studies including action plans should therefore be considered separately.

How the intervention might work

Studies of long-term chronic conditions suggest that self-management support may improve self-efficacy, health status, psychological well-being, coping strategies and physical functioning (Farrell 2004; Griffiths 2005; Siu 2007; Challis 2010). Benefits may be attributable to enhanced adherence to medication, the adoption of appropriate behaviours, and reduced stress and anxiety, though this may also be associated with increased use of healthcare resources (Naylor 2015). Self-management programmes for chronic obstructive pulmonary disease (COPD), defined as above, have improved quality of life and reduced breathlessness and hospital admissions (Zwerink 2014), though there is currently no consensus on the most effective components of self-management interventions (Effing 2012). The evidence of effectiveness in cystic fibrosis is less clear, with interpretation of observed increases in knowledge and changes in behaviour hampered by small, poor-quality trials (Savage 2014).

The objectives of care in bronchiectasis are to treat identifiable underlying causes, control symptoms, reduce the number of exacerbations, prevent deterioration in pulmonary function, improve quality of life and minimise complications (Chalmers 2016; Pasteur 2010). The potential benefits from self-management in individuals with bronchiectasis may include: reduction in symptoms and subsequent improvement in quality of life; and reduction in the number and severity of exacerbations, together with potential reduction in hospital admissions, length of stay, and disease and health status decline.

Non-adherence to therapy may be a significant problem in bronchiectasis with up to 50% of people with severe chest infections not completing prescribed courses of antibiotics, other medicines and airway clearance (McCullough 2014). People who do not adhere to therapy have a shorter time to first exacerbation (Haworth 2014); and a higher annual exacerbations rate compared to those who are adherent (McCullough 2014). Similar to reports from cystic fibrosis (Sawicki 2009), treatment burden may increase with the emergence of new treatments which may in turn lead to more problems with adherence. Non-adherence to antibiotic therapy and airway clearance procedures may be attributable to a range of factors including beliefs about their potential risks and benefits, a younger age and (for antibiotics) a higher number of prescribed medications (McCullough 2015). It is likely that patient self-management programmes may help to improve adherence to prescribed therapy and reduce the negative consequences of poor adherence. With the rise of antimicrobial resistance, adherence to frontline antibiotic therapy may be particularly important for people with bronchiectasis (O'Neill 2016).

Why it is important to do this review

Non-CF bronchiectasis is a chronic disease which causes both persistent day-to-day symptoms such as cough and breathlessness, and intercurrent exacerbations. The long-term management of bronchiectasis focuses on reducing these features of the disease.

Self-management interventions have been shown to be beneficial in the management of other airways diseases associated with management of day-to-day respiratory symptoms and respiratory exacerbations such as asthma and COPD (Zwerink 2014; Peytremann-Bridevaux 2015). Guidelines recommend self-management plans for these diseases and patient education is one of the factors in bronchiectasis management recently prioritised by the European EMBARC group (Aliberti 2016).

This review aims to summarise the evidence for self-management strategies for people with bronchiectasis and will seek to provide guidance for both current recommendations and possible future research needs.

OBJECTIVES

To assess the efficacy and cost-effectiveness of self-management interventions for adults and children with non-cystic fibrosis bronchiectasis.

METHODS

Criteria for considering studies for this review

Types of studies

We will include parallel and cluster-randomised controlled trials (RCTs) of any duration. We will include studies reported as full-text, those published as abstract only, and unpublished data.

Types of participants

Adults (> 18 years) and children with a diagnosis of non-cystic fibrosis bronchiectasis confirmed by plain film chest radiograph, bronchography or high-resolution computed tomography with at least three months of daily sputum expectoration. We will exclude participants with a diagnosis of cystic fibrosis (CF), sarcoidosis or active allergic bronchopulmonary aspergillosis. We will also exclude studies of other long-term health conditions unless results for people with bronchiectasis are reported separately.

