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Early View

Task force report

European Respiratory Society statement on airway clearance techniques in adults with bronchiectasis

Beatriz Herrero-Cortina, Annemarie L. Lee, Ana Oliveira, Brenda O'Neill, Cristina Jácome, Simone Dal Corso, William Poncin, Gerard Muñoz, Deniz Inal-Ince, Victoria Alcaraz-Serrano, Gregory Reychler, Angela Bellofiore, Annette Posthumus, Patient representative, Thomy Tonia, James D Chalmers, Arietta Spinou

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Title: European Respiratory Society statement on airway clearance techniques in adults with bronchiectasis

Authors Beatriz Herrero-Cortina[1,2,3], Annemarie L Lee[4,5], Ana Oliveira[6,7,8,9], Brenda O´Neill[10], Cristina Jácome[11,12], Simone Dal Corso[13,14], William Poncin[15,16,17], Gerard Muñoz[18,19], Deniz Inal-Ince[20], Victoria Alcaraz-Serrano[21,22], Gregory Reychler[23,24,25], Angela Bellofiore[26,27], Annette Posthumus (patient representative)[28], Patient representative[28], Thomy Tonia[29], James D Chalmers[30], Arietta Spinou[31,32].

Affiliations

Beatriz Herrero-Cortina, PhD

1. Hospital Clínico Universitario Lozano Blesa. Avda. C, de San Juan Bosco, 15, 50009 Zaragoza, Spain.
2. Instituto de Investigación Sanitaria (IIS) Aragón. Avda. C, de San Juan Bosco, 15, 50009 Zaragoza, Spain.
3. Universidad San Jorge, Zaragoza, Spain. Campus Universitario, Autovía Mudéjar, km. 299, 50830 Villanueva de Gállego, Zaragoza

Email: beafisiorespi@gmail.com
ORCID: 0000-0002-4749-0444
Twitter: @Beika_Physio

Annemarie L Lee, PhD

4. Department of Physiotherapy, Faculty of Medicine, Nursing and Health Sciences, Monash University, 47-49 Moorooduc Hwy, Frankston, 3199, Victoria, Australia
5. Institute for Breathing and Sleep, Austin Health, 145 Studley Rd, Heidelberg VIC 3084, Australia

Email: annemarie.lee@monash.edu
ORCID: 0000-0002-8631-0135
Twitter: @AnnemarieLLee1

Ana Oliveira, PhD

6. School of Rehabilitation Sciences, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada
7. West Park Healthcare Centre, Toronto, Ontario, Canada
8. Lab3R – Respiratory Research and Rehabilitation Laboratory, School of Health Sciences, University of Aveiro (ESSUA), Aveiro, Portugal

9. iBiMED – Institute of Biomedicine, Department of Medical Sciences, University of Aveiro, Aveiro, Portugal

Email: Ana.Oliveira@westpark.org

ORCID: 0000-0003-4516-6904

Twitter: @wha7tsername

Brenda O´Neill, PhD

10. School of Health Sciences, Ulster University, UK

Email: b.oneill@ulster.ac.uk

ORCID: 0000-0002-6471-1413

Twitter @OneillBon

Cristina Jácome, PhD

11. Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS), University of Porto Faculty of Medicine, Porto, Portugal
12. Center for Health Technology and Services Research (CINTESIS), University of Porto Faculty of Medicine, Porto, Portugal

Email: cristinajacome.ft@gmail.com

ORCID: 0000-0002-1151-8791

Twitter: @CristinaJcome2

Simone Dal Corso, PhD

13. Graduate Program in Rehabilitation Sciences. Universidade Nove de Julho. Rua Vergueiro, 235/249. CEP 01525-000. São Paulo/SP, Brazil.
14. Department of Allergy, Immunology and Respiratory Medicine, Monash University, Melbourne, Victoria, Australia.

Email: si.dal.corso@gmail.com

ORCID: 0000-0001-9190-6796

William Poncin, PhD

15. Institut de recherche expérimentale et clinique (IREC), pôle de Pneumologie, ORL et Dermatologie, Université Catholique de Louvain, Brussels, Belgium
16. Service de Pneumologie, Cliniques universitaires Saint-Luc, Brussels, Belgium
17. Secteur de Kinésithérapie et Ergothérapie, Cliniques universitaires Saint-Luc, Brussels, Belgium

Email: william.poncin@uclouvain.be

ORCID: 0000-0002-7686-2294

Twitter: @WPoncin

Gerard Muñoz Castro, PhD

18. Department of Pneumology, Dr. JosepTrueta University Hospital. Bronchiectasis Group, Girona Biomedical Research Institute. Parc Hospitalari Martí Julià - Edifici M2. C/ del Dr. Castany, s/n, 17190 Salt, Girona
19. Department of Physical Therapy, EUSES & ENTI. University of Girona and University of Barcelona. Carrer del President Francesc Macià, 65, 17190 Salt, Girona

Email: munoz.gerard@gmail.com

ORCID: 0000-0002-5420-0556

Twitter: @gerardmuoz

Deniz Inal-Ince, PhD

20. Hacettepe University, Faculty of Physical Therapy and Rehabilitation, 06100 Samanpazari, Ankara, Turkey

E-mail: dince@hacettepe.edu.tr

ORCID: 0000-0002-8151-0664

Twitter: @Dinalince2

Victoria Alcaraz-Serrano, PhD

21. Barcelona Institute for Global Health (ISGlobal)
22. Blanquerna School of Health Science, Ramon Llull University, Barcelona

Email: victoria.alcaraz.serrano@gmail.com

ORCID: 0000-0001-6036-9545

Twitter: @Vic_Alcaraz

Gregory Reychler, PhD

23. Institut de recherche expérimentale et clinique (IREC), pôle de Pneumologie, ORL et Dermatologie, Université Catholique de Louvain, Avenue Hippocrate 55, 1200 Brussels, Belgium
24. Service de Pneumologie, Cliniques universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium

25. Secteur de Kinésithérapie et Ergothérapie, Cliniques universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium

Email: gregory.reychler@saintluc.uclouvain.be

ORCID: 0000-0002-7674-1150

Angela Bellofiore, BSc

26. Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Internal Medicine Department, Respiratory Unit and Cystic Fibrosis Adult Centre, Milan, Italy.
27. Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Health and Care Professions Department, Milan, Italy.

Email: angela.bellofiore@policlinico.mi.it

ORCID: 0000-0002-0037-1392

Annette Posthumus, patient representative

28. European Lung Foundation (ELF)

Patient representative

28. European Lung Foundation (ELF)

Thomy Tonia, MSc

29. Institute of Social and Preventive Medicine, University of Bern. Mittelstrasse 43, 3012 Bern, Switzerland

Email thomy.tonia@ersnet.org

ORCID: 0000-0001-7896-6188

Twitter: @ThomyTonia

James D. Chalmers, PhD

30. Division of Molecular and Clinical Medicine, Ninewells Hospital and Medical School, Dundee, UK

Email: jchalmers@dundee.ac.uk

ORCID: 0000-0001-5514-7868

Twitter: @ProfJDChalmers

Arietta Spinou, PhD

31. School of Life Course & Population Sciences, Faculty of Life Sciences & Medicine, King's College London, London, UK
32. King's Centre for Lung Health, King's College London, London, UK

Email: arietta.spinou@kcl.ac.uk

ORCID: 0000-0002-3442-4739

Twitter: @AriettaSpinou

Corresponding author

Dr Arietta Spinou

School of Life Course & Population Sciences, Faculty of Life Sciences & Medicine

King's College London, Guy's Campus, Room 2.02, Addison House, SE1 1UL, London, UK

Telephone: +44 (0)20 7848 6618

Email: arietta.spinou@kcl.ac.uk

Twitter: @AriettaSpinou

ORCID: 0000-0002-3442-4739

Abstract

Airway clearance techniques (ACTs) are part of the main management strategy for patients with bronchiectasis. Despite being a priority for patients, accessibility, implementation, and reporting of ACTs are variable in clinical settings and research studies. This European Respiratory Society statement summarises current knowledge about the ACTs in adults with bronchiectasis and makes recommendations to improve future evidence base. A task force of 14 experts and two patient representatives (10 countries) determined the scope of this statement through consensus and defined six questions. The questions were answered based on systematic searches of the literature.

The statement provides a comprehensive review of the physiological rationale for ACTs in adults with bronchiectasis, and the mechanisms of action along with the advantages and disadvantages of each ACT. Evidence on the ACTs in clinical practice indicates that active cycle of breathing techniques, positive expiratory pressure devices and gravity assisted drainage technique are the most frequently used techniques, although there is limited evidence on the type of ACTs used in specific countries. A review of 30 randomised trials for the effectiveness of the ACTs shows that these interventions increase sputum clearance during or after treatment, reduce the impact of cough and the risk of exacerbations, and improve health-related quality of life. Furthermore, strategies for reducing the risk of bias in future studies are proposed. Finally, an exploration of patients´ perceptions, barriers and enablers related to this treatment is also included to facilitate implementation and adherence to ACTs.

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Take home message ERS reviews the evidence for airway clearance techniques in bronchiectasis and suggests areas of further research.

List of abbreviations

ACBT, active cycle of breathing techniques

ACTs, airway clearance techniques

BC, breathing control

BHQ, bronchiectasis health questionnaire

BIM, bronchiectasis impact measure

BSI, bronchiectasis severity index

CI, confidence intervals

CONSORT, consolidated standards of reporting trials

COPD, chronic obstructive pulmonary disease

COSMIN, COnsensus-based Standards for the selection of health Measurement INstruments

CSS, cross-sectional study

ELTGOL, slow expiration with glottis opened in lateral posture

EMBARC, European multicentre bronchiectasis audit and research collaboration

ERS, European Respiratory Society

ESR, erythrocyte sedimentation rate

FEF, forced expiratory flow

FET, forced expiratory technique

FEV_1, forced expiratory volume in 1 second

FRC, functional residual capacity

FVC, forced vital capacity

GAD, gravity-assisted drainage

HFCWO, high-frequency chest wall oscillation

HRQoL, health-related quality of life

HS, hypertonic saline

IC, inspiratory capacity

IMT, inspiratory muscle training

IPV, intrapulmonary percussive ventilation

IQR, interquartile range

IS, isotonic saline

ISWT, incremental shuttle walk test

MD, mean difference

MEP, maximal expiratory pressure

MIP, maximal inspiratory pressure

MMEF, maximal mid-expiratory flow

mMRC, modified Medical Research Council

NR, not reported

O-PEP, oscillating positive expiratory pressure

PEEP, positive end positive expiratory pressure

PEF, peak expiratory flow

PEP, positive expiratory pressure

Qol-B, quality of life - bronchiectasis

RCT, randomised controlled trial

RCX, randomised cross-over trial

RV, residual volume

SEM, standard error of the mean

SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials

TLC, total lung capacity

TPEP, temporary positive expiratory pressure

Summary of statements

Table 1. Summary of the European Respiratory Society (ERS) task force statement on airway clearance techniques (ACTs) in adults with bronchiectasis.

Question 1. What is the physiological rationale for the use of ACTs in adults with bronchiectasis?
- Sputum from people with bronchiectasis is abnormally hyper-concentrated (dehydrated) and mucin concentration is related to disease severity. This indicates that the level of mucus layer dehydration plays an important role in the pathophysiology of the disease. - The main physiological mechanism that promotes mucus clearance involves mechanical stress, such as fluid shear stresses, compressions or stretching, and osmotic shocks. ACTs which implement these mechanisms of action have the potential to enhance mucociliary clearance in bronchiectasis, as they can potentially achieve a greater expiratory to inspiratory flow rate or direct volume of air behind lung regions that are obstructed by mucus accumulation.
Question 2. What is the physiological rationale of each one of the ACTs and what are the advantages and limitations of each technique?
- The ACTs enhance sputum clearance by incorporating one or more of the following mechanism of actions: improvement of collateral ventilation and interdependence, increase of expiratory airflow velocity, reducing the total airway cross-sectional ratio, use of gravity, change of airway pressures and generation of airway oscillations. Data specifically evaluating the above physiological principles in people with bronchiectasis are scarce. - The main advantages of specific ACTs are that they can be performed independently, they are feasible in different environments or can easily be implemented in a daily routine. - The main disadvantages of specific ACTs are the level of concentration and effort that is required to perform them, the need of cleaning and periodic replacements of devices, the noise or size of devices, difficulty of transport, the lack of biofeedback and the cost.

Question 3. Which are the ACTs that are clinically used in the management of adults with bronchiectasis and are there any patterns according to geographical location?

- There is limited evidence about the clinical use of ACTs in specific countries. Based on the available data (i.e., Australia, New Zealand, USA, Japan, UK), the active cycle of breathing technique is the most commonly used ACT in bronchiectasis. Positive expiratory pressure, oscillating positive expiratory pressure, and techniques based on the effect of gravity are also commonly used.
- Studies reporting on the clinical use of ACTs do not always adequately describe the responding population and sample. They also do not always clearly define ACTs.
- Data on the use of ACTs in clinical practice are scarce and some data are likely to be out of date given the progress in bronchiectasis management in the past decade.

Question 4. What is the clinical evidence for the effectiveness of ACTs, in terms of function and disability (e.g., sputum expectoration), activity (e.g., physical activity) and participation (e.g., self-care), in adults with bronchiectasis?

- Although data on the effects of performing ACTs for periods over 6 or 12-months is limited, the findings demonstrate a reduction in the impact of cough, improvement in health-related quality of life and reduction in the risk of exacerbations. These findings support previously published clinical recommendations for the use of ACTs as part of bronchiectasis management in adults. However, no evidence is existing about the optimal frequency or the number of sessions.
- Randomised controlled trials have assessed a variety of ACTs, with oscillating positive expiratory pressure (mainly via Flutter and Acapella), gravity assisted drainage and active cycle of breathing being the most commonly studied techniques. The existing literature does not demonstrate superiority of one technique over another but supports the use of ACTs.
- Wet sputum weight or volume were the most commonly used outcome measures. The ACTs increase the expectorated sputum during or following a single session of ACTs. Despite being frequently used in clinical practice, the interpretation of sputum changes is ambiguous.

- To date, there are no studies that have investigated the effect of ACTs on mortality or changes in disease severity using the bronchiectasis severity index or FACED. There are also no studies providing a health economics estimation for ACTs in bronchiectasis.

Question 5a. What are the experiences and perceived impact of ACTs on adults with bronchiectasis?
Question 5b. What are the perceived barriers to and enablers of ACTs in adults with bronchiectasis?

- Patient experience was generally well rated for ACTs. Preference was mainly based on the independence of technique, patient satisfaction with symptom relief, and perceived efficacy or difficulty.
- Patient adherence to ACTs could be related to older age, good physical function, milder respiratory symptoms, less treatment burden and belief in treatment necessity.
- Optimal engagement of patient and healthcare professionals, adequate motivation, time and resources were some of the barriers and enablers of ACTs.

Question 6. In adults with bronchiectasis, how should studies for ACTs be conducted to reduce the risk of bias, facilitate comparison of findings, as well as conducting future meta-analyses?

- The risk of bias amongst the studies that assess ACTs is heterogeneous, but generally unclear.
- For most studies, reporting was unclear for allocation concealment or there was selective reporting.
- Blinding of the ACTs was also limited for patients and personnel, although this is often challenging due to the nature of the intervention.
- Futures studies should be adequately powered, based sample size estimation of one or two primary outcome measures, which have well-explored psychometrics properties. Blinding of outcome assessment and statistical analysis of the ACTs should be implemented to help minimise bias. Study reporting should be clear and following the CONSORT reporting guidelines.

ACT/ACTs, airway clearance technique/airway clearance technique/s.

Introduction

Bronchiectasis is a chronic respiratory disease defined by abnormal and irreversible dilation of the bronchi [1, 2], with impaired mucociliary clearance. Common features include persistent cough with sputum production and recurrent acute exacerbations [2, 3]. Recurrent exacerbations contribute to progressive lung damage [4], impaired health-related quality of life (HRQoL) [5-7] and are linked to a worse prognosis [8].

Impaired mucociliary clearance is one of the main defects leading to bronchiectasis and disease progression [9, 10]. While some patients with bronchiectasis have an inherited cause of impaired mucociliary clearance, e.g., primary ciliary dyskinesia, in most cases the combined effects of chronic airway inflammation and infection lead to persistently impaired mucus clearance [10]. Enhancing or restoring mucus clearance from airways is, therefore, a key therapeutic strategy, which aims to disrupt the pathogenic vortex of this disease.

The European Respiratory Society (ERS) guidelines for the management of people with bronchiectasis, as well as other national and international reference documents [2, 11-14], highlight airway clearance techniques (ACTs) as an essential strategy to control and address impaired mucociliary clearance and related symptoms [2, 15]. Airway clearance techniques are composed of a range of strategies to facilitate the mobilisation and expectoration of secretions. Nevertheless, access to this treatment is still suboptimal for people with bronchiectasis and clinical practice seems to be highly variable across countries [16, 17]. Preliminary international data suggests that the clinicians' recommendation to perform ACTs is inconsistent [16, 17] and the overall global clinical practice is currently unknown. This may be related to the lack of knowledge about the beneficial effects of ACTs, namely, how to identify people who can benefit

from it, and how to implement and ensure long-term adherence to this treatment. Thus, a statement summarising the current knowledge around this field was required.

The objectives of this ERS task force were: first, to describe the physiological rationale for prescribing ACTs in adults with bronchiectasis and to synthesise their main action mechanisms, highlighting their advantages and disadvantages. Second, to review the current global practice of ACTs and their short-term and long-term effects in this population, outlining suggestions to improve the future research on this topic. Finally, to summarise the patient experience, satisfaction, and preference for ACTs, as well as the perceived enablers and barriers that may influence treatment adherence [18].

Methods

Panel composition

The task force panel, which represented ten countries, included thirteen expert respiratory physiotherapists, two patient representatives, and a respiratory physician with clinical and research expertise in bronchiectasis. Expert physiotherapists were selected by the task force chairs ensuring wide representation, i.e., inclusion of early career researchers and individuals from different countries, after an open invitation to all members of the ERS Group 9.02 – Physiotherapists. The patient representatives were suggested by the European Lung Foundation, considering a representation from one patient who is adherent to ACTs and one who is not. The patient representatives were included in the working teams, actively participating in the online meetings and providing input throughout the project, particularly on topics related to patients' feedback. Moreover, the panel was supported by an experienced ERS methodologist.

All task force members signed a conflict-of-interest disclosure before project commencement, according to ERS policies and adherence to the ERS policy was monitored by the chairs throughout the project. Two external librarians (SDG and KP), from King's College London, collaborated with the task force, through running the search strategies and their updates.

The task force panel identified six main questions of clinical and research interest, by discussion and consensus. The panel members formulated three working groups and addressed two questions each (supplementary material 1, table S1,). Between June 2020 and June 2022, the task force panel met virtually six times and each working group held at least four additional teleconferences. Other communication and review of drafts was performed through email contact and manuscript collaboration on a secure cloud platform.

Literature review

The task force panel designed the search strategies to address the six questions in collaboration with the librarians and the ERS methodologist. Systematic literature searches using MEDLINE (Ovid), Embase, AMED, CINAHL, Cochrane Centrale and PEDro databases were initially run in September 2020 and then updated in November 2021. Original research papers on ACTs in bronchiectasis were used for the sections on global clinical practice, effects of ACTs, research quality assessment and patient´s feedback, barriers, and enablers. For the physiological rationale of the use of ACTs in bronchiectasis and mechanisms of action, secondary articles, i.e., reviews, were also included. Articles in English were selected, except for Question 2, where the panel agreed to include studies in other languages (e.g., French, Spanish, Portuguese, Italian) to ensure the collection of information on ACTs that were not developed in Anglo-Saxon countries. The filters used for the search strategies were species (human) and age (≥ 18 years), except for Question 1 and Question 2, where animal and in vitro studies were allowed.

The panel decided to assess techniques that were specifically developed to enhance airway clearance and improve the management of sputum-related symptoms; therefore, techniques with a different primary objective that have been explored as means of airway clearance, such as exercise, respiratory muscle training and non-invasive ventilation (NIV), were excluded from this statement. The panel also agreed not to consider cough manoeuvres as an individual ACT, since this is a physiological mechanism for sputum expectoration and in trials it is often used as a control treatment arm. Humidification, mucoactive agents and other medications were outside the scope of this task force, which focused on non-pharmacological approaches. Therefore, the aforementioned treatments were only reported if they were a comparative arm of an included study. The full search methodology for each question is available on supplementary material 2.

The sensitivity of all search strategies was checked before screening the results. Search strategies that lacked adequate sensitivity, i.e., Question 1 and Question 2, were re-designed twice (supplementary material 1). For each question, two independent reviewers screened the search results according to pre-specified selection criteria. Disagreements were resolved by consensus from the two reviewers or consultation from a third reviewer. Data extraction was performed using pre-specified spreadsheets, evidence obtained was assessed qualitatively and the quality of studies was assessed in Question 6, using the Cochrane tool for randomised trials risk of bias [19], since the findings of this question aim to improve the methodological quality of future research in this topic.

Results

Question 1 - What is the physiological rationale for the use of ACTs in adults with bronchiectasis?

Understanding the physiology of ACT is fundamental to its application in clinical practice. Therefore, the task force initially sought to review studies examining the airway clearance impairment mainly in people with bronchiectasis, as well as studies investigating the physiological mechanisms of action to enhance mucus clearance.

Evidence overview

A total of 22 studies were identified, all meeting the inclusion criteria (supplementary material 1, figure S1 and table S2). Of these studies, nine studies were primary research [9, 20-27] and 13 were secondary research studies (one systematic review [28] and 12 narrative reviews [3, 29-39]. Eleven studies provided data from in-vitro experiments [20, 21, 23-25, 31-33, 35, 37, 39] and three studies were experimental/clinical trials [20-22]. Six studies reported data from people with bronchiectasis [3, 9, 24, 26-28], five studies provided a mix of data from different respiratory diseases including bronchiectasis [23, 29, 34, 36, 38], seven studies outlined data from other respiratory diseases such as chronic obstructive pulmonary disease (COPD), and cystic fibrosis [25, 31-33, 35, 37, 39] and one study involved healthy adults [22].

Impaired mucociliary clearance in people with bronchiectasis

Impaired mucociliary clearance in people with bronchiectasis is often demonstrated through productive cough, abnormally high presence of sputum or difficulty in sputum expectoration. Abnormalities in mucus production, ciliary function and biophysical and surface mucus properties directly contribute to a decreased mucus clearance rate compared to healthy people

[33, 36, 39]. There are limited data about the function of the airway surface layer in bronchiectasis and the hypothesis that mucus layer dehydration impairs mucus transport is derived from other chronic respiratory diseases [25, 37, 39] . Still, considering that the sputum samples of people with bronchiectasis are abnormally hyper-concentrated (dehydrated), this could be a possible explanation [9].

Firstly, neutrophil elastase activity plays an important role in the pathogenesis and progression of bronchiectasis [26, 28]. Excessive neutrophil elastase activity within the inflamed airway has been reported to decrease ciliary beat frequency and directly stimulates mucin secretion [26, 28]. Mucin 5B (MUC5B) appears to be the most predominant mucin in bronchiectasis [9]. Mucin 5AC (MUC5AC) and higher airway mucin levels are associated with increased disease severity [9, 26]. However, these findings are based on only a few studies in bronchiectasis [9, 26], and further research is needed to confirm them.

An excess of secreted mucins leads to mucus layer dehydration and generates an osmotic imbalance between the mucus layer and the periciliary layer. This phenomenon ultimately compresses the periciliary layer and ciliary system [32]. Consequently, ciliary beating is slowed down and mucus layer adhesion to the airway epithelial surface is facilitated (adhesivity is a surface property of the sputum, defined as the ability to bond to a solid surface [36]); therefore mucus transport is reduced, which results in mucus accumulation [25, 39]. This contributes to perpetuating the pathogenesis of bronchiectasis, which has lately been described as a vicious vortex [3]. In fact, a hyper concentrated mucus layer can lead to local epithelial hypoxia, which may limit the action of cystic fibrosis transmembrane conductance regulator channels and produce higher levels of dehydration in the airway surface layer [24]. Most ciliary dysfunction in bronchiectasis is acquired due to the effects of chronic inflammation, but the genetic condition

primary ciliary dyskinesia, caused by more than 50 recognised gene defects affecting the structure and function of motile cilia, is increasingly recognised [38].

Secondly, when respiratory muscle strength is preserved as in the case of bronchiectasis, mucus adhesivity appears to be the strongest factor determining cough effectiveness for airway clearance [33, 36]. This property is independent of mucus viscosity (the loss of energy from an object through a substance and thus the resistance to flow) and mucus elasticity, (the recoil energy transmitted back to an object) [31, 36]. Greater adhesivity appears when there is high interfacial tension between the mucus layer and the airway epithelium and/or low mucus wettability (the surface energy at a solid-sputum-air interface) [33, 36]. The limited available data from in-vitro experiments suggest that mucus transport via coughing is impaired in bronchiectasis [24].

Consequently, the rationale for the use of ACTs in bronchiectasis is based on improving the biophysical and surface properties of the mucus layer to enhance the clearance of inflammatory markers and to help modulate the pathogenic microorganism load in the airways. This way, ACTs aim to break the pathogenic vortex and slow down the disease progression.