Types of interventions

Self-management interventions are defined as structured interventions for individuals with bronchiectasis designed to improve self-health behaviours and self-management skills. The interventions should include collaborative interaction between participants and healthcare providers, involving goal setting and feedback, with at least two points of contact. Self-management interventions should include at least two of the following components: patient education, airway clearance techniques, adherence to medication, exercise (including pulmonary rehabilitation), and action plans (Pasteur 2010; Chang 2015). Self-management interventions that include action plans will be considered separately (Hagger 2014). We will exclude interventions solely comprising participant education or those focused only on exercise, such as pulmonary rehabilitation delivered in a care setting. We will include studies of self-management interventions delivered in any form (e.g. Internet, mobile device, face-to-face, paper) with the following comparisons.

- Self-management versus usual care.
- Self-management versus an alternate form of self-management (e.g. paper-based booklet versus mobile app).

For comparisons between different types of self-management we will include co-interventions, including types of exercise interventions, provided they are evenly distributed between the groups.

Types of outcome measures

We will include all outcomes irrespective of follow-up duration, but will evaluate the impact of follow-up in sub-group analyses.

Primary outcomes

1. Health-related quality of life using measures validated for patients with bronchiectasis in a clinical setting (e.g. Bronchiectasis Severity Index (BSI; St. George's Respiratory Questionnaire (SGRQ)).
2. Exacerbations (requiring antibiotic therapy) measured as frequency, proportion with one or more, or duration.
3. Serious adverse events (i.e. any adverse even that results in death or is life-threatening).

Secondary outcomes

1. Frequency of hospital admissions measured.
2. Lung function (forced expiratory volume in one second (FEV_1) litres or percent of predicted).
3. Symptoms (e.g. dyspnoea, cough, wheeze), for example using the Leicester Cough Questionnaire (LCQ).
4. Self-efficacy (e.g. Chronic Disease Self-Efficacy Scale).
5. Economic costs (e.g. direct: costs of care such as cost-benefit or cost-effectiveness; indirect: days lost from work or full-time education).
6. Adverse events (e.g. pneumonia).

Reporting of one or more of the listed outcomes is not an inclusion criterion for the review.

Search methods for identification of studies

Electronic searches

We will identify studies from the Cochrane Airways Group's Specialised Register (CAGR), which is maintained by the Information Specialist for the Group. The Register contains trial reports identified through systematic searches of multiple healthcare databases, and handsearching of respiratory journals and meeting abstracts (please see Appendix 1 for further details). We will search all records in the CAGR using the search strategy in Appendix 2.
We will also conduct a search of ClinicalTrials.gov (www.ClinicalTrials.gov) and the World Health Organization (WHO) trials portal (www.who.int/ictrp/en/). We will search all databases from their inception to the present, and we will impose no restriction on language of publication.

Searching other resources

We will check reference lists of all primary studies and review articles for additional references. We will search relevant manufacturers' websites for trial information. We will search the 'grey' literature at OpenGrey (www.opengrey.eu/).
We will search for errata or retractions from included studies published in full-text on PubMed (www.ncbi.nlm.nih.gov/pubmed) and report the date this was done within the review.

Data collection and analysis

Selection of studies

Two review authors (CK and SG) will independently screen titles and abstracts for inclusion of all the potential studies we identify as a result of the search and code them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. We will retrieve the full-text study reports/publication and two review authors (CK and SG) will independently screen the full-text and identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreement through discussion or, if required, we will consult a third review author (SS). We will identify and exclude duplicates and collate multiple reports of the same study so that each study rather than each report is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA flow diagram and a 'Characteristics of excluded studies' table (Moher 2009).

Data extraction and management

We will use a data collection form for study characteristics and outcome data which has been piloted on at least one study in the review. The following characteristics will be extracted from included studies by one review author (DL).

1. Methods: study design, total duration of study, details of any 'run in' period, number of study centres and location, study setting, withdrawals, and date of study.
2. Participants: N, mean age, age range, gender, severity of condition, diagnostic criteria, baseline lung function, smoking history, inclusion criteria, and exclusion criteria.
3. Interventions: intervention, comparison, concomitant medications, and excluded medications.
4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.
5. Notes: funding for trial, and notable conflicts of interest of trial authors.

Two review authors (DL and CK) will independently extract outcome data from included studies. We will note in the 'Characteristics of included studies' table if outcome data were not reported in a usable way. We will resolve disagreements by consensus or by involving a third review author (SS). One review author (SS) will transfer data into the Review Manager 5 file (RevMan 2014). We will double-check that data is entered correctly by comparing the data presented in the systematic review with the study reports. A second review author (CK) will spot-check study characteristics for accuracy against the trial report.

Assessment of risk of bias in included studies

Two review authors (CK and DL) will independently assess the risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve any disagreements by discussion or by involving another review author (SS). We will assess the risk of bias according to the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias.

We will grade each potential source of bias as high, low or unclear and provide a quote from the study report together with a justification for our judgment in the 'Risk of bias' table. We will summarise the risk of bias judgments across different studies for each of the domains listed. We will consider blinding separately for different key outcomes where necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be very different than for a patient-reported quality-of-life scale). Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome.

Assessment of bias in conducting the systematic review

We will conduct the review according to this published protocol and report any deviations from it in the 'Differences between protocol and review' section of the systematic review.

Measures of treatment effect

We will estimate intervention effects using odds ratios with 95% confidence intervals (CI) for dichotomous data and mean difference or standardised mean difference with 95% CI for continuous data. If standard deviations (SD) are not reported but other measures of variance around mean differences, such as standard error, CIs, or P values are reported, we will calculate these according to Section 7.3 in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). In this review it is likely that different scales may be used to measure the same outcome (for example, Bronchiectasis-Quality of Life (B-QoL) and St. George's Respiratory Questionnaire (SGRQ)). In this case, we will use the standardised mean difference (SMD) and its 95% CI, ensuring a consistent direction of effect by reversing scaling where necessary, supported by a statement in the text on direction of interpretation.

We will undertake meta-analyses only where this is meaningful i.e. if the treatments, participants and the underlying clinical question are similar enough for pooling to make sense.

We will narratively describe skewed data reported as medians and interquartile ranges.

Unit of analysis issues

Cross-over trials

Cross-over trials are not appropriate for this intervention as it is not possible to avoid carry-over of knowledge acquisition from the first phase. However, if we identify eligible cross-over studies only data from the first pre-cross-over phase will be included.

Cluster-randomised trials

Large-scale trials are uncommon in bronchiectasis and it is unlikely that we will identify eligible RCTs randomising at the level of group (e.g. by primary care practice). Eligible cluster-randomised RCTs will be analysed in accordance with methods described in Section 16.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), using average cluster size and an estimate of the intraclass correlation coefficient (ICC) to adjust sample sizes to the 'effective sample size'. We will combine single RCTs with cluster-RCTs if the designs and interventions are considered sufficiently similar and the effect of the intervention is unlikely to be influenced by the method of randomisation.

Multiple-arm trials

Where multiple trial arms are reported in a single RCT, we will describe all study groups in the 'Characteristics of included studies' table, but only include the analysis arms that meet our review criteria. If multiple comparisons (e.g. self-management A versus self-management B versus self-management C versus usual care) are combined in the same meta-analysis, we will divide the usual care (control) group by the number of intervention arms to avoid 'double-counting'. Decisions on unit of analysis issues will be described in the text.