Physiological mechanisms to enhance mucociliary clearance

Mechanical stress applied to the airways could stimulate hydration of the mucus layer and enhance airway clearance [23, 35]. During normal breathing, two mechanical stresses are generated during both respiratory phases of inspiration and expiration, and they are essential for the normal regulation of airway surface hydration: the airflow and the trans-airway pressure

gradient [23]. Previous studies reported that fluid shear stress, compression or stretch and osmotic shock are the main physical mechanisms that stimulate airway surface hydration [23]. Additionally, an *in vitro* flow model suggests two conditions that promote airway clearance [20, 21, 29]: the peak expiratory flow rate should be greater than the peak inspiratory flow rate (rate difference >10%) for mucus to move proximally, and a peak expiratory flow rate of 30-60 L/min is required to break the adhesive bonds generated between the mucus layer and the airway epithelial surface. Accordingly, airway clearance strategies are based on generating greater mechanical stress on the airways compared to normal breathing and the achievement of one of the above conditions may play an important role in improving airway clearance for people with bronchiectasis.

Achieving a sufficient volume of air behind the lung regions that are obstructed by mucus accumulation is another mechanism that may be associated with enhancing mucus clearance [29]. Three different strategies have been described to achieve this mechanism. Slow, deep inspirations to take advantage of the parenchymal interdependence and generate traction force to maintain open or re-expand the smaller airways [30]; end-inspiratory breath-hold that reduces asynchronies in time constants between lung regions with different resistance or compliance constants [22]; and promotion of ventilation via collateral channels using adjacent lung units [29]. These mechanisms use the Pendelluft effect, which allows air to move into the lung units that are most obstructed by mucus accumulation [29].

In summary, evidence suggest that sputum-related symptoms result from increased mucus production, dehydration and impaired biophysical properties of mucus and reduced ciliary function due to primary and secondary ciliary dysfunction. The physiological mechanisms by which ACTs could enhance mucociliary clearance include improving the rate of mucus clearance

by stimulating airway surface hydration, increasing the velocity of airflow and thus the air-mucus interaction, and by facilitating a homogeneous distribution of ventilation. These mechanisms provide a physiological justification for the role of ACTs in bronchiectasis.

Question 1: Statements

- Sputum from people with bronchiectasis is abnormally hyper-concentrated (dehydrated) and mucin concentration is related to disease severity. This indicates that the level of mucus layer dehydration plays an important role in the pathophysiology of the disease.
- The main physiological mechanism that promotes mucus clearance involves mechanical stress, such as fluid shear stresses, compressions or stretching, and osmotic shocks. ACTs which implement these mechanisms of action have the potential to enhance mucociliary clearance in bronchiectasis, as they can potentially achieve a greater expiratory to inspiratory flow rate or direct volume of air behind lung regions that are obstructed by mucus accumulation.

Question 1: Recommendations for research

- Investigate how biophysical and surface sputum properties such as viscoelasticity, adhesivity and cohesivity (defined as the tendency for a gel to remain attracted to itself [36]) change across the disease trajectory, in relation to underlying aetiologies, or with different endotype or phenotypes in people with bronchiectasis.
- Investigate how the biophysical and surface sputum properties influence the effectiveness of ACTs in people with bronchiectasis. Evaluate whether these sputum biomarkers could support the identification of good candidates/responders for specific ACTs in order to personalise airway clearance management.

- Explore whether the order or specific combination of the physiological mechanisms described above can improve mucus clearance, specifically in people with bronchiectasis according to their disease aetiology, endotype or phenotype. This may help in selecting the most suitable ACTs or combination of ACTs in clinical practice.

Question 2 - What is the physiological rationale of each one of the ACTs and what are the advantages and limitations of each technique?

To answer this question, we searched for studies that examined or explained the physiological mechanism of mucociliary clearance for each ACT. Considering what could improve long-term adherence to ACTs, we also summarised the views of the panel about the key advantages and disadvantages of each technique, including the views of the patient representatives.

Evidence overview

A total of 30 studies were identified, all meeting the inclusion criteria (supplementary material 1, figure S2 and table S3). Of these studies, 18 were primary research papers, including 14 clinical trials, i.e., one randomised controlled trial [40], nine crossover trials [41-49], and four quasi-experimental [50-53]. Five studies provided data from *in-vitro* or animal experiments [20, 21, 35, 50, 52]. Only four studies reported data exclusively from people with bronchiectasis [49, 54-56], nine studies reported mix data from various respiratory diseases (e.g., bronchiectasis, COPD, and cystic fibrosis) [29, 45, 57-63], nine studies included patients with other respiratory diseases [35, 40-44, 47, 48, 51, 64], and one study reported data from healthy adults [46].

The physiological rationale for each of the following ACTs was considered: forced expiration technique (FET), active cycle of breathing techniques (ACBT), manual percussions, manual

vibrations or shaking, autogenic drainage, slow expiration with glottis opened in lateral posture (ELTGOL), gravity-assisted drainage (GAD) technique, positive expiratory pressure (PEP) devices, positive expiratory pressure devices with oscillation (O-PEP), high-frequency chest wall oscillation (HFCWO), and intrapulmonary percussive ventilation (IPV). These techniques appear to achieve one or several of the physiological principles proposed to enhance sputum clearance: improvement of collateral ventilation and interdependence, increased expiratory airflow velocity, reducing the total airway cross-sectional ratio, use of gravity, change of airway pressures and production of airway oscillations. Specific data on frequencies and flows rates achieved through ACTs in other patient populations can be found in McIlwaine et al.[29]

The identified ACTs have a range of advantages. For instance, many ACTs can be used independently by the patient, and they are portable and easy to learn. Common disadvantages include the need for some level of concentration when performing the techniques, as well as the need for instructions or training to ensure optimal execution, especially when access to a specialist respiratory physiotherapist is limited. If the performance of ACTs includes the use of a device, the need for cleaning, periodic replacement, noise, and/or transport difficulties are the main disadvantages associated with its use. Table S4 (supplementary material 1) presents the physiological rationale for the ACTs and table 2 their advantages and disadvantages from the respiratory physiotherapists and patients´ perspectives. Although some techniques may be combined with others, each technique was reported separately. Further information on the procedures for performing ACTs is available in online resources that include videos and illustrations [65-67].

Table 2. Advantages and disadvantages of each airway clearance technique (ACT).

	FET	ACBT	Manual percussions	Manual vibrations or shaking	GAD	HFCWO	IPV	AD	ELTGOL	PEP	O-PEP
Advantages											
Can be performed independently.	✓	✓	≈ (anterior lung regions)	≈ (anterior lung regions)	✓	✓		✓	✓	✓	✓
Can be combined with some other ACTs	✓ (e.g., GAD)	✓ (e.g., GAD)	✓ (e.g., GAD)	✓ (e.g., ACBT)	✓ (e.g., ACBT)	✓ (e.g., GAD)	✓ (e.g., GAD)	✓ (e.g., O-PEP)	✓ (e.g., O-PEP)	✓ (e.g., AD or ELTGOL)	✓ (e.g., AD or ELTGOL)
Easy to perform in different environments / easy to transport (e.g., when travelling).	✓	✓	✓	✓	✓	≈ (if using a portable HFCWO device)		✓	✓	✓	✓ (except TPEP)
Easy to teach (respiratory physiotherapist) and easy to learn how to perform (patients).	✓	✓				✓				✓	✓
Patient does not require concentration or effort			✓	✓	✓	✓	✓				
Technique can be applied passively, which can be appropriate when patients are too unwell to do independent techniques.			✓	✓	✓	✓	✓				
Generate ventilatory support (e.g., recommended for exacerbations or in more severe patients)							✓				
Patients may prefer this technique compared to other techniques.								✓		✓	✓

Disadvantages											
Less commonly used as a standalone technique because a prolonged treatment time may be needed, especially when the goal is to enhance sputum clearance from peripheral airways.	**X**			**X**	**X**						
Likelihood of airway dynamic collapse using low inspiratory lung volumes [57].	**X**	**X**									
Usually, assistance is required from a respiratory physiotherapist or another person (e.g., caregiver).			**X**	**X**			**≈** (preferably used in clinical settings)				
It may be difficult for the respiratory physiotherapist or caregiver to perform long sessions while still achieving optimal performance.			**X**	**X**					**X** (if it is assisted)		
Patients may experience discomfort (especially those who are frail) or present adverse events (e.g., gastroesophageal reflux, shortness of breath, ventilation/perfusion mismatch, increase intracranial pressure), particularly in severe disease or during acute exacerbations.			**X**	**X**	**X** (especially downward positions)	**X**			**X** (if side-lying position was not tolerated)		
Devices that are difficult to transport (size or weight) and required electrical source if a battery-operated device is not available.						**X**	**X**				**X** (only TPEP)
Cost associated with the device (the prize or because needed to replace periodically)						**X**	**X**			**X**	**X**
Device does not provide feedback on whether it is used correctly or not (e.g., target pressure unless a manometer is used)						**X**	**X**			**X** (except TheraPEP)	**X** (except TPEP)
Noisy						**X**	**X**				**X**
Time required for cleaning and disinfection							**X**			**X**	**X**

Can take time to master the technique and requires concentration and effort compared to other techniques.								X	X		

✓ for advantages; X for disadvantages; ≈ yes, but with exceptions. FET, forced expiratory technique; ACBT, active cycle of breathing techniques; GAD, gravity-assisted drainage; HFCWO, high-frequency chest wall oscillation; IPV, intrapulmonary percussive ventilation; PEEP, positive end expiratory pressure; O-PEP, oscillating positive expiratory pressure; ELTGOL, slow expiration with glottis opened in lateral posture; PEP, positive expiratory pressure; TPEP, temporary positive expiratory pressure.

Question 2: Statements

- The ACTs enhance sputum clearance by incorporating one or more of the following mechanism of actions: improvement of collateral ventilation and interdependence, increase of expiratory airflow velocity, reducing the total airway cross-sectional ratio, use of gravity, change of airway pressures and generation of airway oscillations. Data specifically evaluating the above physiological principles in people with bronchiectasis are scarce.
- The main advantages of specific ACTs are that they can be performed independently, they are feasible in different environments or can easily be implemented in a daily routine.
- The main disadvantages of specific ACTs are the level of concentration and effort that is required to perform them, the need of cleaning and periodic replacements of devices, the noise or size of devices, difficulty of transport, the lack of biofeedback and the cost.

Question 2: Recommendations for research

- Assess if the physiological mechanisms described for each ACT work specifically in people with bronchiectasis and what are the related physiological actions (pressure, frequencies, flow rate, etc) in this population.
- Establish whether the physiological effects of ACTs change depending on the clinical status (i.e., clinical stability *vs.* acute exacerbation) or disease severity (i.e., mild *vs.* severe) of the patients.
- Conduct studies that involve people with bronchiectasis in their design and incorporate strategies that enhance the advantages and mitigate the disadvantages of ACTs in clinical practice.

Question 3 - Which are the ACTs that are clinically used in the management of adults with bronchiectasis and are there any patterns according to geographical location?

Despite ACTs being recommended in national and international guidelines, their clinical implementation across the globe is largely unknown. To identify the use of ACTs in the management of adults with bronchiectasis, we analysed surveys, audits and registries that recorded the clinical use of ACTs, alone or alongside other treatments. Potential location patterns were also assessed.

Evidence overview

A total of 2,934 studies were screened for eligibility and seven papers were included [68-74] (supplementary material 1, figure S3 and table S5). Five studies assessed the clinical use of ACTs via surveys [68-70, 72, 73], and two studies through audit [74] or registry data [71]. One registry recorded the ACTs during a clinically stable stage or exacerbation of the disease [71], and one survey only during exacerbations [73], whilst the other studies were conducted during a clinically stable stage or did not report this information. One study assessed ACTs during Coronavirus disease 2019 (COVID-19) [72].

All surveys were administered to healthcare professionals [68-73], mainly physiotherapists (n=482) [68-70, 73]. In three studies that reported on survey response rates for healthcare centres and professionals, these ranged from 70% to 88% [68-70], whilst it was only 0.5% in the survey that had the highest number of invited healthcare professionals (n=26,000) [73].

All studies assessed a variety of ACTs, apart from Santos et al. [70] that specifically assessed the use of different PEP devices. The ACTs were not always defined, but results were mainly

presented as frequencies of use (figure 1). Based on six studies that compared a variety of ACTs, the most common routinely used ACT was the ACBT, with a range of 48-to 91%. PEP or O-PEP (range 7-75%), techniques based on gravity such as GAD (range 8-76%) and modified-GAD (range 10-55%), and techniques based on optimal positioning (range 35-84%) were also frequently reported. Other, less frequently used ACTs were manual percussion, deep breathing exercises, positions of ease (possibly for ease of breathlessness), manual and high frequency vibrations, sustained maximum expiration, FET, autogenic drainage, or other (figure 1 and supplementary material 1, figure S4).

Evidence for the clinical use of ACTs was mainly available from Australia, and ACBT with FET or directed cough were the most frequently selected choices [69, 72-74]. Due to the limited data from other countries, it was not possible to identify additional geographical patterns.

(Please, insert figure 1 around here)

Question 3: Statements

- There is limited evidence about the clinical use of ACTs in specific countries. Based on the available data (i.e., Australia, New Zealand, USA, Japan, UK), the active cycle of breathing technique is the most commonly used ACT in bronchiectasis. Positive expiratory pressure, oscillating positive expiratory pressure, and techniques based on the effect of gravity are also commonly used.
- Studies reporting on the clinical use of ACTs do not always adequately describe the responding population and sample. They also do not always clearly define ACTs.

- Data on the use of ACTs in clinical practice are scarce and some data are likely to be out of date given the progress in bronchiectasis management in the past decade.

Question 3: Recommendations for research

- Surveys, audits and clinical registries need to assess the ACTs that are currently used in clinical practice in different geographic areas and investigate potential variations.
- Surveys need to consistently report on the responder population and sample characteristics.
- Studies need to clearly and adequately define ACTs in line with the clinical practice of each country, so as to enable future comparisons.

Question 4 – What is the clinical evidence for the effectiveness of ACTs, in terms of function and disability (e.g., sputum expectoration), activity (e.g., physical activity) and participation (e.g., self-care), in adults with bronchiectasis?

Clinical evidence for the effectiveness of ACTs is vital for the management of bronchiectasis. To identify this for adults with bronchiectasis, we analysed randomised clinical trials that assessed the effects of any ACT in the participant's function and disability, activity, and participation. The comparative arm of the studies could be another ACT, a different type of treatment, placebo, sham intervention, or no treatment.

Evidence overview

A total of 1,936 studies were screened for eligibility and 30 papers were included (supplementary material 1, figure S5). Results are presented in table 3. All included studies were randomised; 10 had a parallel group design and 20 had a crossover design. They were mainly short-term studies with a range from 1 day to 4 weeks, whilst two studies had a duration of 3, and 12 months each [75, 76]. Overall, there were 811 participants (57% females), with mean age of 58 years, and mean forced expiratory volume in one second (FEV_1) 59% predicted. Most studies included patients during a clinically stable condition (n=22), three during an acute exacerbation [77-79], and one study during both clinical stages [80], although this was not clearly reported in four studies[81-84].

Most included studies were active comparator studies, with one ACT technique compared to another. Most studies investigated the effectiveness of O-PEP; specifically, Flutter (n=13), Acapella (n=7), Aerobika (n=1), RC Cornet (n=2), Quake (n=1), TPEP (n=1), lung flute (n=1), and

bubble PEP (n=2) were studied in different or the same trials. Studies also assessed GAD (n=13), ACBT (n=11), manual techniques i.e., percussions/vibrations (n=9), ELTGOL (n=4), autogenic drainage (n=4), PEP (n=2) and HFCWO (n=1). The GAD and manual techniques were used alone or in combination with other ACTs; also referred to as conventional physiotherapy treatment. Most techniques were self-administered by the patients at the hospital, predominantly after training by a respiratory physiotherapist or another experienced healthcare professional. Alternatively, clinical supervision was provided in each session or selected ones.

The effectiveness of the techniques was assessed using function and disability outcomes, whilst there were limited trials that used activity and participation measures (supplementary material 1, table S6). Sputum volume or weight during or after treatment (n=30), patient-reported preference and comfort (n=16), dyspnoea (n=11) and HRQoL (n=7) were the most common outcome measures used, whilst most studies did not report on patients' adherence to treatment. Three studies included the number of coughs or presence of cough as one of their secondary outcomes [85-87] and only two studies used frequency of exacerbations or time to first exacerbation [75, 76]. There is no evidence about the optimal frequency, or the number of sessions needed to ensure correct procedure of the ACTs. The studies that assessed ACT adverse events did not identify serious adverse effects that are related to ACTs.

Table 3. Effectiveness of airway clearance techniques.

Author, year, country	Study design	Clinical status	ACTs applied	Prescription of therapy per technique	Outcome measures (units) / * primary outcome	Patient No. (%Females) Age (years) FEV_1 (% pred) Daily sputum quantity	Key findings / * primary outcome /
Studies lasting less than 4 weeks of intervention							
Tsang et al. [78] 2003, China	RCT	Acute exacerbation	GAD+BC *vs.* O-PEP (Flutter)+BC *vs.* BC	Three daily (one supervised) from day 2 to day of discharge / 15 mins per session	Wet sputum weight (g) FVC (L) / FEV_1 (L) / PEF (L/min) SpO_2 (%) Heart rate (bpm) Hospitalisation length (days)	n= 15 (47% F) Age (GAD+BC)= 67±15 Age (O-PEP+BC)= 72±5 Age (BC)= 74±6 FEV_1 (GAD+BC)= 48±24 FEV_1 (O-PEP+BC)= 39±7 FEV_1 (BC)= 36±11 Daily sputum (GAD+BC) (g)= 47.5±23.2 Daily sputum (O-PEP+BC) (g)= 25.6±14.6 Daily sputum (BC) (g)= 26.2±20.3	There were no statistically significant differences between the GAD+BC, O-PEP+BC and BC.
Patterson et al. [88] 2004, UK	RCX	Clinical stability	ACBT+GAD (2 positions) with vibrations *vs.* IMT (80% of MIP)	Single session / maximum of 30 mins	*Wet sputum weight (g) FVC (L; % pred) FEV_1 (L; % pred) PEF (L/min; % pred) SpO_2 (%)	n= 20 (70% F) Age= 54±14 FEV_1= NR	*ACBT+GAD with vibration significantly improved sputum weight (during ACT intervention) when compared to IMT (6.3±6.6 *vs.* 4.0±4.3; MD 2.3; 95% CI 0.5 to 4.1; p=0.01). *ACBT+GAD with vibration significantly improved

						Daily sputum = NR (inclusion criteria → ½ egg cup /day)	sputum weight (including session and 30min post-intervention) when compared to IMT (9.0±7.8 *vs.* 6.5±6.8; MD 2.4; 95% CI 0.4 to 4.4; p=0.02).
Patterson et al. [89] 2005, UK	RCX	Clinical stability	ACBT+GAD (2 positions) with percussion/ vibrations *vs.* O-PEP (Acapella)	Single session per technique / maximum of 30 mins	*Wet sputum weight (g) FVC (L; % pred) FEV_1 (L; % pred) PEF (L/min; % pred) SpO_2 (%)	n= 20 (65% F) Age= 58±11 FEV_1= 64±22 Daily sputum = NR (inclusion criteria → ½ egg cup /day)	No statistically significant differences were found.
Eaton et al. [90] 2007, New Zealand	RCX	Clinical stability	ACBT *vs.* ACBT+GAD *vs.* O-PEP (Flutter)	Single session per technique / maximum of 30 mins	*Wet sputum weight (g) *Wet sputum volume (mL) *FEV_1 (% pred) *SpO_2 (%) *Borg scale dyspnoea (points)	n= 36 (67% F) Age= 62±10 FEV_1= 57.8±19.8 Daily sputum= NR (inclusion criteria → chronic productive cough)	*ACBT+GAD significantly obtained greater sputum quantity (during ACT intervention) when compared to the ACBT and O-PEP (O-PEP *vs.* ACBT-GAD MD -5.6g±8.2 / -5.1mL±8.8; ACBT *vs.* ACBT+GAD -5.9g±9.6 / -5.7mL±10.5; p<0.01) #. *ACBT+GAD significantly obtained greater sputum quantity (including session and 30min post-intervention) when compared to the ACBT and O-PEP (O-PEP *vs.* ACBT-GAD MD -5.6g±8.5 / -4.9mL±8.2; ACBT *vs.* ACBT+GAD -5.6g±9.2 / -5.3mL±9.9; p<0.001).
Patterson et al. [77] 2007, UK	RCT	Acute exacerbation	O-PEP (Acapella)+GAD (2 positions) vs. usual ACTs (ACBT, autogenic drainage, PEP, O-PEP-Flutter or no ACT)	Once (n=2) or twice (n=18) daily for 10-14 days (end day of antibiotics) O-PEP+GAD (min)=15±3	*Wet sputum volume (mL) FVC (L) / FEV1 (L) Vital capacity (L) SpO_2 (%) Borg scale dyspnoea (points) 15-count breathlessness score (points)	n= 20 (50% F) Age= 61± 11 FEV_1= 64.7±21.1 Daily sputum= NR	No statistically significant differences were found.

				Usual ACTs(min)=11±6			
Syed et al. [91] 2009, India	RCX	Clinical stability	ACBT + GAD vs. GAD + percussion and vibrations + BC	Single session / every 3 hours while awake for 30 mins	*Wet sputum weight (g) Wet sputum volume (NR) FVC (L) / FEV_1 (L) / FEV_1/FVC (l)	n= 35 (23% F) Age= 45±11 FEV_1 (ACBT+GAD)= 41±19 FEV_1 (GAD+percussion and vibration + BC)= 43±20 Daily sputum ranging from 30-132mL/day Daily sputum > 50 mL= 11 participants Daily sputum ≤ 50mL=24 participants	A statistically significant difference in FEV_1/FVC values were observed between pre- and post-intervention in ACBT + GAD intervention (48.4±25.5 vs. 56.1±27.9; p<0.001). A statistically significant difference in FEV_1/FVC values were observed between pre- and post-intervention in GAD + percussion and vibration + BC intervention (49.1±23.9 vs. 54.0±26.5; p=0.03).
Naraparaju et al. [81] 2010, India	RCX	NR	O-PEP (Acapella) *vs.* IMT (80% MIP)	Single session / NR	Wet sputum volume (mL)	n= 30 (67% F) Age= 51±6 FEV_1= 44.5±16.2 Daily sputum= NR (inclusion criteria → chronic productive cough)	O-PEP (Acapella) significantly increased sputum volume (including session and 2h post-intervention) when compared to IMT (80% MIP) (7.2±1.1 vs. 6.5±1.1; MD 0.7; 95% CI 0.1 to 1.3; p=0.014).
Shabari et al. [82] 2011, India	RCX	NR	O-PEP (RC-Cornet) *vs.* O-PEP (Acapella)	Single session / maximum of 20-30 min	*Wet sputum volume (mL)	n= 40 (50% F) Age= 52±16 FEV_1%= NR Daily sputum= NR (inclusion	*O-PEP (RC-Cornet) significantly increased sputum volume (including session and 2h post-intervention) when compared to O-PEP (Acapella) (36.6±7.2 *vs.* 34.6±9.0; MD=1.9; 95% CI NR; p=NR)

						criteria → sputum expectoration of more than 30 ml/day)	
Tambasci o et al. [92] 2011, Brazil	RCX	Clinical stability	O-PEP (Flutter) *vs.* PEP (modified Flutter)	Single session, 4 weeks / 30 min	Mucociliary transport (relative velocity) Sputum displacement using simulated cough machine (cm) Contact angle (°)	n= 18 (72% F) Age= 52±18 FEV_1 (83% - 81%)= 3 participants FEV_1 (77% - 62%)= 9 participants FEV_1 (47% - 31%)= 4 participants FEV_1 (29%)= 1 participant Daily sputum= NR (inclusion criteria → not demonstrate a sufficient respiratory secretion quantity for the analysis)	O-PEP significantly increased sputum displacement from pre to post intervention (9.6±3.4 vs. 12.4±10.5; p<0.05). O-PEP significantly increased the contact angle from pre to post intervention (23.3±6.2 *vs.* 29.4±5.7; p<0.05).
Paneroni et al. [93] 2011, Italy	RCX	Clinical stability	IPV *vs.* GAD (3 positions) with percussion and vibration + FET	Single session / 30 min	Wet sputum weight (g) Dry sputum weight (g) Wet sputum volume (ml) SpO_2 (%) Respiratory rate (cpm) Heart rate (bpm) Visual analogue scale dyspnoea (%)	n= 22 (45% F) Age= 64±9 FEV_1= 53±30 Daily sputum= NR (inclusion criteria → daily sputum volume >20 mL for at least 2 consecutive days)	IPV significantly increased respiratory rate when compared to GAD with percussion and vibration + FET (MD -1.6; 95% CI -3.2 to -0.02; p=0.047). IPV significantly reduced dyspnoea from pre to post intervention (35±29 *vs.* 23±20; p=0.004).
Guimarae s et al. [94] 2012,	RCX	Clinical stability	O-PEP (Flutter) *vs.* ELTGOL *vs.* Control (no ACT)	Single session / 15 min	*Dry sputum weight (g) FVC (L) / FEV_1 (L) FEV_1/FVC (L) / $FEF_{25–75}$% (L/s)	n= 10 (80% F) Age= 56±18	*ELTGOL significantly increased sputum weight (during ACT intervention) when compared to O-PEP and control period (median; min-max): [0.4; 2.6-0.1]

Brazil					/ IC (L) / VC (L) / TLC (L) / FRC (L) / RV (L) / RV/TLC (%) / IC/TLC	FEV_1= 53±19 Daily sputum= NR (inclusion criteria → persistent productive cough)	*vs.* [0.1; 1.3-0.1] *vs.* [0.1; 0.6-0.0]; p=NR). ELTGOL and O-PEP significant decreased RV ([-18.7; -71.5-(-10.7)] *vs.* [-29.6; -54.6-(-8.9)] *vs*. [2.9; -8.0-35.1]; p=NR), FRC [-14.5; -55.6-(3.6)]. vs [-28.8; -52.0-(-5.1] *vs.* [4.3; -18.9-22.4]; p=NR) and TLC ([-9.7; -40.0-(-1.9)] *vs.* [-18.3; -42.8-(-6.4)] *vs.* [4.6; -7.4-12.6]; p=NR) when compared to control period. O-PEP significant increased IC/TLC when compared with ELTGOL and control period ([22.8; -3.6-82.5)] *vs.* [17.9; -10.2-57.8)] vs. [6.7; -17.3-21.3]; p=NR).
Figueiredo et al. [95] 2012, Brazil	RCX	Clinical stability	O-PEP (Flutter) *vs.* Sham O-PEP (sham Flutter)	Single session / 15 min	*Wet sputum volume (mL) Impulse oscillometry= R5 (kPa/l/s) dR/dF ([kPa/l/s]/Hz) X5 (kPa/l/s) AX ([kPa/l/s]·Hz) f0 (Hz)	n= 8 (50% F) Age= 47 (SEM 6) FEV_1= 65 (SEM 6.8) Daily sputum (mL) = 47.8 (SEM 7.1)	O-PEP significantly increased sputum volume (during ACT intervention) compared to sham O-PEP (28.0±5.4 *vs.* 19.6±3.6; 95% CI 3.4 to 13.4; p< 0.05). O-PEP (Flutter®) significantly decreased R5 (MD −11.2; 95% CI−4.4 to −18.2; p=NR), dR/dF (MD −20.8; 95% CI−32.4 to −9.0; p=NR) and AX (MD −7.8; 95% CI−11.9 to −3.7; p=NR) when compared to sham O-PEP.
Amit et al. [80] 2012, India	RCX	Clinical stability (n=22) and acute exacerbation (n=13)	O-PEP (RC-Cornet) *vs.* O-PEP (Quake)	Single session / maximum of 15 min	Wet sputum volume (ml)	n= 35 (68% F) Age= 52±14 FEV_1= NR Daily sputum= NR (inclusion criteria → sputum expectoration of more than 20mL/day)	O-PEP (Quake) significantly increased sputum volume (24h post intervention) when compared to O-PEP (RC-Cornet) (36.2±15.4 *vs.* 33.8±12.4; MD 2.4; 95% CI 1.0 – 4.4; p=0.021).

Nicolini et al. [96] 2013, Italy	RCT	Clinical stability	HFCWO (The Vest) *vs.* other ACTs including PEP bottle, PEP mask, ELTGOL, O-PEP (Acapella) *vs.* no ACT (control)	Twice daily for 15 consecutive days/ 30 min for HFCWO - 40 min for the other ACTs	*BCSS (points) *CAT (points) Sputum volume (mL) Haematology (WC (103 cell) / RC (106 cell) /Neutr (%) / Lymph (%) /C-R Prot. (NR)) FVC (ml) FEV_1 (ml) FEV_1/FVC (ml) TLC (ml) RV (ml) MIP (cmH2O) MEP(cmH2O) PaO_2 (mmHg) $PaCO_2$ (mmHg) pH (NR) mMRC dyspnoea (points) Sputum cytology (TCCx 106/mg / Neutrophyls (%) Lymphocytes (%) / Eosinophyls (%) /Macrophages (%))	n= 30 (70% F) Age (HFCWO)= 75±5 Age (other ACTs)= 74±4 Age (no ACT)= 72±7 FEV_1=NR Daily sputum= NR (inclusion criteria → sputum expectoration ≥ 20 mL/day at least 3 consecutive days)	HFCWO and the group of other ACTs significantly increased sputum volume (during session and 1h after intervention) (after values 52.0±16.9 vs. 62.5.±18.9 vs. 77.0±10.6; p=NR), improved TCCx 106/mg (7.225±1.186 vs. 8.490.±2.771 vs. 10517±2514.9; p=NR), neutrophils (59.9±10.1 vs. 62.0.±9.9 vs. 78.1±6.8; p=NR), lymphocytes (11.9±4.9 vs. 13.5.±3.9 vs. 7.2±2.7; p=NR) and macrophages (35.6±15.2 vs. 31.2.±7.5 vs. 32.2±10.8; p=NR), MRC (MD -0.7±0.8 vs. -0.5.±1.1 vs. 1.0±0.8; p=NR), BCSS (-2.7±1.8 vs. -0.2.±1.8 vs. 3.1±1.4; p=NR), CAT (-8.0±4.0 vs. -0.4.±6.8 vs. 9.9±3.6; p=NR), C-R Prot. (-1.0±0.8 vs. -0.0.±0.9 vs. 1.3±1.1; p=NR), when compared to no ACT. HFCWO significantly improved sputum volume, neutrophils, macrophages, CAT, C-R Prot, FVC (MD 192.1±80.9 vs. 54.5.±153.7 vs. -37.0±35; p=NR) and FEV_1 (135.5±93.4 vs. -94.0.±128.3 vs. -21.0±30.7; p=NR) when compared with other ACTs and no ACTs. HFCWO significantly improved WC (103 cell) (MD -673.8±1093.6 vs. 957.0.±915.7; p=NR), RC (106 cell) (73.0±202.5 vs. -82.0.±62.3; p=NR), TLC (-657.0±1088.9 vs. 46.0.±95.6; p=NR), RV (-580.0±1118.1 vs. 65.0.58.5; p=NR), MIP (9.8±10.1 vs. -4.1.±2.5; p=NR) and MEP (6.5±7.2 vs. -8.3.±3.9; p=NR) when compared to no ACT.
Anand et al. [83] 2014, India	RCT	NR	ACBT *vs.* other ACTs (GAD, percussion, pressure-vibration, active bilateral respiratory	Single session/ 30 min	Wet sputum volume (mL) PEF (NR)	n= 30 (NR% F) Age= NR $FEV_{1=}$ NR	ACBT (192±62 *vs.* 210±64) and other ACTs (192±44 *vs.* 288±49) significantly improved PEF from pre to post treatment (p<0.001).

			exercises)			Daily sputum= NR (inclusion criteria -> from 10 to 150 mL / day)	
Semwal et al. [97] 2015, India	RCX	Clinical stability	Autogenic drainage *vs.* O-PEP (Acapella)	Single session / 20-30 min	*Wet sputum weight (g) Wet sputum volume (mL) SpO_2 (%) Respiratory rate (cpm) PEF (mL) Modified Borg Scale dyspnoea (points)	n= 30 (33% F) Age (male)= 46±9 Age (female)= 49±10 FEV_1= NR Daily sputum= NR (inclusion criteria → history of productive cough)	There were no statistically significant differences between autogenic drainage and O-PEP (Acapella).
Ramos et al. [98] 2015, Brazil	RCX	Clinical stability	GAD + FET (huffing) *vs.* GAD + coughing *vs.* GAD + percussion + coughing *vs.* control (coughing)	Single session / 2 period of 20 min	Percentage of solids (dry/wet weight ratio (%)) Mucus viscosity (poise) Mucus elasticity (dynes/cm)	n= 22 (73% F) Age= 51 (range, 18-76) FEV_1= NR Daily sputum (GAD+FET) (mL)= 27.4±8.6 Daily sputum (GAD + percussion + coughing) (mL)= 26.6±9.7 Daily sputum (GAD + coughing) (mL)= 25.8±8.6 Daily sputum (coughing) (mL)= 24.9±10.7	The percentage of solids content at 60 min was significantly greater following GAD+percussion+coughing compared to control (p =0.01). At 90 min, a significant increase was found in the percentage of solids content obtained following GAD+percussion+coughing (p=0.07) and GAD+FET (p=0.03) compared to control. At 90 min, a significant increase was found in the percentage of solids content obtained following GAD+percussion+coughing (p=0.01) and GAD+FET (p=0.04) compared to GAD + coughing. GAD+percussion+coughing significantly obtain greater sputum samples at 60 and 90 min compared to coughing (p=0.02 and p=0.01, respectively) and GAD+coughing (p=0.04).

							GAD+coughing (p=0.01), GAD+percussion+coughing (p=0.001 and GAD+FET (p= 0.001) significantly obtained greater elastic sputum samples in comparison with coughing at 60 min, but only GAD+percussion+coughing (p=0.001) and GAD+FET (p=0.005) significantly obtained greater elastic sputum samples at 90 min.
Herrero-Cortina et al. [99] 2016 Spain	RCX	Clinical stability	Autogenic drainage *vs.* ELTGOL *vs.* O-PEP (TPEP)	Three non-consecutive sessions in the same week/ 40 min	*Wet sputum weight (g) LCQ (points) FVC (L) FEV_1 (L) $FEF_{25–75}$ (L/s) Patients feedback (Likert scale)	n= 31 (71% F) Age= 60±18 FEV_1= 63±23 Daily sputum = 21 mL [15.8 to 36.5] / 21.1 g [15.3 to 35.6]	Autogenic drainage and ELTGOL significantly increased sputum expectoration (during intervention) than O-PEP [Median diff. Autogenic drainage *vs.* TPEP 3.1g (95% CI 1.5 to 4.8); ELTGOL *vs.* TPEP 3.6 g (95% CI 2.8 to 7.1)]. Autogenic drainage, ELTGOL and TPEP significantly reduced the need of expectoration over 24h after intervention compared to baseline assessment [Median diff. Autogenic drainage *vs.* baseline −10.0g (95% CI −15.0 to −6.8); ELTGOL *vs.* baseline −9.2g (95% CI −14.2 to −7.9); TPEP *vs.* baseline −6.0 g (95% CI −12.0 to −6.1)]. Autogenic drainage (Median diff. 0.5 (95%CI 0.1 to 0.5), ELTGOL (0.9 (95%CI 0.5 to 2.1) and TPEP (0.4 (95CI% 0.1 to 1.2) significantly increased the total LCQ score from pre to post intervention.

AbdelHali et al. [79] 2016, Egypt	RCT	Acute exacerbation	ACBT+GAD *vs.* other ACTs (GAD + percussion + breathing control)	Twice daily, 2 weeks / 15-20 min	Wet sputum volume (mL) FVC (% pred) FEV_1 (% pred) FEV_1/FVC (NR) MMEF (% pred) LCQ (points) mMRC dyspnoea (points) PAO_2 (mmHg) PaO_2 (mmHg) $PaCO_2$ (mmHg) $P(A\text{-}a)O_2$ gradient	n= 30 (33% F) Age= 52±15 FEV_1 (ACBT)= 57±14 FEV_1 (other ACTs)= 54±20 Daily sputum (ACBT) (mL)= 43±9 Daily sputum (other ACTs) (mL)= 44±9	ACBT+GAD significantly improved dyspnoea (Pre 2.9 *vs*. Post 1.6; p<0.001) from pre to post intervention. Other ACTs significantly improved dyspnoea (Pre 2.8 *vs*. Post 2.0; p<0.001) from pre to post intervention. ACBT+GAD significantly increased FVC (Pre 70.7 *vs*. Post 74.0; p<0.001) and MMEF (Pre 31.6 *vs*. Post 36.7; p<0.001) from pre to post intervention. Other ACTs significantly increased FEV_1 (Pre 54.1 *vs*. Post 56.7; p<0.04) and MMEF (Pre 32.3 *vs*. Post 38.9; p<0.001) from pre to post intervention. ACBT+GAD significantly reduced $PaCO_2$ (Pre 52.5 *vs*. Post 47.0; p<0.001) increased PaO_2 (Pre 73.0 *vs*. Post 80.8; p<0.001) and PAO_2 (Pre 84.0 *vs*. Post 90.9; p<0.001) from pre to post intervention. Other ACTs significantly reduced $PaCO_2$ (Pre 55.9 *vs*. Post 49.7; p=0.002) increased PaO_2 (Pre 60.7 *vs*. Post 69.1; p<0.) and PAO_2 (Pre 79.8 *vs*. Post 87.6; p=0.002) from pre to post intervention. ACBT+GAD presented significantly higher values of PaO_2 (80.9± 13.0 *vs.* 69.1± 17.0; p=0.043), total LCQ score (14± 3 *vs.* 12± 4.2; p=0.019) and sputum volume and lower values of P(A-a)O2 gradient (10.1± 7.3 *vs.* 18.5± 10.0; p=0.014) and sputum volume (14.7± 4.0 *vs.* 19.0± 5.7; p=0.023) when compared with the other ACTs post intervention.

Silva et al. [100] 2017, Australia	RCX	Clinical stability	O-PEP (Lung Flute) vs. O-PEP (Flutter)	Single session / maximum of 30 min (+ 30 min rest period)	*Wet sputum weight (g) *Dry sputum weight (g)	n= 40 (73% F) Age= 63±16 FEV_1= 66±30 Daily sputum= NR (inclusion criteria → productive of > 25mL / day)	O-PEP (Flutter) significantly increased wet sputum weight (during intervention) than O-PEP (Lung Flute) (5.1±6.3 *vs.* 3.7±3.4; MD 1.3; 95% CI 0.2 to 3.0; p=0.038). O-PEP (Lung Flute) significantly increased wet sputum weight (during 30 min post intervention, not including session) than O-PEP (Flutter) (2.0±3.0 *vs.* 0.7±0.7; MD 1.3; 95% CI 0.5 to 2.2; p<0.001).
De Souza et al. [49] 2019, Brazil	RCX	Clinical stability	O-PEP (Flutter) *vs.* thoracic compression *vs.* no ACTs (control)	Single session / 30 min (+30 min rest period)	Wet sputum weight (g) Dry sputum weight (g) Sputum adhesiveness (Lopez-Vidriero scale) Sputum purulence (Murray scale) Impulse oscillometry: *R5 (kPa/l/s) R20 (kPa/l/s) R5–R20 (kPa/l/s) X5 (kPa/l/s) AX (kPa/l) Fres (Hz) SpO_2 (%) mMRC dyspnoea (points)	n= 20 (NR% F) Age= 57±14 FEV_1= 60±0.28 Daily sputum= NR	O-PEP significantly increased wet (p=0.039) and dry (p=0.005) sputum compared to no ACTs (control). O-PEP significantly decreased total airway resistance (p=0.04), peripheral resistance (p=0.005) and reactance area (p=0.001) from pre to post treatment. Thoracic compression significantly decreased peripheral resistance (p=0.001) and reactance area (p=0.001) from pre to post treatment.
Santos et al. [85] 2020, Australia	RCX	Clinical stability	ACBT *vs.* O-PEP (bottle PEP) *vs.* no ACT (control)	Single session / 30 min (+ 60min rest period)	*Wet sputum weight (g) Dry sputum weight (g) FVC (L; % pred) / FEV_1 (L; % pred) / FEV_1/FVC (L; % pred) / MEF_{25-75}	n= 35 (68% F) Age= 75±8	*ACBT and O-PEP significantly increased wet sputum weight during active intervention (ACBT *vs.* no ACT 1.6, 95%CI 0.8 to 2.3; O-PEP *vs.* no ACT 1.0, 95%CI 0.3 to 1.6) and during the total time of the session (30 min

					(L; % pred) No. ACT cycles No. coughs 0-10 scale dyspnoea (points) 1-5 scale fatigue (points) SpO_2 (%) Heart rate (cpm)	FEV_1= 72.0±20.0 Daily sputum= NR (inclusion criteria → daily sputum production)	of intervention + 60 min of rest) (ACBT *vs.* no ACT 1.3, 95%CI 0.2 to 2.4; O-PEP *vs.* no ACT 2.1, 95C%CI 0.9 to 3.3). ACBT and O-PEP significantly increased dry sputum weight during active intervention (ACBT *vs.* no ACT 0.04, 95%CI 0.01 to 0.07; O-PEP *vs.* no ACT 0.03, 95%CI 0.01 to 0.05) and during the total time of the session (30 min of intervention + 60 min of rest) (ACBT *vs.* no ACT 0.03, 95%CI 0.01 to 0.05; O-PEP *vs.* no ACT 0.05, 95C%CI 0.01 to 0.10) when compared to no ACT. ACBT significantly improved dyspnoea, SpO_2, increase heart rate and fatigue (all p< 0.005) compared to no ACT. O-PEP significantly increased FVC (%), heart rate, fatigue and improved dyspnoea and SpO_2 (all p< 0.005) compared to no ACT. ACBT required significantly more treatment cycles when compared to O-PEP (MD −2.5; 95% CI −3.1 to −2.0; p<0.05).
Studies lasting at least 4 weeks of intervention							
De Oliveira et al. [101] 2001, Brazil	RCT	Clinical stability	GAD + manual percussion and/ or vibration *vs.* O-PEP (Flutter)	Twice a week, 4 weeks / 60 min session (10 min of inhalation + 20 min of ACT + 30 min of rest)	Wet sputum weight (g) Dry sputum weight (g) PEF (L/min) Respiratory rate (cpm) SpO_2 (%) Heart rate (bpm)	n= 10 (60% F) Age= 59±14 FEV_1= 58±18 Daily sputum= NR	O-PEP significantly decreased oxygen saturation from pre to week 3 (95±2 *vs.* 93±3; p<0.05). Cardiac frequency also showed a statistically significant diminution in weeks 1 and 4 with O-PEP (77±9 *vs.* 72±7; 79±12 *vs.* 75±10; both p<0.05).

Thompson et al. [102] 2002, UK	RCX	Clinical stability	ACBT *vs.* O-PEP (Flutter) + FET Both groups could use GAD if necessary	Twice daily, 4 weeks / Until there was no further sputum to expectorate (29min± 17 for ACBT + FET *vs.* 26min± 11 for OPEP + FET)	Wet sputum weight (g) PEF (L/min) / FEV_1 (L) / FVC (L) CRQ (points) Borg scale dyspnoea (points) Session's length (minutes)	n= 22 (64% F) Age (ACBT)= 68±16 Age (O-PEP)= 59±8 FEV_1 (ACBT)= 70±42 FEV_1 (O-PEP)= 67±38 Daily sputum= NR (inclusion criteria → productive bronchiectasis)	There was a statistically significant improvement in FEV_1 with the O-PEP#, but this did not achieve a clinically meaningful change (Data NR).
Murray et al. [76] 2009, UK	RCX	Clinical stability	O-PEP (Acapella) vs. no ACT	Twice daily, 3 months / 20-30 mins per session	*LCQ (points) Wet sputum volume (ml) FVC (Ll; % pred) / FEV_1 (L; % pred) / FEV_1/FVC (L; % pred) / FEF_{25-75}% (L/s; % pred) MIP / MEP (cmH2O; % pred) ISWT (m) Sputum bacterial load (cfu/mL) SGRQ (points) No. exacerbations	n= 20 (40% F) Age=73 [72-77] FEV_1= 75.7 [48.3-98.1] Daily sputum (mL)= 5 [1.2 – 15]	*O-PEP significantly improved the total score of LCQ (Median, 1.3; IQR, -0.2-3.2 vs. 0; -1.5-0.5; p=0.002) compared to no ACT. O-PEP significantly increased the 24-h sputum volume (Median 2; IQR 0-6 vs. -1; -5-0; p=0.02), ISWT (40; 15-80 vs. 0; -10-20; p=0.001) and in SGRQ (7.8; -1.0-14.5 vs. -0.7; -2.3-0.0; p=0.005) compared to no ACT.
Senthil et al. [84] 2015, India	RCT	NR	ACBT *vs.* ACBT + O-PEP (Acapella)	Once day, 4 weeks / 30 min	FVC (L) FEV_1 (L)	n= 30 (NR% F) Age= 55±3 FEV_1= NR	ACBT (Pre 2.31±0.42 *vs.* Post 2.42±0.43; p=0.029) and ACBT + O-PEP (Pre 2.33±0.73 *vs.* Post 2.853±0.663; p=0.000) significantly increased FEV_1 from pre to post intervention. ACBT + O-PEP significantly increased FVC from pre to post intervention (Pre 3.22±0.67 vs. Post 3.41±0.97; p=0.01).
Tambascio et al. [103]	RCX	Clinical stability	O-PEP (Flutter) vs. Sham O-PEP (sham Flutter)	Once daily, 4 weeks / 30 min	Sputum adhesiveness (points) / mucociliary transport (relative velocity) / sputum displacement	n= 17 (59% F) Age= 55±14	O-PEP significantly increased sputum displacement (Pre 9.9±3.1 *vs.* Post 14.0±5.7; p=NR) and decreased sputum contact angle (Pre 26.5±3.2 *vs.* Post 22.8±3.6;

2017, Brazil					(cm) / contact angle (°) Sputum purulence (Murray scale) / Sputum cytology (nº inflammatory cells (10^6) / eosinophils (%) / neutrophils (%) / macrophages (%) / lymphocytes (%) Microbiology (bacterial isolation and colony-forming units)	FEV_1= 42±17 Daily sputum= NR (inclusion criteria → at least >0.5 mL of respiratory secretion)	p=NR) from pre to post treatment.
Üzmezoglu et al. [87] 2018, Turkey	RCT	Clinical stability	ACBT + GAD *vs.* O-PEP (Flutter)	Twice daily, 4 weeks / 15-20 min	Sputum production (4-category changes) SF-36 (points) mMRC scale dyspnoea (points) Borg scale dyspnoea (points) FVC (% pred) / FEV_1 (% pred) /FEV_1 / FVC (NR) PEF (% pred) Presence of cough, wheezing, fatigue and loss of appetite	n= 40 (55% F) Age= 54±11 FEV_1 % pred= 70.8±28.2 to 60.6±23.4 Daily sputum (ACBT)= 14 participants (72%) Daily sputum (Flutter)= 12 participants (60%)	O-PEP significantly improved general health (40.0±21.6 *vs.* 35.6±27.9; p=0.048) and pain (86.7±17.8 vs. 69.9±25.4; p=0.011) in the SF-36 when compared to ACBT + GAD, post intervention. O-PEP significantly improved pain (p=0.005) and physical state assessment (p=0.005) in the SF-36 and dyspnoea (p=0.012 evaluated by mMRC; p=0.006 evaluated by Borg scale) from pre to post treatment. ACBT+GAD significantly improved dyspnoea (p=0.002 evaluated by mMRC) and a reduction in the number of patients presenting cough (Pre n=14; Post=4; p=0.002) from pre to post treatment. O-PEP significantly reduced the number of patients presenting fatigue (Pre n=12; Post=4; p=0.021) from pre to post treatment. ACBT+GAD (n=4; p=0.004) and O-PEP (n=5; p=0.003)

							significantly increased the number of patients with greater sputum production from baseline.
Muñoz et al. [75] 2018, Spain	RCT	Clinical stability	ELTGOL *vs.* Upper limb stretches ("placebo" intervention)	Twice daily, 12 months / 15 min if only one lung was affected or 30 min when both lungs were affected	*Wet sputum volume (mL) FEV_1 (L; % pred) 6MWT (m) SGRQ (points) LCQ (points) No. exacerbations (12 month) Time 1st exacerbation (days) ESR (mm) Leukocytes (10^3/ µL) Neutrophils (%) C-R Prot. (mg/dL) Fibrinogen (mg/dL)	n= 44 (52% F) Age (ELTGOL)= 63±13 Age (Upper limb stretches)= 64±8 FEV_1 (ELTGOL)= 58±23 FEV_1 (Upper limb stretches)= 65±28 Daily sputum (ELTGOL) (mL)= 20 [15-40] Daily sputum (upper limb stretches) (mL)= 15 [15-20]	*ELTGOL significantly increased sputum volume (obtained 24h post intervention) after the first session (Median 17.5; 95%CI 10.0 to 26.2 *vs.* -5; 95%CI -11.2 to 0.0; p<0.001) and at month 12 (Median 10.0; 95%CI -5.0 to 25.0 *vs.* 0.0; 95%CI -10.0 to 3.7; p=0.015) than upper limb stretches. ELTGOL significantly improved the total LCQ score (−1.96; 95%CI 0.2 to 3.8 *vs.* -2.0; 95%CI -2.8 to -1.2; p<0.001), SGRQ (−6.8; 95%CI −15.1 to 1.5 vs. 11.4; 6.9 to 15.9; p<0.001) and reduced the no. of exacerbations (Median −0.8; 95%CI −1.5 to -0.1 *vs.* 0.35; 95%CI -0.5 to 0.35; p=0.042) when compared to upper limb stretches.
Livnat et al. [104] 2021, Israel	RCT	Clinical stability	O-PEP (Aerobika) *vs.* Autogenic drainage	Once daily, 4 weeks / 15-20 min	*Lung clearance index (points) Sputum quantity (mL; self-reported) Sputum purulence scale (points) FEV_1 (% pred) QoL-B (points)	n= 51 (64% F) Age (O-PEP)= 66±13 Age (autogenic drainage)= 67±13 FEV_1 (O-PEP)= 81±18 FEV_1 (autogenic drainage)= 96±18	Patients performing autogenic drainage reported a significantly higher sputum reduction compared to those using O-PEP [less sputum 6 (24%) *vs.* 12 (52%); more sputum (19 (76%) *vs.* 11 (48%); p=0.044]. Autogenic drainage significantly increased social functioning score (Pre Median 50 IQR [21-67] *vs.* Post 58 [37-76]; p=0.04) from pre to post treatment. Autogenic drainage significantly increased health perceptions score (Pre 33 IQR [25-58] *vs.* Post 42 [33-65]; p=0.04) from pre to post treatment.