Dealing with missing data

We will contact investigators of included studies to provide unreported data such as missing outcomes, missing data, means or SDs. We will note differential dropout between study groups and note reasons for withdrawal. Where a particular outcome includes substantial loss to follow-up ($\geq$ 50%), we will report this in the text and mark the data with an asterisk. We will also note reasons for missing data and differences in missing data between groups where reported. We will use available cases for data analysis and will not impute missing data. Where studies include analyses based on the imputation of missing values, we will include data at low risk of bias and report data separately for those at higher risk of bias in the text of the review. Multiple imputation methods that include sensitivity analyses pre-specified in published protocols are considered at low risk of bias (Little 2012; Gewandter 2014). Imputation of missing data related to trial outcomes, using methods such as last observation carried forward, are not considered appropriate. For example, completion of missing data (e.g. relating to an efficacy outcome) following an intervention-related death would be inappropriate (Gewandter 2014).

Where missing data are thought to introduce high risk of bias (substantial loss to follow-up or inappropriate imputation), we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis**.**

Assessment of heterogeneity

In this review, the specific nature of the intervention, population, outcomes and methodological quality may vary considerably between studies. We will assess potential sources of variability between studies in the following ways.

1. Clinical variability: we will compare the distribution of participants, interventions, and outcomes across the included studies. We will discuss and agree potential clinical heterogeneity by consensus.
2. Methodological variability: we will compare study designs and study quality using risk of bias criteria.
3. Statistical heterogeneity (where variability in the effects of interventions is greater than expected by chance alone): we will evaluate the statistical significance of heterogeneity using the Chi² test (P = 0.10 is significant). However, this test may be unreliable, lacking power to detect important heterogeneity with few or small studies and the potential to detect clinically insignificant heterogeneity with large numbers of studies. It is also possible for trials to show large consistent effects in the face of significant heterogeneity. Therefore, in addition to assessing evidence of heterogeneity using the Chi² test as above, we will also quantify the magnitude of heterogeneity using the ^{2} (random-effects model only), and I² statistics with the following interpretation thresholds, based on recommendations in Section 9.5 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):

   i) 0% to 40%: might not be important;
   ii) 30% to 60%: may represent moderate heterogeneity;
   iii) 50% to 90%: may represent substantial heterogeneity;
   iv) 75% to 100%: considerable heterogeneity.

We will report substantial heterogeneity (> 50%) and explore possible causes by prespecified subgroup analysis.

Assessment of reporting biases

We will compare the results of data from published and unpublished studies as a direct test of publication bias. If there are a sufficient number of studies (10 or more), we will explore potential bias arising from small-study effects using Egger's method, to test for asymmetry in funnel plots (Egger 1997). If smaller studies show

larger intervention effects compared to larger studies, we will evaluate potential causes (for example, poor methodological quality; differences in populations or interventions) and report studies at high risk of bias in the text of the review.

Data synthesis

Studies will be included in meta-analyses where the study designs, interventions and outcomes are similar. Where substantial heterogeneity (> 50%) is identified we will report outcomes in the text, giving direction and size of the effect along with the strength of the evidence (risk of bias). It is likely that included studies will vary by population, design and outcomes, therefore meta-analysis using a random-effects model would be most appropriate. However, where there are few studies or the effects of interventions across studies are not randomly distributed (for example, with publication bias), the random-effects model estimates may be unreliable or biased. It is likely that this review will only include a small number of low powered studies, therefore we will use a fixed-effect model and evaluate the impact of model choice using a sensitivity analysis. We will synthesise and report dichotomous and continuous data separately for a given outcome, should the need arise (e.g. exacerbation/no exacerbation or exacerbation duration). Where end-of-study point estimates and change from baseline scores are reported we will analyse these separately. We will perform the analyses using Review Manager 5 (RevMan) (RevMan 2014).

Summary of findings table

We will create a 'Summary of findings' table using the following primary and secondary outcomes: health-related quality of life, hospital admissions, serious adverse events, exacerbations, lung function, self-efficacy and economic costs. We will tabulate the quality of each outcome using the five GRADE criteria (study limitations, consistency of effect, imprecision, indirectness and publication bias) (GRADE 2014). We will use methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), using GRADEpro software (GRADEpro GDT). We will justify all decisions to down- or up-grade the quality of studies using footnotes and we will make comments to aid the reader's understanding of the review where necessary.

Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses.

1. Age: adults (> 18 years) versus children.
2. Duration of follow-up (less than 12 months vs 12 months or longer).

We will use the following outcomes in subgroup analyses.

1. Health-related quality of life.
2. Hospital admissions.
3. Adverse events.

We will use the formal test for subgroup interactions in Review Manager 5 (RevMan 2014).

Sensitivity analysis

We plan to carry out the following sensitivity analyses.

1. We will exclude studies at high risk of selection bias.
2. Analyses using a random-effects model.
3. Missing data (studies with > 50% or those using inappropriate imputation).

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. Sources and search methods for the Cochrane Airways Group's Specialised Register (CAGR)

Electronic searches: core databases

Database	Frequency of search
MEDLINE (Ovid)	Weekly
Embase (Ovid)	Weekly
CENTRAL (the Cochrane Library)	Monthly
PsycINFO (Ovid)	Monthly
CINAHL (EBSCO)	Monthly
AMED (EBSCO)	Monthly

Handsearches: core respiratory conference abstracts

Conference	Years searched
American Academy of Allergy, Asthma and Immunology (AAAAI)	2001 onwards
American Thoracic Society (ATS)	2001 onwards
Asia Pacific Society of Respirology (APSR)	2004 onwards
British Thoracic Society Winter Meeting (BTS)	2000 onwards
Chest Meeting	2003 onwards
European Respiratory Society (ERS)	1992, 1994, 2000 onwards
International Primary Care Respiratory Group Congress (IPCRG)	2002 onwards
Thoracic Society of Australia and New Zealand (TSANZ)	1999 onwards

MEDLINE search strategy used to identify trials for the CAGR

Bronchiectasis topic search

1. exp Bronchiectasis/
2. bronchiect$.mp.
3. bronchoect$.mp.
4. kartagener$.mp.
5. (bronchial$ adj3 dilat$).mp.
6. or/1-5

Filter to identify RCTs

1. exp "clinical trial [publication type]"/
2. (randomised or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. Animals/
10. Humans/
11. 9 not (9 and 10)
12. 8 not 11

The MEDLINE strategy and RCT filter (Lefebvre 2011) are adapted to identify trials in other electronic databases.

Appendix 2. Search strategy to identify relevant trials from the CAGR

#1 BRONCH:MISC1
#2 MeSH DESCRIPTOR Bronchiectasis Explode All
#3 bronchiect*
#4 #1 or #2 or #3
#5 MeSH DESCRIPTOR Self Care Explode All
#6 MeSH DESCRIPTOR Education
#7 MeSH DESCRIPTOR Patient Education as Topic
#8 educat*
#9 self-manag*
#10 "self manag*"
#11 self-car* or "self car*"
#12 train* or instruct*
#13 "patient cent*" or patient-cent*
#14 patient-focus* or "patient focus*"
#15 patient-education or "patient education"
#16 "management plan" or management-plan
#17 management* NEAR1 program*
#18 behavior* or behaviour*
#19 disease* NEAR2 management*
#20 self-efficac*
#21 empower*
#22 #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21
#23 #4 AND #22

[In search line #1, MISC1 denotes the field in the record where the reference has been coded for condition, in this case, bronchiectasis]

CONTRIBUTIONS OF AUTHORS

SS, CK, DL and SG drafted the protocol.

For the review, CK and SG will select studies for inclusion; DL, CK and SS will extract data from the studies and assess the risk of bias; SS will enter data into RevMan and perform the analyses; SS, CK, DL and SG will draft the final review.

SS has overall responsibility for the review.

DECLARATIONS OF INTEREST

Sally Spencer - none known.

Carol Kelly - none known.

Dave Lynes - none known.

Seamus Grundy - none known.

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Employer of Seamus Grundy

External sources

- No sources of support supplied