Data is presented as mean ± standard deviation, unless otherwise stated. Studies have been classified according to the intervention length (<4 weeks or ≥4 weeks). ACBT, active cycle of breathing techniques; ACT, airway clearance technique; AX, integral of reactance between 5 Hz and resonant frequency; BC, breathing control; CI, confidence intervals; dR/dF, dependency of resistance as a function of oscillation frequency; ELTGOL, slow expiration with the glottis opened in the lateral posture; ESR, erythrocyte sedimentation rate; f0, resonant frequency; FEF, forced expiratory flow; FET, forced expiration technique; FEV1, forced expiratory volume in one second; FRC, functional residual capacity; FVC, forced vital capacity; GAD, gravity-assisted drainage; HFCWO, high frequency chest wall oscillation; HS, hypertonic saline; Hz, hertz; IQR, interquartile range; IC, inspiratory

capacity; IMT, inspiratory muscle training; IS, isotonic saline; ISWT, Incremental shuttle walk test; MD, mean difference; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; MMEF, maximal mid-expiratory flow; mMRC, modified Medical Research Council; NR, not reported; O-PEP, oscillatory positive expiratory pressure; PEF, peak expiratory flow; Qol-B, quality life questionnaire - bronchiectasis; R5, resistance at 5 Hz; RCT, randomised controlled trial; RCX, randomised cross-over trial; RV, residual volume; SEM, standard error of the mean; TLC, total lung capacity; X5, reactance at 5 Hz. * Reported as primary outcomes in the study. Note: Table does not include patient preference, barriers and enablers, as these are presented in Question 5.

Question 4: Statements

- Although data on the effects of performing ACTs for periods over 6 or 12-months is limited, the findings demonstrate a reduction in the impact of cough, improvement in health-related quality of life (HRQoL) and reduction in the risk of exacerbations. These findings support previously published clinical recommendations for the use of ACTs as part of bronchiectasis management in adults [2,11-14]. However, there is no evidence about the optimal frequency or number of ACTs sessions.
- Randomised controlled trials have assessed a variety of ACTs, with oscillatory positive expiratory pressure devices (O-PEP) (mainly via Flutter and Acapella), gravity-assisted drainage (GAD) and active cycle of breathing techniques (ACBT) being the most commonly studied techniques. The existing literature does not demonstrate superiority of one technique over another but supports the use of ACTs.
- Wet sputum weight or volume were the most commonly used outcome measures. The ACTs increase the expectorated sputum during or following a single session of ACTs. Despite being frequently used in clinical practice, the interpretation of sputum changes is ambiguous.
- To date, there are no studies that have investigated the effect of ACTs on mortality or changes in disease severity using the bronchiectasis severity index or FACED. There are also no studies providing a health economics estimation for ACTs in bronchiectasis.

Question 4: Recommendations for research

- Investigate the effectiveness of ACTs using large-scale and prospective randomised controlled trials, particularly during acute exacerbations.

- Assess the effect of ACTs in the long-term, particularly in reducing exacerbations, hospitalisations, bronchiectasis disease severity and mortality. A follow-up of at least 6 months needs to be implemented in these studies.
- Assess the cost-effectiveness of ACTs based on direct and indirect costs, such as savings on medications and hospitalisation compared to therapist time and equipment expenses.
- Consider including patient adherence and disease-specific health-related quality of life (HRQoL) questionnaires as a primary or secondary outcome in all clinical trials.
- Include alternative assessment tools and outcomes for the ACTs studies, such as impulse oscillometry for pulmonary function, lung clearance index for ventilation impairment, magnetic resonance or high-resolution computed tomography imaging and airway inflammatory markers or changes in airway microbiota.
- Identify the optimal frequency of ACTs and factors that enhance accessibility to physiotherapy, such as home techniques and telehealth.

Question 5a - What are the experiences and perceived impact of ACTs on adults with bronchiectasis?

Identifying patients´ beliefs on the use of ACTs is essential for effective implementation in the long term, a necessary step to improve clinical outcomes in bronchiectasis. To support patient-reported strategies for optimising treatment implementation, we analysed crossover studies and parallel or crossover RCTs, which explored patients´ perspective of ACTs and how this treatment impacts on patients' daily life.

Evidence overview

A total of 22 studies met the inclusion criteria (supplementary material 1, figure S6); nine studies were included for examining participant experience and impact on symptoms [78, 81, 88, 90, 91, 93, 105-107], 17 studies examined preference for techniques or adherence [75, 77, 81, 82, 85, 86, 88, 90, 97, 99, 100, 102, 104, 105, 107-109] and one study explored participant satisfaction with ACTs [110]. Two studies were conducted in people experiencing an acute exacerbation [77, 78], while the remaining studies were in clinically stable individuals [81, 82, 85, 86, 88, 90, 93, 97, 99, 100, 102, 104, 105, 107] or the clinical state was unspecified [106, 108-110]. The instruments used to evaluate patient satisfaction and perceived experience were an adapted questionnaire that was validated in cystic fibrosis [110], visual analogue scales [91, 93, 107], Likert scales [78, 81, 85, 90, 106], tools developed by the authors [78, 81, 85, 90, 106], or the instrument was unspecified [88]. Adherence rates were measured by diary card recording [75, 104], while assessment of patients' preference was heterogeneous and ranged from Likert scales and standard questionnaires [77, 81, 85, 86, 99, 100, 102, 108], visual analogue scales [97, 107], asking the subject to indicate the preferred ACT [88, 90], or were not reported [105, 109].

There are mixed reports related to patient satisfaction, preference, experience related to symptoms and perceived impact of ACTs (table 3). Three studies focused on patient satisfaction after a single ACT session or following an unclear duration. A cross-sectional study [110] evaluated patient satisfaction for a mix of ACTs that did not require equipment (manual-assisted or self-administered) and O-PEP. Efficacy, convenience, comfort, satisfaction, and cost-effectiveness were rated highly for all techniques. It was proposed that conventional chest physiotherapy (GAD, manual vibrations or percussions) may be easy to learn, cost-effective and convenient for home use, but ACBT and O-PEP were highly rated due to the patient's active participation, independence, convenience, and/or device portability.

Ten studies [75, 85, 86, 90, 97, 99, 102, 104, 105, 109] compared O-PEP (Acapella or Flutter) to a mix of ACTs that did not require equipment (ACBT with or without GAD and manual vibration or percussions, autogenic drainage and ELTGOL) or a control condition in individuals in a stable clinical state. A short-term study showed that most participants preferred autogenic drainage (49%) followed by ELTGOL (35%) [99]. In contrast, Semwal et al [97] identified a lower preference for autogenic drainage over O-PEP (Acapella), which may be linked to the complexity of autogenic drainage. Eaton et al. [90] found that ACBT-GAD was considered more valuable at clearing sputum compared to ACBT, but was less preferable compared to O-PEP (Flutter). This finding was also demonstrated in three other studies, with their treatment ranging from single sessions to four weeks of ACBT-GAD or O-PEP (Acapella, Flutter or Bottle PEP), with a greater preference for O-PEP [86, 102, 109]. In contrast, a recent study found O-PEP (Bottle PEP) more useful for clearing secretions compared to ACBT (seated position) or no therapy, but still more tiring and with similar levels of discomfort to ACBT [85]. A different study [105] reported no difference in time consumption, tediousness, or need for additional training between O-PEP (Bottle PEP) and ACBT.

Two studies recruited people experiencing an acute exacerbation of bronchiectasis [77,78]. GAD with breathing control, O-PEP (Flutter) with breathing control, and breathing control only were all perceived to be similar in ease of application. GAD and O-PEP were reported as equally effective and superior to breathing control for clearing secretions [78]. Patients in the same clinical state demonstrated a greater preference for O-PEP (Acapella) when it was newly introduced, versus their usual ACT, with a proportion of patients still using the O-PEP device daily at one month follow-up [77].

Seven studies [81, 82, 88, 91, 93, 100, 106] compared a combination of techniques that were administered simultaneously (GAD, manual vibrations, or percussions and/or ACBT) or equipment techniques (O-PEP, HFCWO, IPV). A preference for the RC-Cornet over Acapella, based on usefulness for clearing secretions, convenience, comfort, and performance [82] and Flutter over the Lung Flute based on usefulness for clearing secretions, convenience, comfort, and performance, [100] was demonstrated in single studies.. The Acapella was perceived to be more helpful in clearing secretions and a preferred technique compared to inspiratory muscle training [81], but ACBT-GAD was patient-reported as more effective compared to inspiratory muscle training, despite an equal patient preference for both techniques [88]. Moreover, both intrapulmonary percussive ventilation (IPV) and combination of GAD, FET, or manual percussion and vibrations achieved patient-reported improvements in subjective perception of sputum expectoration [93]. Post-treatment discomfort was lower with IPV, which may be related to frequent position changes incorporated into GAD. Following a year of HFCWO use, there were improvements in subjective ratings of respiratory health and ability to clear secretions, compared to not using this treatment [106]. In the only comparison between techniques not requiring any equipment, Syed et al. [91] found greater comfort with ACBT with GAD compared to GAD with deep breathing and manual vibrations and percussions, which may influence compliance for the treatment.

Table 4. Patient satisfaction, preference, and perceptions of airway clearance techniques.

Study authors	Study design	Patient No.	Daily sputum quantity	ACTs applied	Prescription of therapy per technique	Tools applied to evaluate patient satisfaction, preference, and perceptions	Key findings
Thompson et al. [102] 2002, UK	RCX	17	NR	ACBT-FET O-PEP (Flutter) + FET [Both groups could use GAD if necessary]	25-30 mins, twice daily, 4 weeks	Investigator-derived questionnaire for patient preference	65% preferred O-PEP (Flutter), 18% preferred ACBT-GAD, 18% had no preference.
Tsang et al. [78] 2003, Hong Kong	RCT	15	NR	GAD + BC O-PEP (Flutter) + BC BC	15 mins, three times daily (one supervised) from day 2 to discharge	Likert scale (4-point scale) for ease of application of technique and effectiveness	No difference in ease of application between techniques. O-PEP (Flutter) perceived to be more effective than BC on each treatment day, but there was no difference between GAD and O-PEP (Flutter) on any treatment day.
Patterson et al. [88] 2004, UK	RCX	20	½ egg cup/day	ACBT-GAD with vibrations IMT (80% of MIP)	Maximum of 30 mins, single session	Patient preference for each method and perceived effectiveness	20% of patients rated IMT more effective, 55% rated ACBT-GAD with vibrations more effective and 25% rated similar efficacy for both. 50% preferred IMT for home use and 50% preferred ACBT-GAD with vibrations.
Patterson et al. [86] 2005, UK	RCX	20	½ egg cup/day	ACBT-GAD (2 positions) with manual percussion/vibrations O-PEP (Acapella)	Maximum of 30 mins (15 min in each position), once daily,	Patient preference for each technique recorded using a standardised questionnaire	While a greater proportion of patients preferred Acapella (70%), this was not significant (mean difference 0.4, 95% CI -0.04 to 0.71).

					single session per technique		
Eaton et al. [90] 2007, New Zealand	RCX	37	NR	ACBT (seated position) ACBT-GAD O-PEP (Flutter)	Maximum 30 mins, once daily, single session per technique	At final visit (conclusion of intervention), patients recorded their preferred clearance technique.	ACBT-GAD was perceived as more useful in clearing secretions than ACBT (mean difference 1.0 (SD 1.9). ACBT-GAD associated with more discomfort (0.7 (1.4)) than ACBT, more time consuming than ACBT (1.3 (1.4)) or O-PEP (Flutter) (1.1 (1.8)) and harder to perform compared to O-PEP (Flutter). The O-PEP (Flutter) interfered less with daily life compared to ACBT-GAD (1 (1.6)). All techniques were well accepted and tolerated. 44% preferred O-PEP (Flutter), 33% preferred ACBT-GAD, 22% preferred ACBT in seated position.
Patterson et al. [77] 2007, UK	RCT	20	NR	O-PEP (Acapella) + GAD (2 positions) Usual ACT (ACBT, autogenic drainage, PEP, Flutter or no ACT)	Maximum of 30 mins, once or twice daily for 10-14 days	Short questionnaire administered to those in the Acapella Group determining preference of Acapella compared to their previous technique	35% preferred O-PEP (Acapella) to their usual ACT, 10% preferred their usual ACT, 5% reported no preference.
Syed et al. [91] 2009, India	RCX	35	NR	GAD + manual percussions/vibrations ACBT	Single occasion, every 3 hours while awake for 30 mins	Visual analogue scales used to quantify the degree of comfort during each therapy session (anchor of uncomfortable and	Greater comfort for ACBT.

						comfortable on a 10-cm line)	
Naraparaju et al. [81] 2010, India	RCX	30	>30 mL/day	O-PEP (Acapella) IMT (80% of MIP)	Single occasion	Patient preference was recorded on an investigator-derived scale	O-PEP (Acapella) was more useful than IMT in clearing secretions (mean (SD) 1.17 (0.89) vs 0.67 (1.03), p=0.03), but there was no difference in convenience, comfort, and overall performance between techniques. Preference for clearing secretions was greater for O-PEP (Acapella).
Morgan et al. [109] 2011, Australia	RCX	12	NR	GAD O-PEP (Flutter)	Twice daily, 4 weeks	NR	Reported patient preference was greater for O-PEP (Flutter).
Paneroni et al. [93] 2011, Italy	RCX	22	>20 mL/day	IPV GAD + manual percussions/vibrations with FET	30 mins, single session	Patient subjective discomfort and sensation of phlegm encumbrance and dyspnoea measured with visual analogue scales (anchors of 0 to 100%)	Improvement in sensation of sputum encumbrance was similar between ACTs (p=0.48). Less discomfort with IPV compared to GAD (p=0.03).
Shabari et al. [82] 2011, India	RCX	40	>30 mL/day	O-PEP (RC-Cornet) O-PEP (Acapella)	15-20 mins, single session	Patient preference scale (5-point scale) for usefulness in clearing secretions,	RC-Cornet was preferred over Acapella on usefulness for clearing secretions, convenience, comfort and overall performance (p<0.05).

						convenience, comfort and overall performance	
Vishteh et al. [105] 2011, Iran	CSS	29	NR	ACBT O-PEP (RC-Cornet)	Maximum of 30 mins, single session	Seven questions for patient satisfaction	No difference in understanding the method, degree of time consumption, tediousness, need for additional training and overall satisfaction ($p>0.05$). Patients believed they can do physiotherapy with O-PEP (RC-Cornet) at home over ACBT and preferred this technique (25 *vs.* 15, $p=0.02$).
Semwal et al. [97] 2015, India	RCX	30	NR	Autogenic drainage O-PEP (Acapella)	20-30 mins, single session	Visual analogue scale for patient preference	Higher preference for O-PEP (Acapella) versus autogenic drainage (mean VAS was 6.87 *vs*. 5.77)
Herrero-Cortina et al. [99] 2016, Spain	RCX	31	≥15 mL/day	Autogenic drainage (self-administered) ELTGOL (both lateral positions and respiratory physiotherapist assisted) O-PEP (TPEP, 1 cmH_2O pressure)	40 mins, daily for 3 non-consecutive days over 7 days	Likert questionnaire (self-administered) to indicate preference for technique at the end of each treatment arm.	48.4% preferred autogenic drainage, 35.4% ELTGOL. Preference was attributed to increased sputum expectoration, independence, and personal satisfaction with autogenic drainage.

Kamimura et al. [107] 2017, Japan	RCX	1	Expectoration of sputum >5 times/day	O-PEP (Acapella) Tracheal vibration (at 80Hz)	10 mins, twice daily, 4 weeks	Patient rating of device efficacy on a scale of 0-100, with preference for Acapella or Tracheal vibration device using the visual analogue scale at opposite ends	Preference for tracheal vibration.
Silva et al. [100] 2017, Australia	RCX	40	25 mL/day	O-PEP (Lung Flute) O-PEP (Flutter)	Maximum of 30 mins, single session	Patient asked to state their preferred technique at final review	63% preferred Flutter, 10% preferred Lung Flute, 28% did not have a preference.
Nayak et al.[110] 2018, India	CSS	140	NR	GAD + manual percussions/vibrations, ACBT, FET, O-PEP (Flutter, Acapella, Quake, RC-Cornet)	NR	Questionnaire consisting of 21 questions including technique efficacy, convenience, comfort, satisfaction and cost-effectiveness	GAD + percussion + vibrations: efficacy 97%, convenience 95.7%, comfort 100%, satisfaction 95.7%, cost-effectiveness 93.7%. ACBT: efficacy 100%, convenience 100%, comfort 100%, satisfaction 100%, cost-effectiveness 100%. FET: efficacy 100%, convenience 100%, comfort 100%, satisfaction 100%, cost-effectiveness 95.8%. O-PEP: efficacy 100%, convenience 100%, comfort 100%, satisfaction 95.7%, cost-effectiveness 100%.
Muñoz et al. [75] 2018, Spain	RCT	44	≥ 10 mL/day	ELTGOL (affected lung in inferolateral position) + chest and abdominal	15 min if one lung was affected or 30 min if both lungs	Adherence measured at each visit with a physiotherapist by diary card (good adherence =	Adherence of 80% or more was recorded for all participants in the ELTGOL group and 75% of the repetitive upper limb stretches.

				compressions during expiration Repetitive upper limb stretches (biceps, triceps, deltoids, pectoralis major, latissimus dorsi)	were affected, twice daily, 12 months	80% or more sessions were performed)	
Nicolini et al. [108] 2019, Italy	RCT	60	NR	HFCWO (SmartVest, 13-15 Hz with pressure 2-5cmH_20) HFCWO (RespIn 11, focused pulse)	NR	Likert scale (5-point) to evaluate patient preference	Higher score for patient preference with RespIn 11.
Santos et al. [85] 2020, Australia	RCX	35	Reported daily sputum	ACBT O-PEP (Bottle PEP) No therapy	30 mins per technique, single session	Likert scales measuring patient perceptions of usefulness, ease of intervention in clearing secretions, ease of performing interventions, discomfort when performing interventions, if interventions were tiring, ease of understanding instructions and if	ACBT was more useful in clearing secretions than O-PEP (Bottle PEP) (mean difference -0.6, 95% CI -0.9 to -0.2). Both techniques were more useful, with greater ease of clearing secretions compared to control. Bottle PEP was easier to perform as an intervention compared to control (mean difference -0.3, 95% CI -0.6 to -0.0). Both Bottle PEP and ACBT were more tiring compared to control, with Bottle PEP being more tiring than ACBT (mean difference 0.4, 95% CI 0.2-0.7). The instructions for all techniques were easy to understand, with similar levels of discomfort for all techniques.

						perceived worthwhile to perform recorded 60 mins post intervention period. Likert scale for which technique they preferred	47% preferred Bottle PEP therapy, 35% preferred ACBT, 18% reported no preference.
Barto et al. [106] 2020, USA	CSS	2596	NR	HFCWO (inCourage system, RespTech)	NR	Likert scale (5-point) for ratings of overall respiratory health and ability to clear secretions at baseline, 1, 3, 6, 12 months and at 6-month intervals thereafter	The proportion of patients who answered positively to the question "how would you rate your overall respiratory health" increased from 13.6% to 60.5% after 1 year ($p<0.001$). The proportion of patients who answered positively to the question "how would you rate your ability to clear your lungs?" increased from 13.9% to 76.6% after 1 year ($p<0.001$). Most improvement occurred within the first month and was sustained for 1 year.
Livnat et al. [104] 2021	RCT	55	NR	O-PEP (Aerobika) Autogenic drainage	15-20 mins or until no further sputum was produced, daily, 4 weeks	Patient-reported adherence to therapy recorded daily by participants and reported weekly by telephone calls	Adherence to O-PEP was 88%, adherence to autogenic drainage was 87%.

ACBT, active cycle of breathing techniques; ACT, airway clearance technique; CI, confidence intervals; CSS, cross-sectional study; BC, breathing control; ELTGOL, slow expiration with the glottis opened in the lateral posture; FET, forced expiration techniques; GAD, gravity-assisted drainage; HFCWO, high-frequency chest wall oscillation; Hz, hertz; IMT, inspiratory muscle training; mins, minutes; MIP, maximal inspiratory pressure; mL, millilitres; No, number; NR, not reported; O-PEP, oscillatory positive expiratory pressure; RCT, randomised controlled trial; RCX, randomised cross-over trial; > , greater than; ≥ , greater than or equal to.

Question 5b - What are the perceived barriers to and enablers of ACTs in adults with bronchiectasis?

A better understanding of the main factors influencing the routine use of ACTs from the perspectives of both people with bronchiectasis and healthcare professionals is crucial for designing strategies to overcome disease-specific problems and limitations arising from comorbidities and to enhance airway clearance self-management. It is also necessary for treatment adherence and the provision of patient-centred care. Therefore, a search strategy was conducted to identify studies exploring barriers and enablers of ACTs in adults with bronchiectasis.

Evidence overview

Five studies addressed barriers and/or enablers together with adherence to ACT in a mix of study designs, including cohort [111, 112] and qualitative studies [113-115] (supplementary material 1, figure S6). In all studies, participants were in a clinically stable state. A study for predictors of adherence measured the compliance to ACTs over a 12-month period [112]. A total of 41% of patients self-reported adherence to ACT. Those who were adherent to ACTs had a better Physical Function domain score on Quality of Life - Bronchiectasis (QOL-B) compared to those who were non-adherent (mean (SD), 42 (28) *vs*. 29 (26), respectively) [112]. Higher adherence to ACT was associated with lower Treatment Burden domain score on QoL-B (regression coefficient (95% CI) -15.46 (-26.54 to -4.37)) and lower Respiratory Symptoms domain score on QoL-B (regression coefficient (95% CI) -10.77 (-21.45 to -0.09)) [112]. This cohort who reported using ACBT (53%) or O-PEP (Acapella) (61%) also completed a modified “Beliefs about Medicine” questionnaire specific to ACTs. In determining independent predictors of adherence, those adherent to ACT (41%) were older (odds ratio (95% CI) 2.94 (2.74-3.18)), based on a 10-year

increase in age, and believed their ACT was necessary (odds ratio (95% CI) 1.3 (1.1-1.53)). Those with fewer concerns about treatment were also more likely to be adherent to ACTs [111].

Three qualitative studies with patients and clinicians, including respiratory physicians, respiratory physiotherapists and nurses described barriers and enablers to ACTs [113-115]. From the patient perspective, identified barriers were late referral to the multidisciplinary team, lack of engagement with a healthcare professional [114], lack of perceived health benefit, motivation and time commitment [113]. Enablers were working with a multidisciplinary team, which incorporates chronic disease management and support, recognition of the patient role in management and their substantial burden of disease, and a personalised approach to therapy [113, 114]. From the clinicians' perspective, barriers to management were availability of resources for ACTs, time and space restrictions, and funding. Enablers were working with the multidisciplinary team and using a chronic disease approach, as well as patient engagement [115].

Question 5: Statements

- Patient experience was generally well rated for ACTs. Preference was mainly based on the independence of technique, patient satisfaction with symptom relief, and perceived efficacy or difficulty.
- Patient adherence to ACTs could be related to older age, good physical function, milder respiratory symptoms, less treatment burden and belief in treatment necessity.
- Optimal engagement of patient and healthcare professionals, adequate motivation, time and resources were some of the barriers and enablers of ACTs.

Question 5: Recommendations for research

- Further investigate the barriers and enablers of ACTs from the patient and healthcare professionals' perspectives, and the factors that influence patient preference and adherence to treatment, in qualitative studies. Within this topic, examine the patient perspectives upon changing techniques, through mixed methods study designs.
- Investigate the barriers and enablers of using ACTs in varying geographical locations and the underlying training and clinical experience of therapists that may be challenges or facilitators to ACT therapy.
- Use standardised patient-reported outcome measures (PROMs) and patient-experience outcomes measures (PREMs), including patient perceptions and preferences. To allow standardisation and comparison among studies, there are available disease-specific PROMs but, there is a need to develop and validate PREMs in bronchiectasis.
- Conduct pragmatic trials, which consider the patient preference, experience, and satisfaction to ACT prescription in their design. For instance, trials investigating the effectiveness of two or more interventions, could use stratified randomisation based on patient preferences; thus providing a more accurate reflection of real-life.
- To facilitate clinical implementation and patient-adherence, standardised tools that assess patient-related factors such as discomfort, fatigue, ease of performing ACTs, perceived impact of treatment effect, and preference, should be considered in ACTs trials. Future studies need to embed patient, stakeholders, and public's perspectives in their design and delivery, through the patient and public involvement or study co-production.

Question 6 – In adults with bronchiectasis, how should studies for ACTs be conducted to reduce the risk of bias, facilitate comparison of findings, as well as conducting future meta-analyses?

The methodological quality of studies impacts directly on the evidence that underpin clinical practice. Hence, identifying the most frequently used outcome measures, including those previously suggested as core outcomes [116], and reducing the biases in the randomised trials for ACTs in bronchiectasis can lead to improvements in future studies and therefore clinical practice. To address this question, randomised trials for ACTs in bronchiectasis were analysed for risk of bias; this included all studies on Question 4. To additionally capture recently conducted work, studies that met the same criteria but were presented as conference abstracts were also included.

Evidence overview

Thirty-four randomised trials (30 full papers and 4 abstracts) were included (supplementary material 1, figure S7). The majority were cross-over studies (n=21), conducted at a single-centre (n=30) in European countries (n=13). A total of 915 patients with bronchiectasis were included. Twenty-eight studies reported gender, with females (n=445; 59%) being more represented than males (n=306; 41%). The mean age range was 39-75 years, while lung function (FEV_1) ranged from 29 to 96% predicted. Most studies included patients in a clinically stable condition (n=30), who had a productive cough or self-reported sputum expectoration; when reported, daily sputum volume ranged from 1.2 to 132 mL.

Sample size estimation was reported in 16 (53%) of the full-text studies, range was 8 and 68 participants, with only 3 full-text studies including possible dropout rates (range 20-25%) in their sample size calculation. Primary endpoints were clearly reported in 20 (59%) studies, sputum quantity being the most frequent outcome measure used (wet sputum weight, n=8 (24%); dry sputum weight, n=2 (6%); wet sputum volume, n=7 (21%)). Sputum was collected during the ACTs intervention in seven studies (21%) and post-intervention in ten studies (30%). Lung function, sputum quantity, HRQoL, symptoms (particularly breathlessness), and patients´ feedback were other common outcomes (supplementary material 1, table S6).

The risk of bias of the included studies is presented in figure 2. Only one study had low risk of bias (74) and when considered across studies, none of the risk assessment domains were free of bias (supplementary material 1, table S7). The remaining 33 trials did not consistently report sufficient information to adequately assess risk of bias. For the domains of the Cochrane Risk of Bias Tool that could be assessed as high or low risk of bias (i.e., not unclear), there were six assessment domain scores that had a high risk of bias and 78 that had a low risk of bias.

On the risk of bias, allocation concealment, blinding and selective reporting, were frequently classified as unclear (figure 2). Most studies failed to provide sufficient information about the method used to conceal the allocation sequence (selection bias) and most trials did not blind participants nor personnel (performance bias), although we need to acknowledge that the Cochrane tool was designed for placebo-controlled drug studies. Most studies combined objective and subjective (e.g., self-reported) outcome measures, which is a strong point. Nevertheless, data collection procedures for the subjective outcomes were often unclear. Selective reporting was classified as unclear risk of bias in most studies, due to insufficient information. Eight trials were included on a clinical trial registry and were classified as low risk,

since their results reported all primary outcomes and most secondary outcomes [75, 76, 94, 96, 99, 103, 104, 117].

(Please, insert figure 2 around here)

Question 6: Statements

- The risk of bias amongst the studies that assess ACTs is heterogeneous, but generally unclear.
- For most studies, reporting was unclear for allocation concealment or there was selective reporting.
- Blinding of the ACTs was also limited for patients and personnel, although this is often challenging due to the nature of the intervention.
- Futures studies should be adequately powered, based on sample size estimation of one or two primary outcome measures, which have well explored psychometrics properties. Blinding of outcome assessment and statistical analysis of the ACTs should be implemented to help minimise bias. Study reporting should be clear and following the CONSORT reporting guidelines.

Question 6: Recommendations for research

- Ensure that study reporting is clear and facilitates risk of bias assessment, by following the CONSORT reporting guidelines. To reduce the risk of reporting bias, we recommend registering the studies in clinical trial registries or publishing their protocol in clinical journals, according to SPIRIT reporting guidelines.

- To minimise bias and maximize the validity of the results, trials should blind as many individuals as possible. Blinding of outcome assessment and statistical analysis of the ACTs is usually feasible and needs to be implemented. Where possible, studies should use blinding of the investigators who direct or supervise the treatment and/or the patients who perform ACTs. To achieve this last point, sham interventions, placebo-controlled designs for treatment-naive patients, or cluster trials that include settings where ACTs are not part of standard care can be implemented.
- Studies should be adequately powered, based on sample size estimation of one or two primary outcome measures. Recruitment from multiple centres that can follow standardised procedures may be an optimal strategy.
- Future trials that use a core set of outcome measures, with well-explored psychometric properties according to COSMIN, could simplify future meta-analysis and support stronger conclusions. Current suggestions for core outcomes in bronchiectasis [116] together with exploration of core outcomes which are specific to physiotherapy [118] should be considered in future trials.

Discussion

This task force statement panel included international experts, incorporating a wide geographical representation, and two patient representatives with bronchiectasis. Our patient representatives were invited to participate through the European Lung Foundation and were purposefully selected for their different behaviour regarding ACTs treatment, i.e., one who is adherent to ACTs and the other who is not; thus, the statement had input from different perspectives. All statement questions were formulated with the aim to be clinically relevant,

important, and include the patient's perspective. Additionally, the statement results were based on systematic work.

Bronchiectasis is characterised by a dehydrated mucus layer, in part due to an abnormal increase in mucin secretion, which may play an important role in the disease progression [9]. The impaired mucociliary clearance in this population has prompted the use of ACTs to enhance mucus clearance rate and reduce sputum-related symptoms. Clinical recommendations in adults with bronchiectasis consider ACTs an important strategy to disease self-management, although our understanding of their exact mechanisms of action is based on studies that are not specific to bronchiectasis.

Based on the physiology, effective ACTs are those that break the mucous layer by generating adequate mechanical stress in the airway [23] and those that move the mucus layer towards the proximal airways by enhancing peak expiratory flow [20, 21]. The ACTs that were explored in bronchiectasis by clinical trials appear to achieve these physiological principles (suplemmentary material, table S4), and they were effective in the short term, in improving sputum expectoration, respiratory symptoms and HRQoL in patients with stable disease. Although the hydration or generation of an osmotic shock in the airways (as another mechanism of action for enhancing clearance) was outside of this task force, we need to consider the potential complementary role of the hydration, humidification and mucoactive drugs in the efficacy of the ACTs [119, 120].

The ACTs that have been used in studies investigating efficacy in bronchiectasis varied. Most studies investigating the efficacy of ACTs were focused on O-PEP (table 3). It is unclear if this is

due to heterogeneity of airway clearance clinical management across the world or reflects research availability. Findings suggest that ACBT and O-PEP devices are the most used ACTs in clinical practice. However, data come mainly from Australia, New Zealand, the United Kingdom, and the United States; thus, may not reflect the clinical practice in other countries.

A 12-month long study for ACTs in bronchiectasis showed that performing ELTGOL twice daily can reduce the risk of exacerbations, improve HRQoL and reduce the impact of cough. In the short-term, most ACTs in bronchiectasis enhance sputum removal, although no ACT has been shown to be more effective than another one. Therefore, respiratory physiotherapists need to be aware of available ACTs and offer to individual patients the opportunity to try more than one techniques, considering their advantages and limitations (table 2). The choice of the most appropriate ACTs will be based on the patient's own experience and preference, including ease of performance, perceived efficacy in relieving symptoms, and time consumption. When more robust evidence becomes available from pragmatic trials, clinical guidelines can guide the best approach to select the most appropriate ACTs for individuals with bronchiectasis.

Most studies examining the efficacy of ACTs had an unclear risk of bias in most categories and particularly in the performance, detection and reporting bias. In studies examining ACTs, blinding participants and healthcare professionals in charge of the interventions may be challenging to establish and maintain over time. Different methods of blinding, such as use of sham interventions, blinding the assessors (masking) or recruiting previously treatment-naive patients could improve the quality of the evidence base.

EMBARC [18] and US registries [121] have previously identified important research priorities in bronchiectasis. Further studies of treatment efficacy, in both a stable state and during an acute exacerbation, and with larger sample sizes that include patients from different countries or regions should be conducted. Following other interventions in bronchiectasis, these studies should incorporate long term follow up, i.e., not less than three months for PROMs and not less than six months for exacerbations, hospitalisations or cost-effectiveness. Although sputum quantity is the most frequent outcome measure selected as primary outcome in ACTs trials in bronchiectasis, its measurement properties are ambiguous [122]; thus, its interpretation is still unclear [123]. Future trials should incorporate more robust measures, such as exacerbation frequency, hospital admission and patient-reported outcomes, particularly validated disease-specific questionnaires that have a clear interpretation [124, 125]. Currently, disease-specific questionnaires are the QoL-B with 37 items and 8 domain scores[126], the Bronchiectasis Health Questionnaire (BHQ) with 10 items and a total score [127] and the Bronchiectasis Impact Measure (BIM) assessing 8 domains with one item each[128]. A consensus on the essential outcomes in future trials, and a better definition, common terminology, and consistent reporting in ACTs, will facilitate the comparison between study findings. Importantly, the use of standardised assessments for patient preference and adherence, and patient and stakeholders' input into study design will ensure a pragmatic approach.

Self-management and adherence are the cornerstone for the long-term management of any chronic disease, so it is crucial to identify the enablers and barriers to using ACTs. When teaching ACTs, empowering the patient through clinical education on the benefits and limitations of the treatments, offering advice to reduce treatment burden, scheduling regular reviews and setting reminders could improve engagement and treatment adherence. This strategy also optimises the therapeutic relationship between the health care professionals and patients [114, 115].

This ERS statement was focused on techniques that were specifically developed to enhance mucus clearance, and based on our working definition for ACTs, techniques such as NIV or exercise were excluded. NIV is commonly evaluated in combination with other ACTs (e.g., FET, ACBT) in end-stage, severe disease or during exacerbations [129, 130]; it has been shown to reduce breathlessness and respiratory rate, prevent airway dynamic collapse and maintain oxygenation[129, 130]. Exercise and its role in enhancing mucus clearance in bronchiectasis remains complex, since it usually does not exclude practicing ACTs. On the contrary, ACTs are often part of pulmonary rehabilitation, practically or as part of the education [131, 132]. Therefore, our ability to assess the role of exercise as an ACT is currently limited. Future work with a wider definition for ACTs and good control of potential confounders should investigate the role of NIV and exercise in airway clearance for bronchiectasis. Moreover, the role of other potential devices for ACTs in bronchiectasis, such as Simeox, free aspire advanced, mechanical insufflation-exsufflation and intermittent positive pressure breathing should be also evaluated in future studies.

Conclusion

The current evidence supports that ACTs is an effective treatment and has a crucial part in the usual care of adults with bronchiectasis. Accessibility to ACTs should be facilitated and ideally delivered by a specialist respiratory physiotherapist. However, there is limited evidence establishing the physiological effect of these techniques and current clinical practice based on geographical regions, remains largely unclear. The use of data from large patient registries could help to better understand the ACTs practice globally. Randomised clinical trials indicate that ACTs increase the expectorated sputum, improve disease symptoms and HRQoL and reduce the risk of exacerbations, although they often have an unclear risk of bias or a poor description of their techniques. There is a great need for studies to investigate the role of ACTs during acute

exacerbations of bronchiectasis and in the long-term. Additionally, researchers can consider different settings, new modes of application, and novel outcomes for future ACTs studies. Importantly, to achieve optimal care, study designs need to incorporate patient-centred outcomes and patient voice.

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132. Chalmers JD, Crichton ML, Brady G, Finch S, Lonergan M, Fardon TC. Pulmonary rehabilitation after exacerbation of bronchiectasis: a pilot randomized controlled trial. *BMC Pulm Med 2019 May 6;19(85):Epub* 2019.

Figure legends

Figure 1. Clinical use of airway clearance techniques (ACTs). The graph presents the ACTs that were reported as the most routinely used.

The terminology of the graphs follows the terminology of the original studies, i.e., PEP *vs.* PEP-mask and Flutter *vs.* O-PEP. Gravity-assisted drainage was presented as postural drainage in the original studies. The study by Santos et al, [70] was not included in the graphs as it reported on the frequency of a specific type of ACTs, positive expiratory pressure devices. Results of this study, presented as percentage of physiotherapists, were: PEP-mask 2%, PEP-mouthpiece: 32%, PEP-bottle 72%, Flutter 36% and Acapella 46%. Percentages do not add up to 100% due to allowing the physiotherapists to choose all ACTs that apply. ACT, airway clearance technique; ELTGOL, slow expiration with glottis opened in lateral posture; PEP, positive expiratory pressure; O-PEP, oscillatory positive expiratory pressure.

Figure 2. Risk of bias graph, based on reviewer's judgements for each risk of bias item and presented as percentages across all included studies (n=34).

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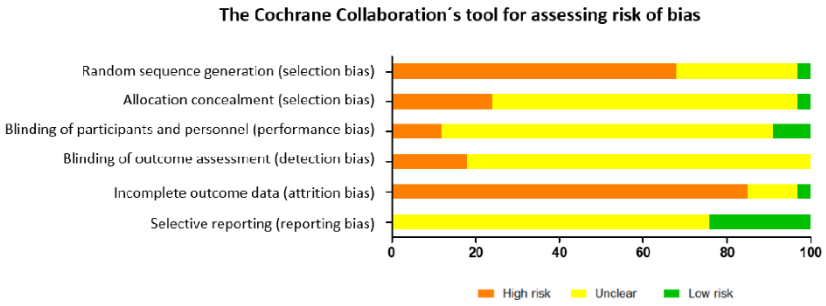


Figure 2. Risk of bias graph, based on reviewer's judgements for each risk of bias item and presented as percentages across all included studies (n=34).

Supplementary material - 1

Title: European Respiratory Society statement on airway clearance techniques in adults with bronchiectasis.

Authors: Beatriz Herrero-Cortina, Annemarie L Lee, Ana Oliveira, Brenda O´Neill, Cristina Jácome, Simone Dal Corso, William Poncin, Gerard Muñoz, Deniz Inal-Ince, Victoria Alcaraz-Serrano, Gregory Reychler, Angela Bellofiore, Annette Posthumus (patient representative), Patient representative, Thomy Tonia, James D Chalmers, Arietta Spinou.

Table S1. Professional background and working groups of the European Respiratory Society (ERS) Task Force panel.

Members	Speciality	Country	Working group
Beatriz Herrero-Cortina	Respiratory Physiotherapist, Co-chair	Spain	Questions 1 and 2
Annemarie Lee	Respiratory Physiotherapist	Australia	Questions 5 and 6
Ana Oliveira	Respiratory Physiotherapist	Portugal	Questions 3 and 4
Brenda O´Neill	Respiratory Physiotherapist	UK	Questions 1 and 2
Cristina Jàcome	Respiratory Physiotherapist	Portugal	Questions 5 and 6
Simone Dal Corso	Respiratory Physiotherapist	Brazil	Questions 5 and 6
William Poncin	Respiratory Physiotherapist	Belgium	Questions 1 and 2
Gerard Muñoz	Respiratory Physiotherapist	Spain	Questions 3 and 4
Deniz Inal-Ince	Respiratory Physiotherapist	Turkey	Questions 5 and 6
Victoria Alcaraz-Serrano	Respiratory Physiotherapist	Spain	Questions 1 and 2
Gregory Reychler	Respiratory Physiotherapist	Belgium	Questions 3 and 4
Angela Bellofiore	Respiratory Physiotherapist	Italy	Questions 1 and 2
Annette Posthumus	European Lung Foundation representative	Netherlands	Questions 1 and 2
Patient Representative	European Lung Foundation representative	Israel	Questions 5 and 6
James Chalmers	Respiratory Physician	UK	Questions 3 and 4
Arietta Spinou	Respiratory Physiotherapist, Co-chair	UK	Questions 3 and 4

UK, United Kingdom.

Selection criteria for the studies

Types of studies

For a representative overview of the use of airway clearance techniques (ACTs) in bronchiectasis, a wide variety of studies were considered in our general search: clinical trials (randomised controlled trials, randomised crossover trials; quasi-experimental trials); observational studies (cross-sectional, case-control and cohort studies) and qualitative studies. However, only randomised controlled trials and randomised crossover trials were included to explore the Question 4 (clinical effectiveness) and Question 5 (risk of bias and facilitate comparison between findings). Secondary studies i.e., narrative and systematic reviews, were only included in Question 1 and Question 2. This was due to the topic addressed (physiological /pathophysiological rationale), which is commonly updated using reviews and the difficulty in finding relevant original articles (failed sensitive analysis) despite re-designing the search strategy twice. More detailed information on the specific criteria used for selecting studies for each Question is available in supplementary material 2.

Participants

Our generic selection criteria were adults (≥18 years) with a diagnosis of bronchiectasis using high-resolution computed tomography and clinical symptoms without any restriction based on disease severity, daily sputum expectoration and/or clinical status (e.g., stable or exacerbation). Overlap syndromes (e.g., bronchiectasis with chronic obstructive pulmonary disease, COPD, or bronchiectasis with asthma) were included, but people with cystic fibrosis were excluded. Data from studies recruiting with different respiratory diseases (e.g., bronchiectasis and COPD) were only included if it was possible to separately extract data from people with bronchiectasis.

Specifically for the physiological/pathophysiological Questions 1 and 2, the selection criteria were extended to in vitro and animal model studies, due to the limited information on this topic in bronchiectasis. The panel also agreed to extend the population to muco-obstructive respiratory diseases (e.g., cystic fibrosis, COPD, etc.) and to healthy people for Questions 1 and 2. Additional information in methodology is available in supplementary material 2.

Intervention

Airway clearance techniques were defined as all manual or instrumental techniques and devices that were developed with the main purpose to enhance mucus clearance and manage sputum. We considered single and combined interventions, irrespective of the treatment duration (short and long-term) and based on HERMES (harmonised education in respiratory medicine for European specialists) physiotherapy curriculum [1].

As the panel agreed to focus only on the interventions specifically developed primarily to increase sputum clearance and improve the management of sputum-related symptoms; therefore, techniques with a different primary objective, such as exercise, respiratory muscle training, education of ACTs in a rehabilitation programme and non-invasive ventilation were excluded from this statement. The current evidence on exercise as a potential therapy option to enhance airway clearance is mostly based on pulmonary rehabilitation trials, where ACTs are considered an active component of the programme or an educational approach [2, 3]. Therefore, the ability to identify the effect of the ACTs undertaken by participants in addition to the exercise training (combination of aerobic and resistance training) is not currently possible. Furthermore, the measurements used in these trials do not specifically focus on sputum-related outcomes[2-4] and it is hard to comment on its use as an ACT. Moreover, ACTs may be part of the usual care of patients with bronchiectasis participating in pulmonary rehabilitation/exercise trials (similar to patients with cystic fibrosis). In these studies, since

it is unusual to consider the use of ACTs as an exclusion criterion for the trial, there is a great risk of confounding and bias.

On the other hand, most of the evidence of the role of NIV as an ACT comes from patients with cystic fibrosis, especially, in end-stage severe disease or during exacerbations. The use of NIV helps to reduce patient fatigue and respiratory rate, avoid airway dynamic collapse, and maintain oxygenation during airway clearance sessions. In fact, it is common to evaluate the effect of NIV in combination with other ACTs (e.g., forced expiratory technique, active cycle of breathing technique)[5, 6]. Therefore, the panel agreed that NIV is used as support for the ACTs and is considered more often an adjuvant to ACTs rather than an ACT in itself. Thus, the definition of ACTs we agreed on in our methods resulted in excluding NIV from our work. Finally, other airway clearance methods such as humidification, muco-active agents, other drugs and invasive methods were also outside the scope of this task force.

Search methods

The databases Medline (Ovid), EMBASE, Scopus, AMED, CINAHL, Cochrane CENTRAL and PEDro were used to identify studies. Only articles in English were selected from their inception in these databases. For Question 2, articles in other languages (e.g., French, Spanish, Portuguese, Italian) were allowed to ensure the collection of information on ACTs not developed in Anglo-Saxon countries. These studies were analysed by members of the panel who are native speakers of that language. First literature searches were conducted in November 2020 and an update search was conducted at the end of November 2021. Panel agreed to use the reference lists of all full text articles included in Question 4 for identification of potential reports for Questions 1 and 2 after search strategies failed to find relevant original articles (failed the sensitivity analysis).

Additional information about methodology applied

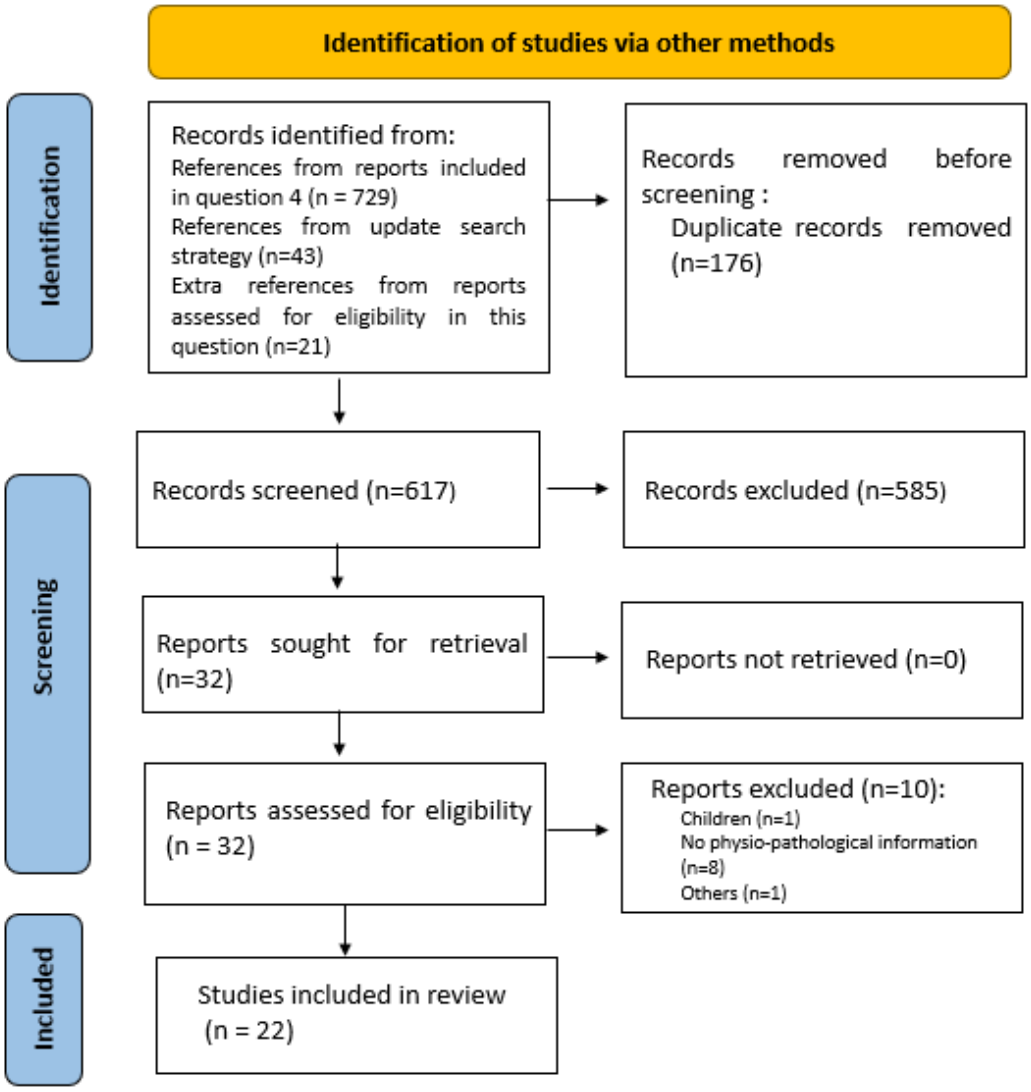


Figure S1. Literature search flow diagram for Question 1 - *What is the physiological rationale for the use for ACTs in adults with bronchiectasis?*

Table S2. Summary of the main features of studies included for Question 1 - *What is the physiological rationale for the use for ACTs in adults with bronchiectasis?*

First author, year, country	Publication type	Study design	Human / animal / in vitro / others	Population / origin of samples	Topic	Relevant findings related to this question
Mead et al.[7] 1970, USA	Secondary	Narrative review	Mathematical models	N/A	Airway physiology (interdependence / collateral ventilation)	The main function of the mechanical interdependence seems to be to promote a homogeneous air opening. The interdependence of air-space distension influences the size of air spaces, the static and dynamic stability of air spaces, the dryness of air spaces, the forces distending airways and blood vessels within lungs, and the distribution of pulmonary oedema.
Kim et al.[8] 1986, USA	Primary	Experimental	In vitro	Sputum samples with similar rheological properties than healthy and people with respiratory diseases	Airway clearance	Mucus transport by two-phase gas-liquid flow mechanism depends on the airway surface liquid layer thickness and rheological properties of fluid.
Kim et al.[9] 1987, USA	Primary	Experimental	In vitro	Sputum samples with similar rheological properties than healthy and people with respiratory diseases	Airway clearance	Effective mucus clearance can be achieved by two-phase gas-liquid flow mechanism in patients with excessive bronchial secretions with biased tidal breathing favouring the expiratory flow and that the clearance can be further promoted by changing rheological properties of mucus.
Crawford et al.[10] 1989, Australia	Primary	RXT	Human	Healthy people	Airway physiology (ventilation distribution)	The main factor of ventilation distribution below closing capacity is the inhomogeneous closure of airways subtending regions in the lung periphery that are close together.
Girod et al.[11] 1992, France	Secondary	Narrative review	In vitro	Chronic bronchitis Cystic fibrosis	Biophysical properties of mucus/sputum	Airway mucus needs appropriate rheological (viscoelasticity and spinnability) and physical surface (adhesiveness, wettability) properties

						for the protection, hydration and lubrication of the underlying airway epithelium.
Randell et al.[12] 2006, USA	Secondary	Narrative review	In vitro / human	Cystic fibrosis, CODP	Airway clearance	Summary of the structure and function of airway clearance system, its regulation and how genetic or acquired disease impacts on its functionality.
Button et al.[13] 2008, USA	Primary	CSS	In vitro / human	Bronchiectasis, Cystic fibrosis, Chronic bronchitis	Airway clearance	Airway mechanical stress stimulates mucus clearance via increases in rates of ATP release into the luminal compartment, resulting in increases in ASL hydration.
Rubin et al.[14] 2010, USA	Secondary	Narrative review	Human	Cystic fibrosis, Chronic bronchitis	Cough clearance / biophysical properties of mucus	The greatest determinant of cough transportability is not viscoelasticity but tenacity, which is the product of adhesivity and cohesivity. Treatments for ineffective cough should consider the interaction between biophysical properties and cough mechanism.
Rubin et al.[15] 2010, USA	Secondary	Narrative review	In vitro / human	Bronchiectasis, Cystic fibrosis, Chronic bronchitis PCD	Airway clearance	Summary of the composition and structure of mucus and phlegm, the mucin secretion and how is the function of the mucus clearance system. Therapies to improve mucus clearance were also described.
Tambascio et al.[16] 2013, Brazil	Primary	CSS	In vitro / human	Bronchiectasis	Biophysical properties of mucus / sputum	Respiratory secretions in individuals with bronchiectasis have poor transport properties, which manifest as reduced mucociliary transport, reduced mucus transport by cough, and higher contact angle. These features were more accentuated in the purulent samples.
Button et al.[17] 2013, USA	Secondary	Narrative review	In vitro / human	Cystic fibrosis	Airway clearance / Action mechanism of ACTs	The application of mechanical stress on airway epithelia promotes changes in ion transport and increases ASL hydration. ACTs used in CF are described based on their mechanism of action.
Rubin et al.[18] 2014, USA	Secondary	Narrative review	Human	Bronchiectasis, Cystic fibrosis, Chronic bronchitis Lung cancer, Allergy Asthma, Fucosidosis, Plastic bronchitis	Biophysical properties of mucus / sputum	Mucus production and biophysical properties of sputum change with the progression of the airway diseases. Thus, sputum samples may be a good biomarker to identify the severity of airway diseases.

Anderson et al.[19] 2015, USA	Primary	CSS	In vitro / human	Chronic bronchitis	Airway clearance	Alterations in the outcomes related to mucus concentration (e.g., extracellular nucleotide / nucleoside-dependent, airway hydration and mucin secretion rates) may slow mucociliary clearance and contribute to disease pathogenesis and loss of lung function in chronic bronchitis.
Sibila et al.[20] 2015, UK	Primary	CSS	Human	Bronchiectasis	Airway infection	Airway mucin (MUC2) levels were higher in bronchiectasis patients colonised with PPM compared with those without airway colonisation, especially in patients with P. aeruginosa. These findings suggest that airway-secreted mucins levels may play a role in the pathogenesis of airway infection in bronchiectasis
Button et al.[21] 2016, USA	Secondary	Narrative review	In vitro / human	Chronic bronchitis Cystic fibrosis	Airway clearance	In health, the osmotic modulus/ pressure of the PCL exceeds that of the mucus layer, resulting in efficient, low-friction movement of mucus. In disease, through multiple mechanisms, the osmotic pressure of the mucus begins to exceed basal PCL values, resulting in compression of the cilia and slowing of mucus transport. Mucus hyperconcentration (mucin overproduction and/or abnormal regulation of ion/water transport), may be a simple method to diagnose chronic bronchitis, monitor its progression, and serve as a biomarker for development of new therapies.
Bennett et al.[22] 2016, USA	Secondary	Narrative review	In vitro / human	Chronic bronchitis Cystic fibrosis	Airway clearance	There is growing evidence that chronic bronchitis and cystic fibrosis may have parallels in disease pathogenesis as well, including cystic fibrosis transmembrane conductance regulator dysfunction, mucus dehydration, and defective mucociliary clearance.
Chalmers et al.[23] 2017, UK	Primary	CSS	Human	Bronchiectasis	Airway inflammation	Sputum neutrophil elastase activity is a biomarker of disease severity and future risk in adults with bronchiectasis.

Mcllwaine et al.[24] 2017, Canada	Secondary	Narrative review	Human	Chronic suppurative lung diseases (including bronchiectasis)	Airway clearance	Description on how to provide a personalised approach to selecting the most appropriate ACT for each patient. It is based on a synthesis of the physiological evidence that supports the modulation of ventilation and expiratory airflow as a means of assisting airway clearance.
Gramegna et al.[25] 2017, Italy	Secondary	Systematic review	Human	Bronchiectasis	Airway inflammation	Sputum neutrophil elastase is useful as an inflammatory marker both in stable state bronchiectasis and during exacerbations and local or systemic antibiotic treatment. Neutrophil elastase has also been associated with risk of exacerbation, time to next exacerbation and all-cause mortality.
Flume et al.[26] 2018, UK	Secondary	Narrative review	Human	Bronchiectasis	Pathophysiology	Description of the pathophysiology of bronchiectasis and an in-depth understanding of the endotypes and clinical phenotypes of this disease.
Contarini et al.[27] 2018, UK / Italy	Secondary	Narrative review	Human	PCD Bronchiectasis	Pathophysiology	Primary ciliary dyskinesia (PCD) is a genetic cause of bronchiectasis in which failure of motile cilia leads to poor mucociliary clearance. This study summarises the current literature describing why, when and how to investigate PCD in adult patients with bronchiectasis.
Ramsey et al.[28] 2020, USA	Primary	CSS	Human	Bronchiectasis	Airway clearance	Bronchiectasis sputum exhibited increased percent solids, total and individual (MUC5B and MUC5AC) mucin concentrations, osmotic pressure and elastic and viscous moduli compared with healthy sputum. Hyperconcentrated airway mucus likely contributes to disease pathophysiology in bronchiectasis.

ASL, airway surface layer; CF, cystic fibrosis; PCD, primary ciliary dyskinesia; PCL, periciliary layer; PPM, potentially pathogenic microorganisms; ACT, airway clearance techniques; CSS, cross-sectional; RXT, randomised crossover trial; NA= not applied

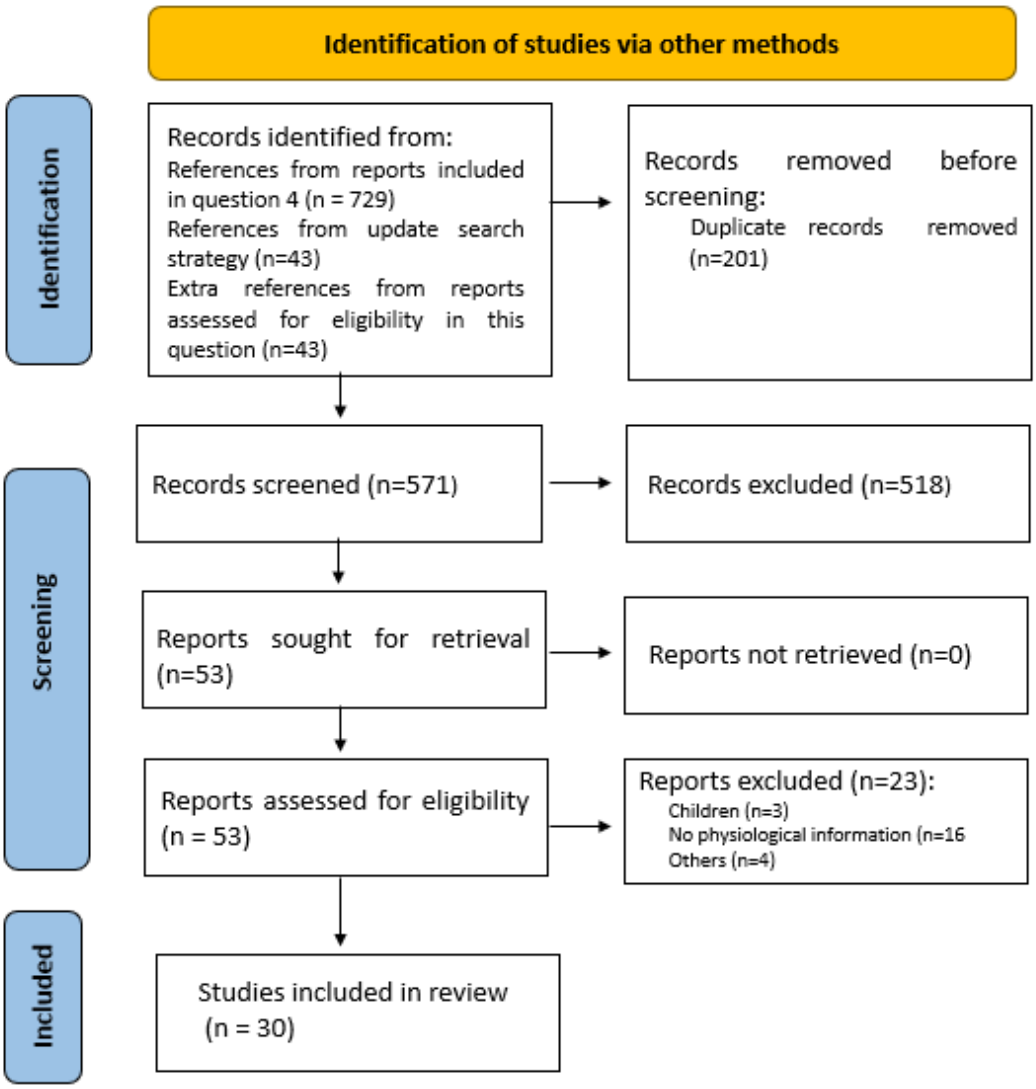


Figure S2. Literature search flow diagram for Question 2 - *What is the physiological rationale of each one of the ACTs and what are the advantages and limitations of each technique?*

Table S3. Summary of the main features of studies included for Question 2 - *What is the physiological rationale of each one of the ACTs and what are the advantages and limitations of each technique?*

First author, year, country	Publication type	Study design	Human / animal / in vitro / others	Population / Origin of samples	Topic	Relevant findings related to this question
Mead et al.[29] 1967, USA	Primary	Cross-sectional	Mathematical models	N/A	Airway physiology (equal pressure points)	Equal pressure points refer to the points where the pressure at the inner wall of the airways is equal to the pleural pressure. During forced expirations, there are points within airways that equal pleural pressure, and the pressure drop from alveoli to these points approximates the static recoil pressure of the lungs. The resistance of these segments has a frictional component which increases as lung volume decreases and an accelerative component which decreases as lung volume decreases.
Pryor et al.[30] 1979, UK	Primary	RXT	Human	Cystic fibrosis	ACTs	During a forced expiratory manoeuvre, there are forces tending to collapse or compress the airways downstream (towards the mouth) of the equal pressure point. This dynamic compression is an essential part of the mechanism of a huff or cough, which is therefore effective only at the compression points (choke points) downstream of the equal pressure point. These choke points move upstream (towards the alveoli) as the lung volume decreases. The FET + GAD cleared more sputum in less time than manual percussion applied by a physiotherapist + GAD in people with cystic fibrosis.
Kim et al.[8] 1986, USA	Primary	Experimental	In vitro	Sputum samples with similar rheologic properties than healthy and people with	Airway clearance	Mucus transport by two-phase gas-liquid flow mechanism depends on the airway surface liquid layer thickness and rheological properties of fluid.

				respiratory diseases		
Kim et al.[9] 1987, USA	Primary	Experimental	In vitro	Sputum samples with similar rheological properties than healthy and people with respiratory diseases	Airway clearance	Effective mucus clearance can be achieved by two-phase gas-liquid flow mechanism in patients with excessive bronchial secretions with flow-bias tidal breathing favouring the expiratory flow and that the clearance can be further promoted by changing rheological properties of mucus.
Postiaux et al.[31] 1990, France	Primary	RXT	Human	COPD	ACTs	It is described how to perform the ELTGOL technique and showed that ELTGOL technique enhances greater mucus clearance than control period in lateral position (especially in the dependent lung) using scintigraphy.
Lannefors et al.[32] 1992, Sweden	Primary	RXT	Human	Cystic fibrosis	ACTs	No difference in mucus clearance using scintigraphy was observed between GAD, PEP and exercise in people with cystic fibrosis. Surprisingly, GAD in the left position promoted greater mucus clearance in the dependent lung (left) than in the right lung.
App et al.[33] 1998, Canada	Primary	RXT	Human	Cystic fibrosis	ACTs	Oscillations applied using an O-PEP device (Flutter) are capable of decreasing mucus viscoelasticity in patients with cystic fibrosis.
van der Schans et al.[34] 1999, Netherlands	Secondary	Narrative review	Human	Bronchiectasis COPD Cystic fibrosis Asthma	ACTs	Description the mechanism of actions of various ACTs and outcome measures to assess the effects of ACTs combined data from different respiratory diseases.
Pryor et al.[35]1999, UK	Secondary	Narrative review	Human	Bronchiectasis Cystic fibrosis Asthma	ACTs	Description of how to perform each technique and its physiological principles.
Cecins et al.[36] 1999, Australia	Primary	RXT	Human	Bronchiectasis Cystic fibrosis PCD	ACTs	No difference was observed in sputum expectorated between ACBT in gravity-assisted drainage positions with or without a head-down tilt. However, breathlessness was higher following the technique in head-down tilt. Patients preferred the ACBT without a head-down tilt.

Wong et al.[37]2003, Singapore	Primary	Quasi-experimental	Animal model	N/A	ACTs	Manual clapping, vibration, and shaking applied by physiotherapists increase expired tidal volume but not peak expiratory flow rate in an animal model. No significant hemodynamic effects were observed during the manoeuvres. The rates achieved during vibrations and shaking are related to physiotherapists' characteristics, particularly clinical experience.
Dosman et al.[38] 2005, Canada	Secondary	Narrative review	Human	Various respiratory diseases	ACTs	Description the history, mechanism of actions and global effectiveness of HFCWO
McCarren et al.[39] 2006, Australia	Primary	RXT	Human	Healthy people	ACTs	During manual vibration the chest behaves as a highly linear system. Changes in intrapleural pressure occurring during vibration appear to be the sum of changes in pressure due to lung recoil and the compressive and oscillatory components of the technique, which suggests that all three components are required to optimise expiratory flow.
McCarren et al.[40] 2006, Australia	Primary	RXT	Human	Cystic fibrosis	ACTs	Peak expiratory flow rate of manual vibration was greater than Flutter (O-PEP), manual percussion, Acapella (O-PEP) and PEP. Vibrations generate lower oscillations of the airflow than Acapella and Flutter (both O-PEP), but similar to manual percussion.
Agostini et al.[41] 2007, UK	Secondary	Narrative review	Human	Cystic fibrosis Chronic bronchitis	ACTs	Description of the technique (based on previous report from J. Chevallier), offering explanations about how the technique works to enhance sputum clearance and evidence supporting its use
Martins et al.[42] 2012, Brazil	Primary	RXT	Human	COPD	ACTs	ELTGOL significantly increased mucus clearance in the peripheral area of the infralateral lung in patients with stable chronic bronchitis, most of whom had mild to moderate COPD.
Riffard et al.[43] 2012, France	Secondary	Narrative review	N/A	N/A	ACTs	Description of the device (IPV), its action mechanism to improve ventilation and enhance sputum clearance and how to set it according to your target treatment.

Button et al.[17] 2013, USA	Secondary	Narrative review	In vitro / human	Cystic fibrosis	Airway clearance / Action mechanism of ACTs	The application of mechanical stress on airway epithelia promotes changes in ion transport and increases ASL hydration. ACTs used in CF are described based on their mechanism of action.
Testa et al.[44] 2015, Italy	Primary	Quasi-experimental	Human	COPD	ACTs	Short-term combination of IPV and various techniques (ELTGOL, PEP mask, PEP bottle, FET and cough) improves PO_2, SpO_2 and perceived dyspnea than the other techniques in patients with COPD and productive cough.
Lanza et al.[45] 2015, Brazil	Primary	Cross-sectional	Human	Bronchiectasis	ACTs	ELTGOL mobilised more than 80% of expiratory reserve volume in subjects with moderate airway obstruction; there is no difference in ERV exhaled during the technique applied by a physiotherapist or by the subject.
Fagevik-Olsen et al.[46] 2015, Sweden	Secondary	Narrative review	Human	Bronchiectasis Cystic fibrosis COPD Asthma	ACTs	Description of the purpose, performance, clinical application, and underlying physiology of PEP when it is used to increase lung volumes, decrease hyperinflation or improve airway clearance.
Terry et al.[47] 2016, USA	Secondary	Narrative review	Human	Various respiratory diseases	Airway physiology (interdependence / collateral ventilation)	Description of the anatomical pathways of collateral ventilation, their physiology and relationship to disease states, their modulatory effects on gas exchange, treatment considerations, and their effect on diagnostic procedures.
Mcllwaine et al.[24] 2017, Canada	Secondary	Narrative review	Human	Chronic suppurative lung diseases (including bronchiectasis)	Airway clearance	Description on how to provide a personalised approach to selecting the most appropriate ACT for each patient. It is based on a synthesis of the physiological evidence that supports the modulation of ventilation and expiratory airflow as a means of assisting airway clearance.
Lee et al.[48] 2017, Australia	Secondary	Systematic Review	Human	Bronchiectasis	ACTs	Systematic review providing extensive information about physiological rationale for PEP devices, especially explained how the intervention might work
Taher et al.[49] 2018, USA	Primary	Quasi-experimental	Human	Healthy subjects COPD	Airway physiology (interdependence / collateral ventilation)	Chest wall strapping induces breathing at low lung volumes but also increases parenchymal elastic recoil. Chest wall strapping increases expiratory airflow in normal subjects as well as subjects with mild to moderate COPD.

Nicolini et al.[50] 2018, Italy	Primary	RCT	Human	COPD	ACTs	HFCWO and IPV improved daily life activities and lung function in patients with severe COPD. IPV demonstrated a significantly greater effectiveness in improving some pulmonary function tests linked to the small bronchial airways obstruction and respiratory muscle strength and scores on health status assessment scales as well as a reduction of sputum inflammatory cells compared with HFCWO.
Wong et al.[51] 2018, New Zealand	Secondary	Narrative review	Human	Bronchiectasis	ACTs	In the ELTGOL technique, the volume of the dependent lung is reduced by placing the patient in the lateral decubitus position and by limiting breathing to expiratory reserve volume. This reduces the total cross-sectional area of the peripheral airways where mucus is primarily produced. Since maximum airflow velocity is inversely proportional to airway diameter, the velocity of airflow in the peripheral airways is increased. Airway patency is maintained by increasing intraluminal pressure via slow expiration through an open glottis. Overall, this results in greater clearance of mucus from the peripheral airways.
Reychler G. et al.[52] 2018, Belgium	Secondary	Systematic Review	Human	Bronchiectasis Cystic fibrosis COPD Asthma	ACTs	The main findings showed that IPV improves gas exchange during exacerbation and could reduce the hospital length of stay for patients with COPD. In subjects with cystic fibrosis, neither lung function nor other parameters were improved. IPV is poorly studied in bronchiectasis (only one study was included).
de Souza et al.[53] 2019, Brazil	Primary	RXT	Human	Bronchiectasis	ACTs	The oscillatory PEP technique was effective for the removal of secretions and in decreasing total and peripheral respiratory system resistance, thoracic compression had comparable positive effects on the peripheral resistance
Demchuck et al.[54] 2021, USA	Primary	Quasi-experimental	In vitro	N/A	ACTs	PEP devices behaved similarly, with increased pressure with increased flow (flow resistors) or flow independence (threshold resistors). There was much greater variation in the performance

						of the O-PEP devices. A higher oscillation index indicates better mechanical performance characteristics.

RXT, randomised crossover trial; RCT, randomised controlled trial; FET, forced expiration technique; GAD, gravity-assisted drainage; PEP, positive expiratory pressure; O-PEP, oscillations positive expiratory pressure; ACTs, airway clearance techniques; HFCWO, high frequency chest wall oscillations; COPD, chronic obstructive pulmonary disease; IPV, intrapulmonary percussive ventilation; PCD, primary ciliary dyskinesia; NA= not applied

Table S4. Description and physiological rationale of each airway clearance technique (ACT).

Airway clearance techniques not requiring devices	
Forced Expiration Technique (FET)	
Description Consists of forced expirations through the mouth while maintaining an open glottis (huffs). Huffing or FET from low lung volumes moves secretions downstream (towards the mouth) from more peripheral airways. Huffing or FET from mid and high lung volumes clears secretions from the central airways	*Mechanisms of action* ▪ The underlying principle is based on the equal pressure point, i.e., the point at which pressure in the airways is equal to pressure outside the airways (pleural pressure) [29, 30]. ▪ Lung volumes are voluntarily altered, depending on the depth of inspiration and this can facilitate movement of the equal pressure point. ▪ FET displaces the position of the equal pressure point to a more distal or proximal airway position. ▪ Additionally, high expiratory flows are generated during the FET, which helps create shearing forces to move mucus through the airways [34]
Active Cycle of Breathing Techniques (ACBT)	
Description	*Mechanisms of action*

The ACBT has 3 key components: breathing control (relaxed breathing at tidal volume), thoracic expansion exercises (deep breathing above tidal volume towards full inspiration) and FET (Please see above section on FET). Thoracic expansion exercises can include a breath hold at the end of full inspiration; a sniff at the end of full inspiration can also be added to further promote increase in lung volumes. When thoracic expansion exercises are facilitated by a respiratory physiotherapist, the physiotherapist can place their hands over the patient's lower and lateral rib cage; however, the ACBT is effective with or without any assistance [30, 35].	▪ Relaxed rhythmical breathing helps control the respiratory rate and respiratory effort during breathing control. ▪ Thoracic expansion exercises generate a greater trans-airway pressure gradient than in normal breathing [29] enhancing lung volumes via interdependence and collateral ventilation and allowing a decrease in airway resistance to facilitate some air entry behind airway mucus. Collateral ventilation in the lungs is proposed to occur via the alveolar pores of Kohn, inter-bronchiolar channels of Martin and bronchoalveolar channels of Lambert [17, 47]. ▪ Same mechanisms described for FET in the above section.
Manual percussions	
Description Rhythmical external oscillations that are applied manually on the chest wall by the physiotherapist.	*Mechanisms of action* ▪ Transmitting the external oscillation to the airways, with the intention to reduce the adhesivity of the mucus layer, change mucus viscoelastic properties and detach mucus from the bronchial wall (decrease adhesivity). ▪ This effect seems to be dependent on the frequency of oscillations transmitted to the thorax and adequate frequency may be difficult to achieve [34]. Therefore, the manual application of the percussion manoeuvre by the respiratory physiotherapist does not necessarily achieve the optimal frequencies for airway clearance and could be ineffective [37]
Manual vibrations or shaking (compression and external oscillation)	
Mechanisms of action	*Mechanisms of action*

The respiratory physiotherapist / caregiver places their hands over an area of the rib cage/thoracic cavity and apply pressure to the rib cage/thorax as the patient exhales. In addition to the pressure created by the compression, oscillations may be created by the respiratory physiotherapist using their hands to create small undulating movements. [37, 39, 53].	▪ It is anticipated that the mechanical effect created by the pressure and oscillations is transmitted through the ribs into the lungs and airways to loosen and move airway mucus. ▪ There is a resultant increase in intrapulmonary pressure as well as expiratory flow rate and expired tidal volume, which contribute to loosening airway mucus [37, 39, 53]. ▪ Slow thoracic compressions may reduce peripheral respiratory system resistance [53]. ▪ Vibrations have been shown to increase peak expiratory flow rates in patients with cystic fibrosis and produce oscillations with frequencies which can enhance mucus transport [40]. ▪ Oscillations may alter sputum viscoelastic properties further helping clearance [24]. McCarren et al. [39] have shown that there is a strong linear relationship between the force applied to the chest wall by the respiratory physiotherapists' hands, the chest wall displacement, the intrapleural pressure, and the expiratory flow rate during vibrations [39]. ▪ Additionally, the impact of compression and oscillation combined together is greater than each technique alone [39].
Gravity-Assisted Drainage (GAD) technique	
Description The patient is positioned with the relevant lung segment in a semi vertical position (as able), so that the bronchopulmonary segment with excess of airway mucus is positioned higher than the central airway.	*Mechanisms of action* ▪ These positions theoretically promote flow of airway mucus from distal to proximal airways, using the effects of gravity. ▪ The angle of the drainage position, length of time spent in the position as well as the size and resistance in the airway can all impact on the effectiveness of GAD positions [36]. ▪ Gravity is believed to be the main physiological effect for enhancing mucus clearance with this technique, but interestingly greater mucus clearance rates have been observed in dependent lung areas compared to non-dependent lung areas [32, 42]. Thus, the reduction of airway cross-sectional area in dependent lung regions may play a more important role in improving mucus clearance than gravity.
Autogenic Drainage	
Description	*Mechanisms of actions*

Patients start breathing repeatedly using low lung volumes in the expiratory reserve volume, with slow and short inspirations, and with active but gentle expiratory phases ("stage 1 or loosening phase"). During this breathing pattern, patients need to keep the glottis opened and a breath-hold may be included after the inspiratory phases. The technique progresses by encouraging patients to breath progressively using high lung volumes into the inspiratory reserve volume and shorten the expiratory phase ("stage 2 and 3 or collect and move up phase) [41]	▪ During the first phase of the technique, a reduction of the cross-sectional area of the airways is attempt [41], and therefore, the lineal air velocity increases, particularly in the peripheral and medium airways, to produce an effective shearing stress on the mucus layer obstructing the bronchial lumen [51]. ▪ Patients need to keep the glottis open during expiratory phases which increases the intrapleural pressure [41]. ▪ The breath-hold included after the inspiratory phases promotes collateral ventilation and air movement behind the obstructed lung regions [24]. This physiological effect is emphasised during the second and third phases of the technique, when the patient breathes progressively using high lung volumes towards the inspiratory phase [41]. In order to avoid dynamic compression during the technique, it is recommended to modulate expiratory effort and coughing is restrained until the mucus has built up into the proximal airways, particularly in patients with reduced elastic recoil [41].
Slow expiration with glottis opened in lateral posture (ELTGOL)	
Description The patient lies in lateral decubitus position with the affected lung in the dependent position. If both lungs are affected, the patient will perform the technique in both lateral decubitus. The patient's breathing pattern during the technique involves active slow expirations from functional residual capacity to the end of the expiratory reserve volume with the glottis opened [45]. The technique may be assisted by a respiratory physiotherapist / caregiver by placing their hands on the upper rib cage and infra-umbilical region [45]	*Mechanisms of action* ▪ Mucus clearance is enhanced by increasing the airflow velocity in the medial and peripheral airways, while the airway cross-section in the dependent lung is reduced [56] [51] [31]. ▪ The patient's breathing pattern during the active slow expirations with the glottis opened [45] also facilitates a reduction of the cross-sectional ratio of the airways while maintaining the airway patency; thus, enhancing the air-gas interaction without dynamic compression [31, 51]. ▪ The volume of air exhaled seems to be similar regardless if the technique is performed independently or with assistance [45]

Airway clearance techniques requiring devices

Positive expiratory pressure (PEP) devices (*PEP mask, PiPEP, Threshold PEP, TheraPEP, Resistex, etc.)*	
Description	*Mechanisms of action*
Positive expiratory pressure (PEP) therapy involves the use of a device. During PEP therapy, the patient exhales through a mouthpiece or mask against a mild resistance (positive pressure), which is provided by a flow resistor, threshold resistor or an external flow source during expiration [54].	▪ A mild resistance (positive pressure), generally between 10 and 20 cmH_2O, is usually the target expiratory pressure to achieve with the use of these devices [48] ▪ The increase in pressure is transmitted to airways, creating back pressure which splints open the airways during exhalation, preventing premature airway closure and reducing gas trapping [46]. ▪ PEP therapy may promote collateral ventilation, and therefore hypothetically improve the delivery of air behind the mucus and facilitate airway clearance.
Oscillating positive expiratory pressure (O-PEP) devices *(Acapella, Flutter, Aerobika, VibraPEP, ShurClear, PocketPEP, RC Cornet, TurboForte, Shaker, Quake, Bottle PEP, Flute, Uniko TPEP, etc.)*	
Description	*Mechanisms of action*
Oscillating positive expiratory pressure (O-PEP) devices are used through a mouthpiece and provide short interruptions during expiration, with the aim to generate positive oscillatory airway pressure and flow waveforms [54].	▪ Although the mechanisms of action for the generation of the oscillations is different between the O-PEP devices, the generation of these oscillations or interruptions induce shear forces on the mucus layer and, mechanically reduce the viscoelasticity of airway mucus; thus, enhance mucociliary clearance and ciliary beat [33]. ▪ Same mechanisms described for PEP devices in the above section.
High-Frequency Chest Wall Oscillation (HFCWO)	
Description	*Mechanisms of action*
It is a self-administered technique delivered by a pneumatic vest or band placed around the chest. A high-output compressor or a battery generates a background pressure, which inflates the vest and	▪ External oscillation is a physical mechanism to stimulate the mucus layer hydration and reduce the interfacial tension between the mucus layer and the airway epithelium (adhesivity), change the viscoelastic properties of mucus, and increase the ciliary beating [38]

compresses the patient's chest. A superimposed frequency of air pressure then oscillates with a sinusoidal or triangular waveform [38]	Alternative methods of compression applied (e.g., chest strapping) have been shown to reduce the pulmonary compliance and increase the lung elastic recoil [49]. Both principles seem to reduce airway resistance (particularly in the smaller airways) and increase expiratory airflow, which facilitates mucus clearance proximally through the two-phase gas-liquid mechanism (airflow bias) [8, 9].
Intrapulmonary Percussive Ventilation (IPV)	
Description It is an instrumental ACT designed to provide internal thoracic percussion by intermittent high-frequency positive pressure burst of gas [44].	*Mechanisms of actions* ▪ The rapid variation and the high amplitude of the pressure peaks lead to oscillation effects on the airways [43], which enhance mucus clearance, reduce its adhesivity and cohesivity and improve the viscoelastic properties of mucus. ▪ Moreover, the asymmetric flow pattern allows the expiratory flow to be greater than the inspiratory flow, and therefore, improves mucus clearance as well [8, 9, 52] . A positive end expiratory pressure (PEEP) is an effect also described in the IPPV that allows recruitment of poorly ventilated lung zones and improves distribution of ventilation [43, 50].

Techniques were classified according to whether they require the use of a device or not. FET, forced expiratory technique; ACBT, active cycle of breathing techniques; GAD, gravity-assisted drainage; HFCWO, high-frequency chest wall oscillation; IPV, intrapulmonary percussive ventilation; PEEP, positive end expiratory pressure; O-PEP, oscillating positive expiratory pressure; ELTGOL, slow expiration with glottis opened in lateral posture; PEP, positive expiratory pressure; TPEP, temporary positive expiratory pressure. Note: This table does not include the potential contraindications of ACTs and clinicians should check those before using any ACT. Contraindications could include undrained pneumothorax, bullae, shock or severe hemodynamic instability, haemoptysis or active pulmonary haemorrhage, acute bronchospasm (relative contraindication), etc.

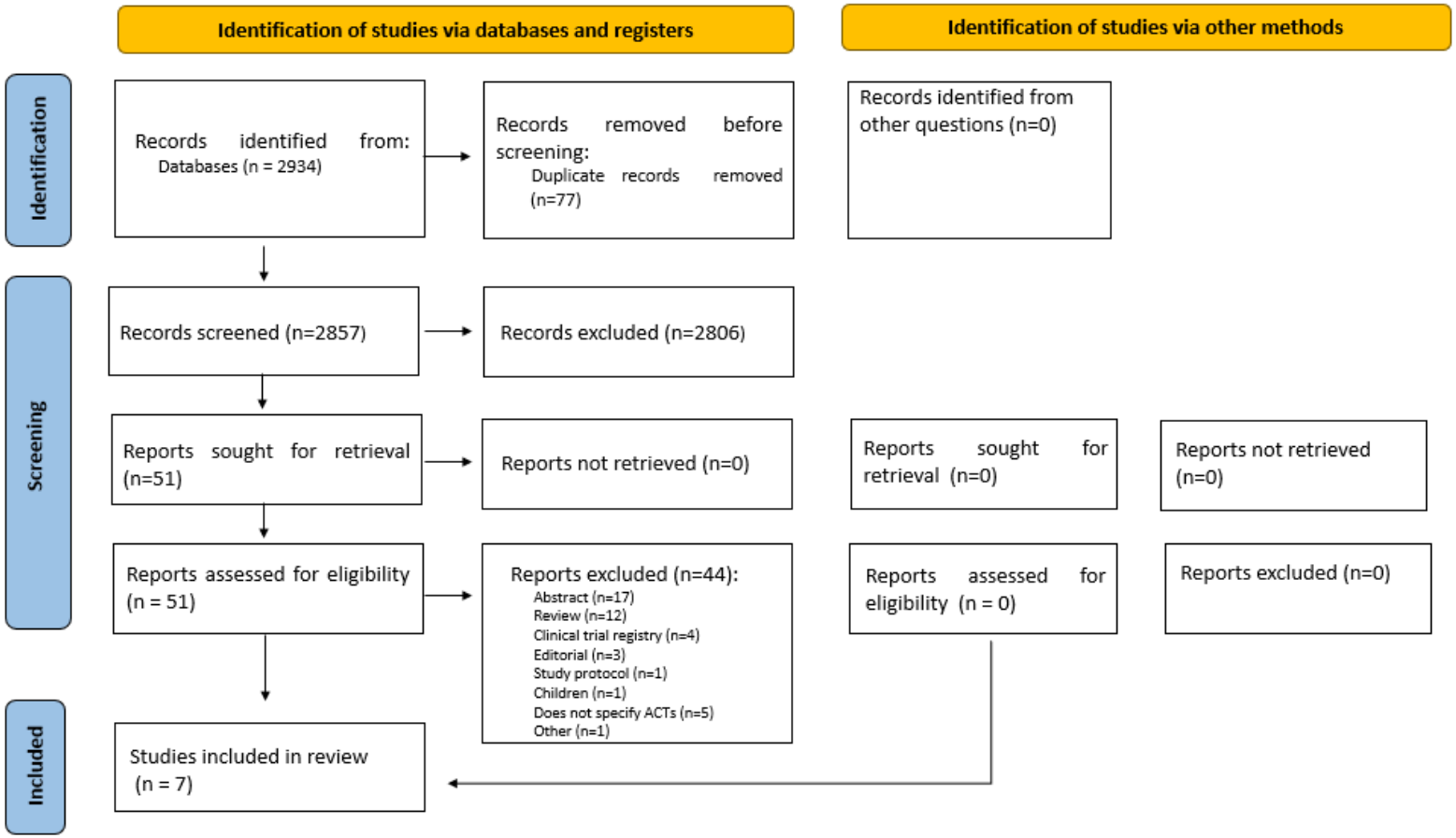


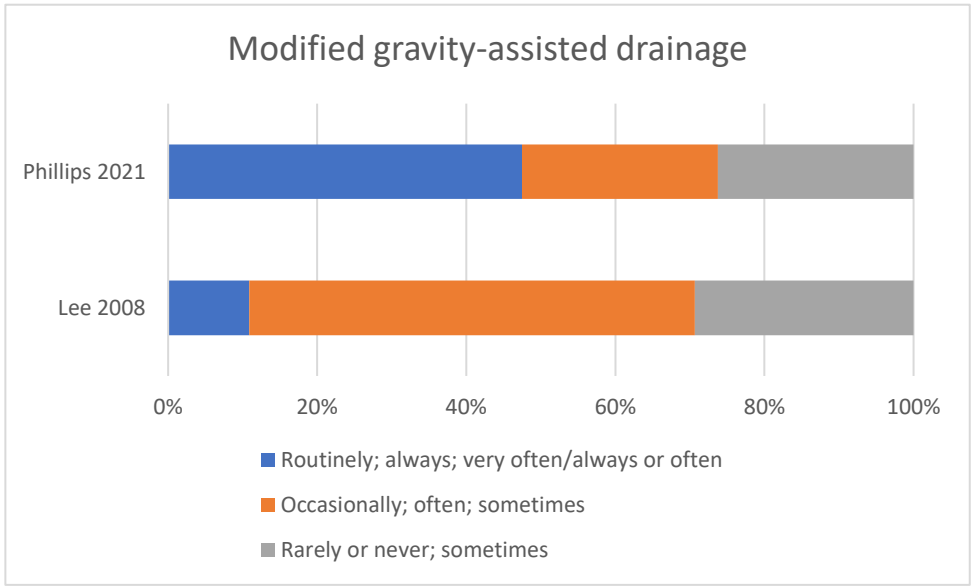
Figure S3 Literature search flow diagram for Question 3 - *Which are the ACTs that are used in the management of adults with bronchiectasis and are there any patterns according to geographical location?*

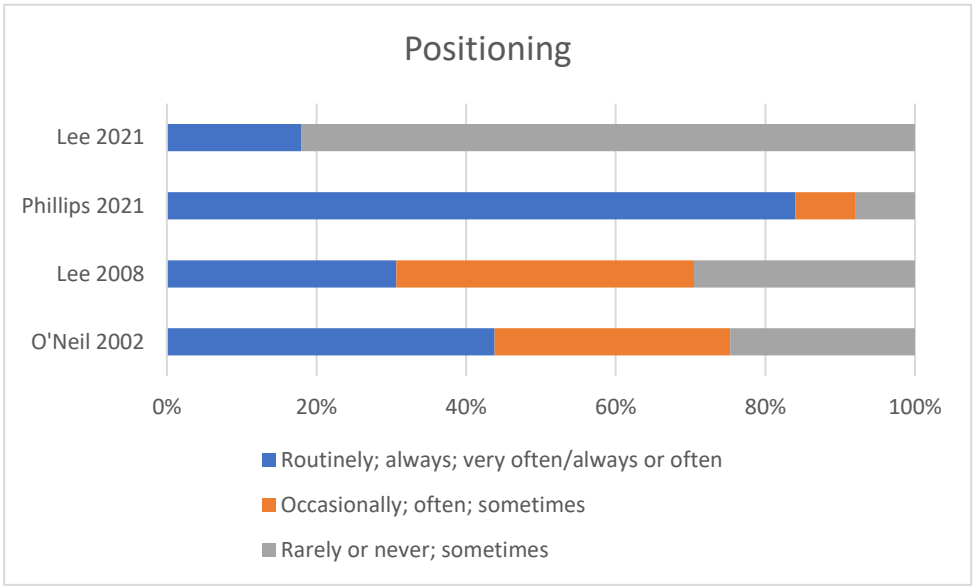
Table S5. Summary of the main features of studies included in Question 3 - *Which are the ACTs that are used in the management of adults with bronchiectasis and are there any patterns according to geographical location?*

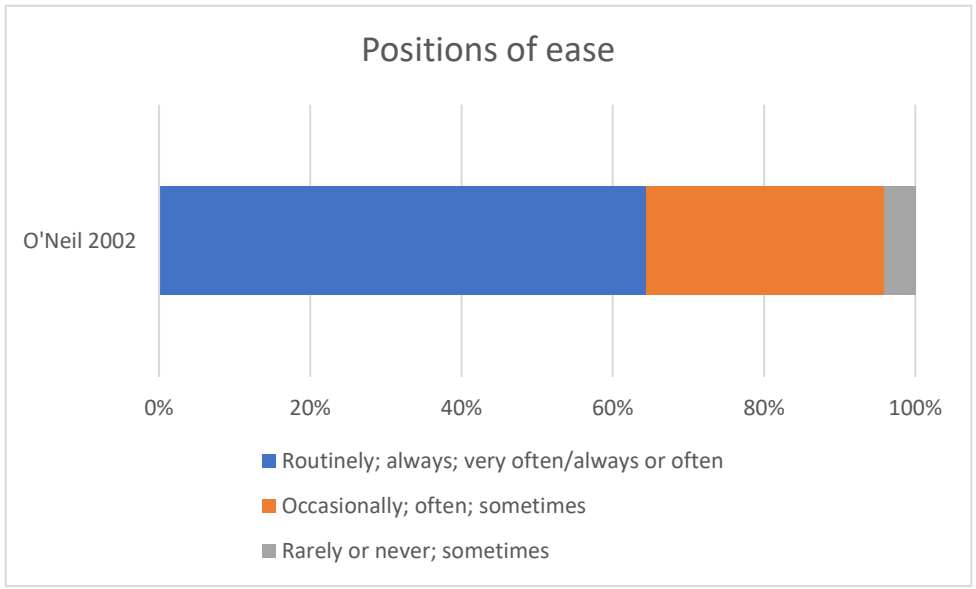
First Author, year	Country	Study start - end date	Data collection	Study design	Sites response rate	HCP response rate	Nº of participants and response rate	Years' experience	Areas of work	Location (urban *vs.* rural)	Responders	Clinical stage of disease
O'Neill et al.[55] 2002	UK	NR	Survey (NR)	Cross-sectional	82%	82%	n=82 (82%)	NR	NR	NR	Physiotherapists	NR
Lee et al.[56] 2008	Australia and New Zealand	NR	Survey (mail)	Cross-sectional	85%	85%	n=102 (85%)	10 (2-42)	Inpatients (93%) and outpatients (70%)	Public/private (6%); tertiary (65%); large major city (1%); large regional/rural (16%)	Cardiorespiratory physiotherapists	NR
Santos et al.[57] 2016	Australia	July 2012 - May 2013	Survey (mail)	Cross-sectional	88%	70%	n=169 (55%)	<1 2%; 1-5 37%; 6-10 24%; >10 28%	Surgical 54%; General medicine 49%; Intensive care/high-dependency unit 43%; Respiratory 43%; Outpatients 36%; Orthopedics 33%; Rehabilitation 20%; Gerontology 18%; Community 15%; Neurology	Tertiary/ teaching hospitals 47%; rural hospitals 33%; generalist hospitals 9%, private hospitals 6%, specialist hospitals 4%	Physiotherapists	NR

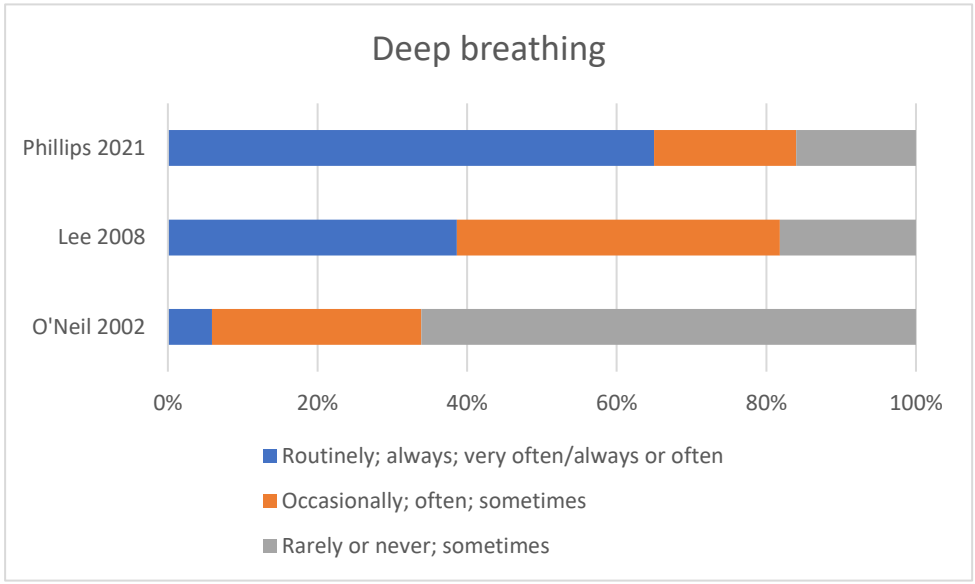
									14%; Oncology 13%; Cardiology 11%; Palliative care 11%; Pediatrics 7%; Others 4%			
Basavaraj et al.[58] 2020	USA	2008 - 2019	Registry	Retrospe ctive	NR	NR	n= 535 NR	NR	NR	NR	Patients	Stable + exacerbation
McShane et al.[59] 2020	Japan	April 2020 - NR	Survey (email)	Cross-sectional	NR	NR	n=51	NR	inpatients, outpatients and home settings	NR	Medical doctors (86.8%) Other (13.2%)	NR
Phillips et al.[60] 2021	Australia and New Zealand	August 2016 - April 2017	Survey (online)	Cross-sectional	NR	0.5%	n=130 (0.24%)	<5 28%; 6-10 17%; 11-15 16%; 16-20 13%; >21 16%	inpatients and outpatients	NR	Physiotherap ists	Exacerbation
Lee et al.[61] 2021	Australia	June 2018 - June 2019	Audit	Cross-sectional	NR	NR	n=54	NR	NR	NR	NR	NR

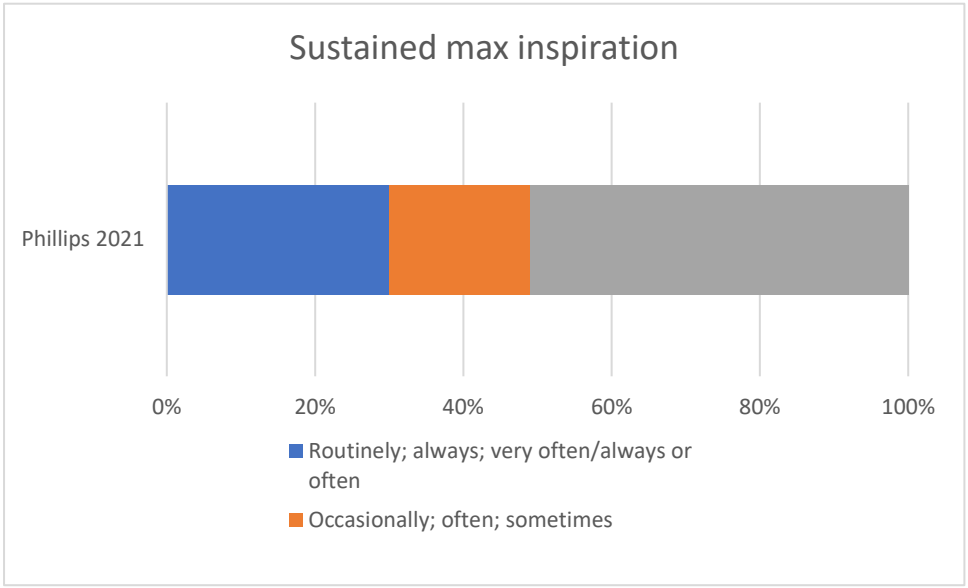
NR, not reported.

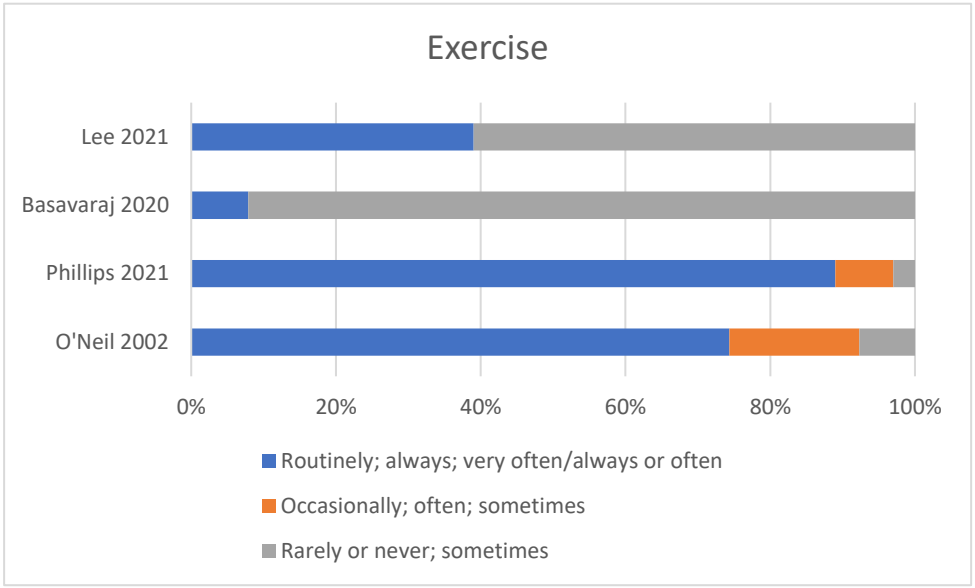

Modified gravity-assisted drainage
Phillips 2021
Lee 2008
0%
20%
40%
60%
80%
100%
Routinely; always; very often/always or often
Occasionally; often; sometimes
Rarely or never; sometimes

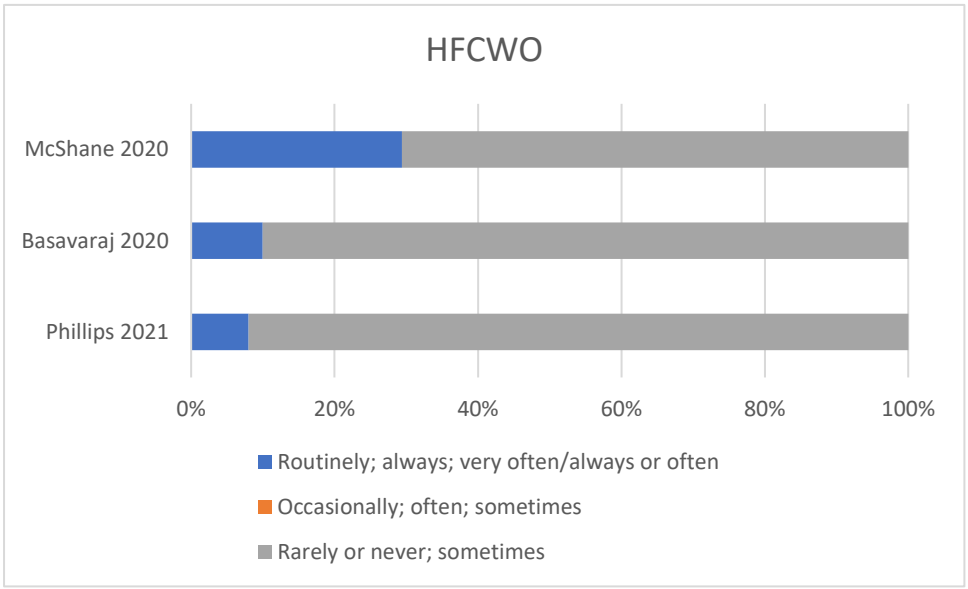

Positioning
Lee 2021
Phillips 2021
Lee 2008
O'Neil 2002
0%
20%
40%
60%
80%
100%
Routinely; always; very often/always or often
Occasionally; often; sometimes
Rarely or never; sometimes

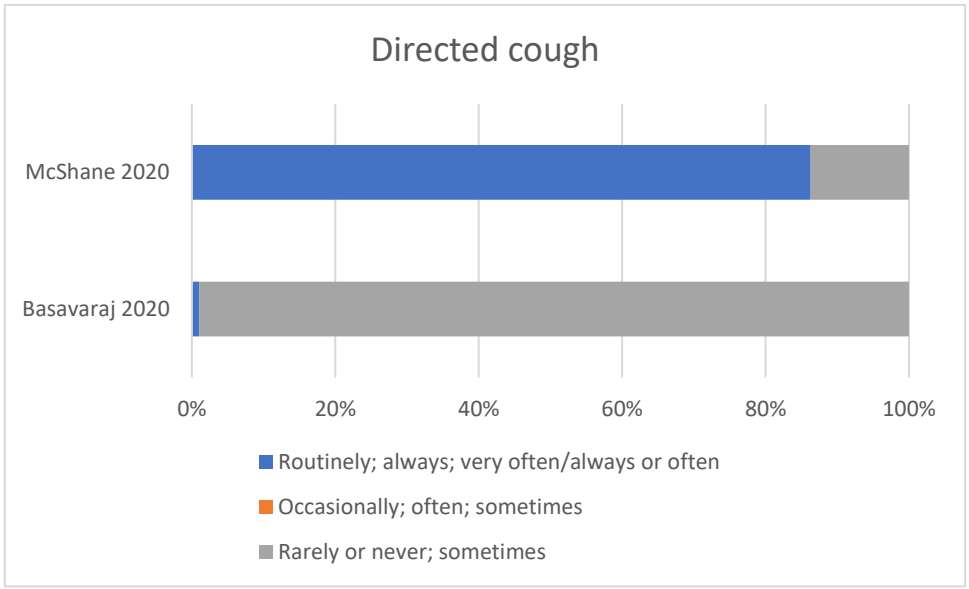

Positions of ease
O'Neil 2002
0%
20%
40%
60%
80%
100%
Routinely; always; very often/always or often
Occasionally; often; sometimes
Rarely or never; sometimes

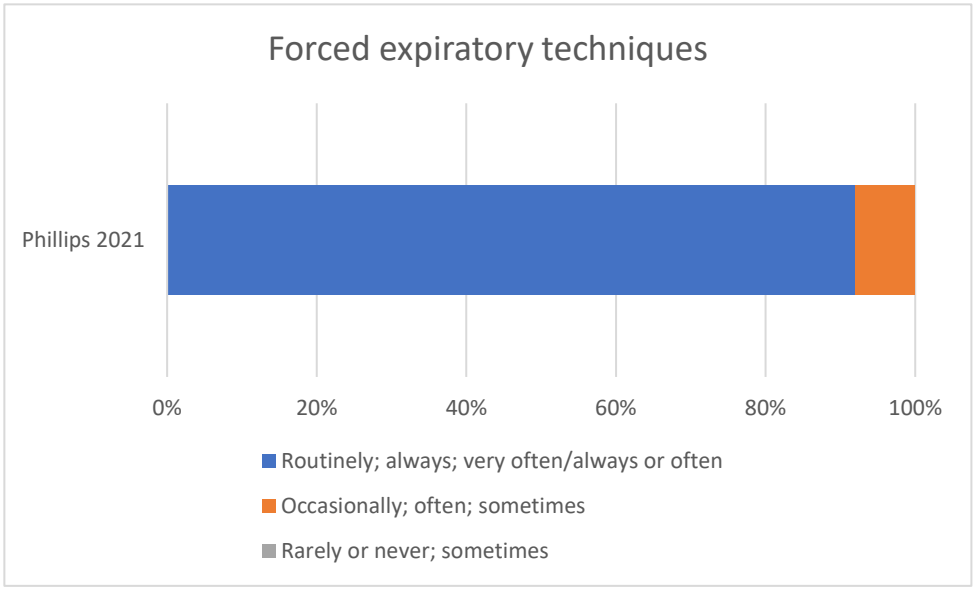

Deep breathing
Phillips 2021
Lee 2008
O'Neil 2002
0%
20%
40%
60%
80%
100%
Routinely; always; very often/always or often
Occasionally; often; sometimes
Rarely or never; sometimes

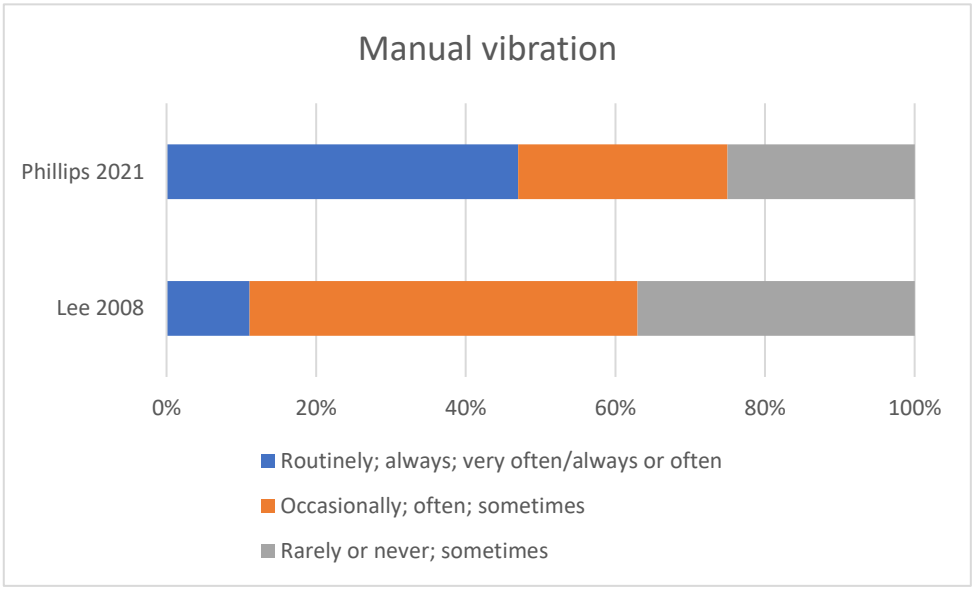

Sustained max inspiration
Phillips 2021
0%
20%
40%
60%
80%
100%
Routinely; always; very often/always or often
Occasionally; often; sometimes


Exercise
Lee 2021
Basavaraj 2020
Phillips 2021
O'Neil 2002
0%
20%
40%
60%
80%
100%
Routinely; always; very often/always or often
Occasionally; often; sometimes
Rarely or never; sometimes


HFCWO
McShane 2020
Basavaraj 2020
Phillips 2021
0%
20%
40%
60%
80%
100%
Routinely; always; very often/always or often
Occasionally; often; sometimes
Rarely or never; sometimes


Directed cough
McShane 2020
Basavaraj 2020
0%
20%
40%
60%
80%
100%
Routinely; always; very often/always or often
Occasionally; often; sometimes
Rarely or never; sometimes





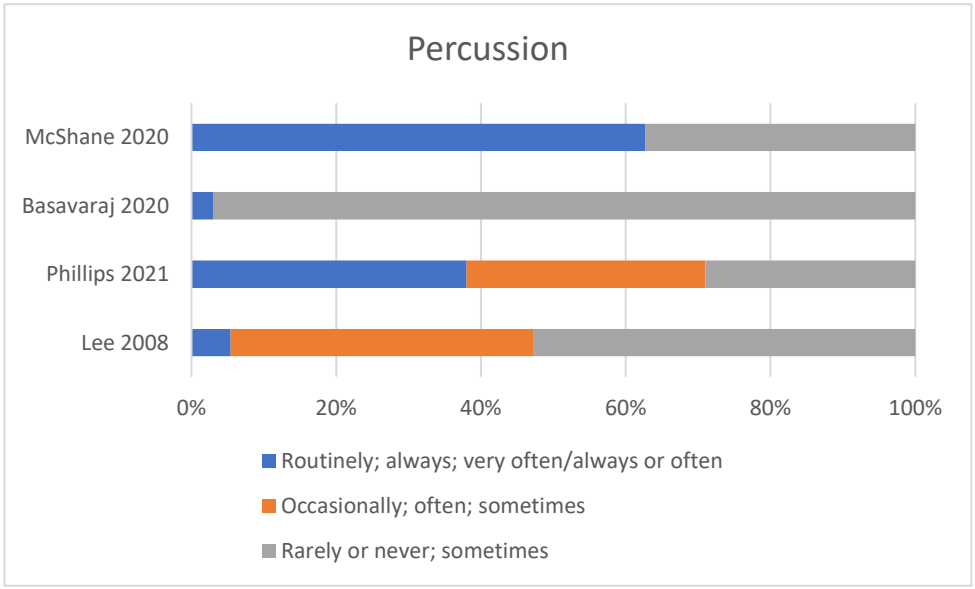


Figure S4. Question 3 - Which are the ACTs that are used in the management of adults with bronchiectasis and are there any patterns according to geographical location? Clinical use of airway clearance techniques (ACTs) which were reported as used less frequently compared to other ACTs. The terminology of the graphs follows the terminology of the original studies. Modified gravity-assisted drainage was presented as modified postural drainage in the original studies. HFCWO, high-frequency chest wall oscillation.

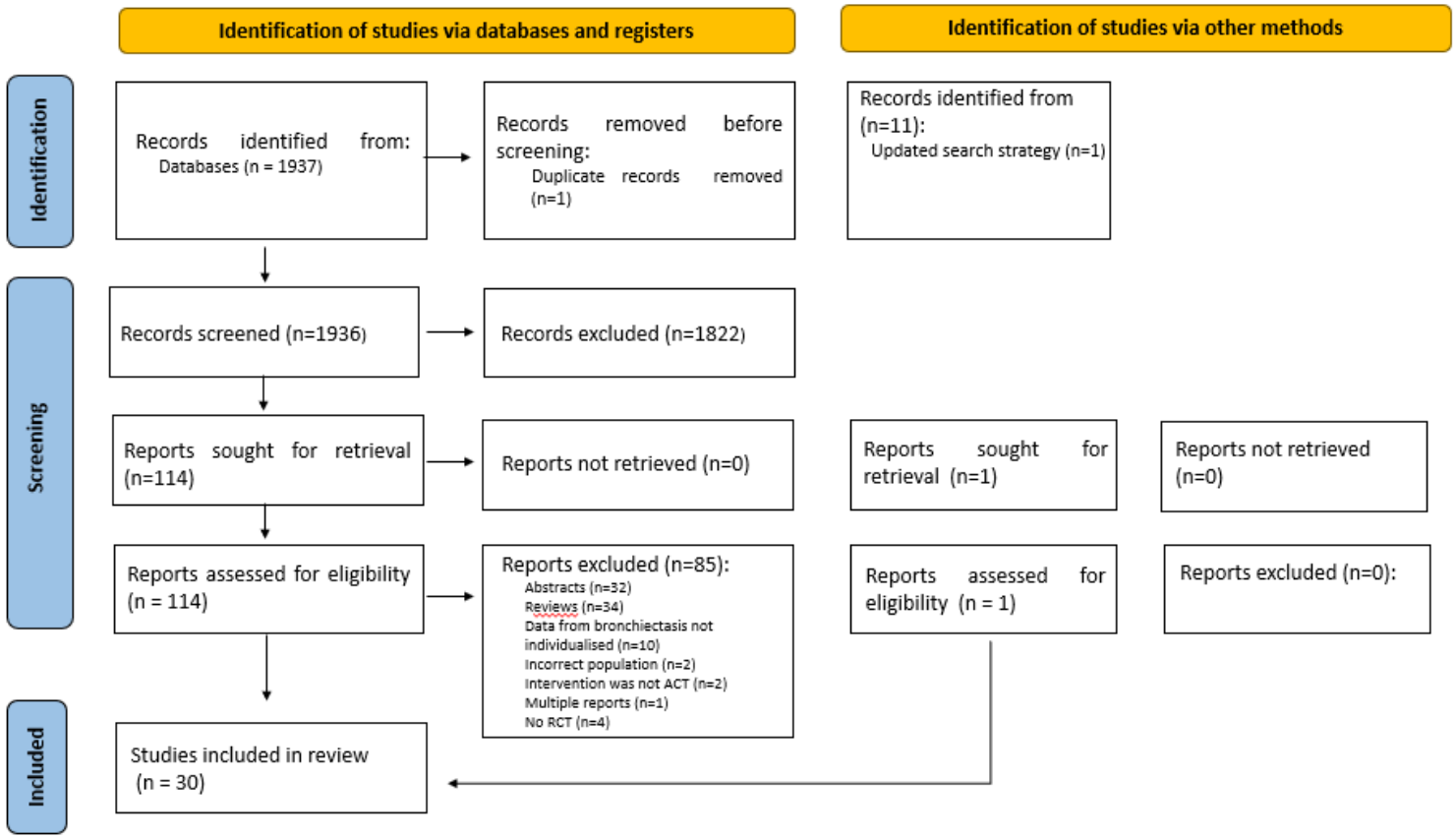


Figure S5. Literature search flow diagram for Question 4 - *What is the clinical evidence for the effectiveness of ACTs, in terms of function and disability (e.g., sputum expectoration), activity (e.g., physical activity) and participation (e.g., self-care), in adults with bronchiectasis?*

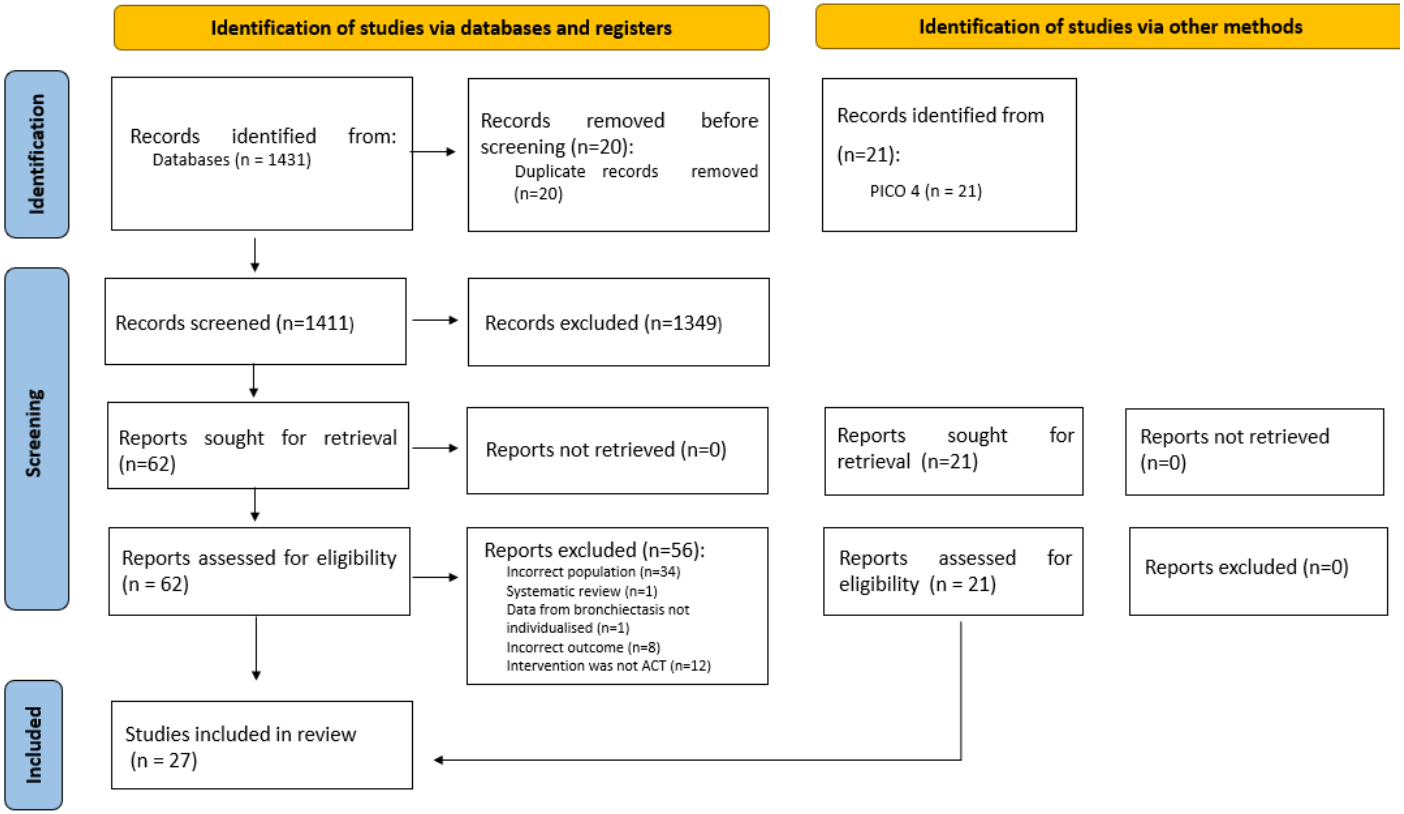


Figure S6. Literature search flow diagram for Question 5 - *a. What are the experiences and perceived impact of ACTs on adults with bronchiectasis? b. What are the perceived barriers to and enablers of ACTs in adults with bronchiectasis?* One search strategy was conducted for both questions.

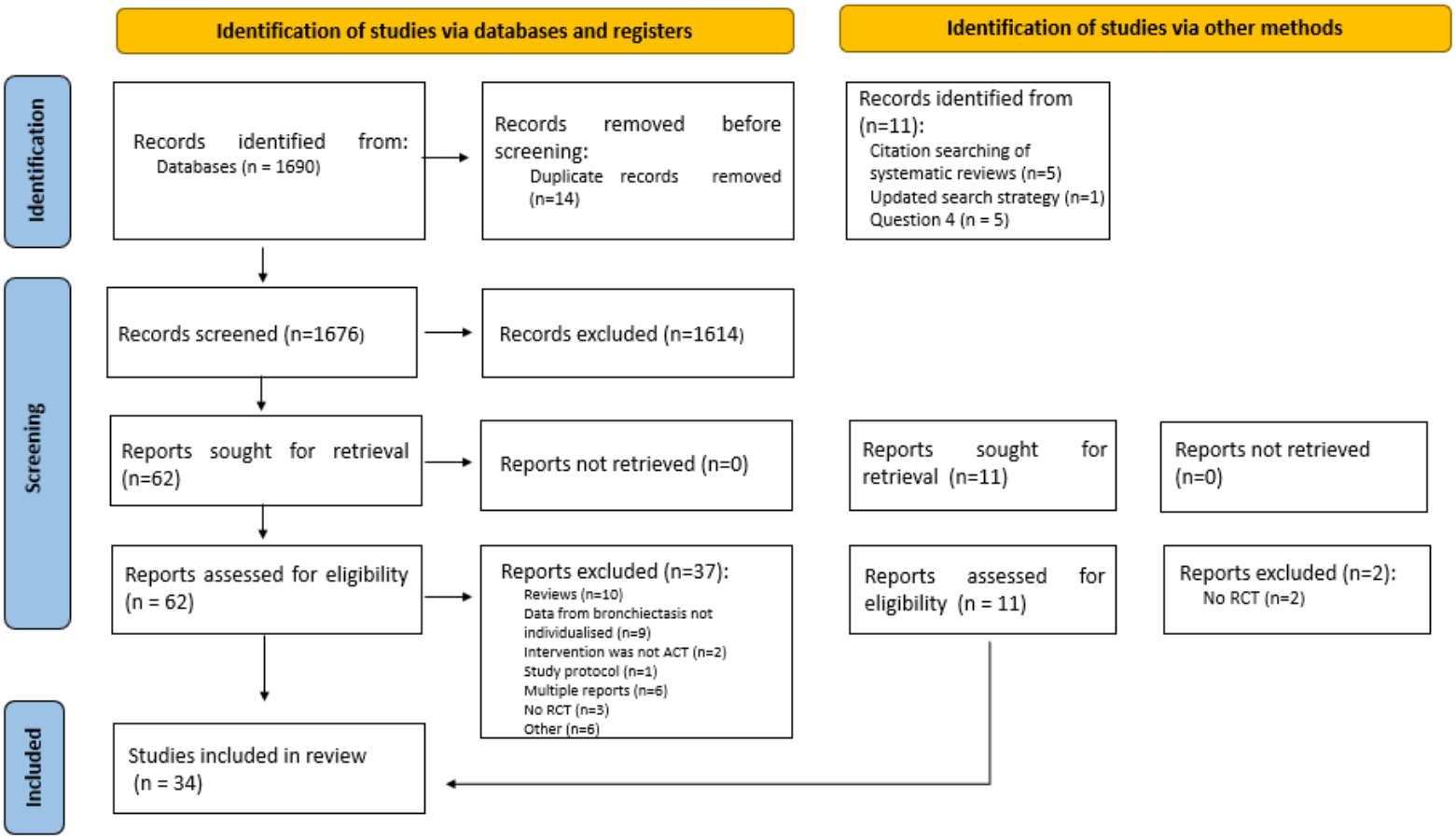


Figure S7. Literature search flow diagram for Question 6 - *In adults with bronchiectasis, how should studies for ACTs be conducted to reduce the risk of bias, facilitate comparison of findings, as well as conducting future meta-analyses?*

Table S6. Description of the outcome measures used in the included studies for Question 6 - *In adults with bronchiectasis, how should studies for ACTs be conducted to reduce the risk of bias, facilitate comparison of findings, as well as conducting future meta-analyses?*.

Outcome measures	Timeframe	Nº of studies that used this outcome measure as primary endpoint	Nº of studies that used this outcome measure to estimate the sample size #	Nº of studies that used this outcome measure as secondary endpoint or not specified
Sputum quantity				
Wet sputum weight	During intervention	4 (12%)	3 (10%)	5 (15%)
	≤4h-after intervention	4 (12%)	4 (13%)	9 (26%)
	24-h after intervention	0	0	3 (9%)
Dry sputum weight	During intervention	2 (6%)	2 (6%)	4 (12%)
	≤4h-after intervention	0	0	5 (15%)
	24-h after intervention	0	0	0
Wet sputum volume	During intervention	1 (3%)	1 (3%)	12 (35%)
	≤4h-after intervention	4 (12%)	0	3 (9%)
	24-h after intervention	2 (6%)	1 (3%)	2 (6%)
Self-reported sputum quantity (Likert scale, VAS, etc.)	During intervention	0	0	0
	≤4h-after intervention	0	0	0
	24-h after intervention	0	0	1 (3%)
Sputum colour	Pre / Post intervention	0	0	2 (6%)
Sputum properties				
Percentage of solids	Pre / Post intervention	0	0	1 (3%)
Mucociliary transport (relative velocity)	Pre / Post intervention	0	0	2 (6%)
Displacement	Pre / Post intervention	1 (3%)	1 (3%)	1 (3%)

Contact angle	Pre / Post intervention	0	0	1 (3%)
Adhesiveness	Pre / Post intervention	0	0	2 (6%)
Viscosity	Pre / Post intervention	0	0	1 (3%)
Elasticity	Pre / Post intervention	0	0	1 (3%)
Self-reported sputum characteristics	Pre / Post intervention	0	0	1 (3%)
Sputum cytology	Pre / Post intervention	0	0	2 (6%)
Microbiology (bacterial isolation, colony-forming units)	Pre / Post intervention	0	0	2 (6%)
Lung function				
FEV_1, FVC, FEF_{25-75}%, PEF	Pre / Post intervention	1 (3%)	0	20 (59%)
TLC, IC, VC, RV, FRC	Pre / Post intervention	0	0	4 (12%)
LCI	Pre / Post intervention	1 (3%)	1 (3%)	0
Oscillometry	Pre / Post intervention	1 (3%)	1 (3%)	1 (3%)
HRQoL				
LCQ	Pre / Post intervention	2 (6%)	1 (3%)	5 (15%)
QoL-B	Pre / Post intervention	0	0	2 (6%)
SGRQ	Pre / Post intervention	0	0	2 (6%)
CRQ	Pre / Post intervention	0	0	1 (3%)
CAT	Pre / Post intervention	0	0	1 (3%)
BHQ	Pre / Post intervention	0	0	1 (3%)
SF36	Pre / Post intervention	0	0	1 (3%)
Nº exacerbations	Follow-up period	1 (3%)	0	3 (10%)
Time to first exacerbations	Follow-up period	0	0	2 (6%)
Nº hospitalisations	Follow-up period	0	0	1 (3%)

Hospitalisation length	During intervention	0	0	1 (3%)
Exercise capacity				
6MWT	Pre / Post intervention	0	0	2 (6%)
ISWT	Pre / Post intervention	0	0	1 (3%)
Respiratory muscle (MIP/MEP)	Pre / Post intervention	0	0	2 (6%)
Respiratory sounds	Pre / Post intervention	1 (3%)	0	0
Nº of coughs	During intervention	0	0	1 (3%)
Symptoms				
Breathlessness	Pre / Post intervention	1 (3%)	0	8 (23%)
BCSS	Pre / Post intervention			
Other self-reported symptoms (e.g., fatigue, pain, etc)	Pre / Post intervention	0	0	4 (12%)
ABG	Pre / Post intervention	0	0	3 (10%)
Biochemistry and haematology	Pre / Post intervention	0	0	3 (10%)
Vital signs (HR, SpO2, RR)	Pre / Post intervention	1 (3%)	0	9 (26%)
Session length	During intervention	0	0	2 (6%)
Patients´feedback	After the intervention	0	0	18 (53%)

VAS, visual analogical scale; FEV_1, forced expiratory volume in the first second; FVC, forced vital capacity; $FEF_{25-75\%}$,forced expiratory flow between 25-75% of vital capacity; PEF, peak expiratory flow; TLC, total lung capacity; IC, inspiratory capacity; VC, vital capacity; RV, residual volume; FRC, functional residual capacity; LCI, lung clearance index; LCQ, Leicester cough questionnaire; QoL-B, quality of life of bronchiectasis; SGRQ, Saint George respiratory questionnaire; CRQ, chronic respiratory disease questionnaire: CAT, COPD assessment test; BHQ, bronchiectasis health questionnaire; SF36, 36 item short form survey; 6MWT, six minute walk test; ISWT, incremental shuttle walk test; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; BCSS, breathlessness, cough and sputum scale; ABG, arterial blood gas; HR, heart rate; SpO2, oxygen saturation; RR, respiratory rate. # As sample size estimation is not usually included in abstracts, only full text manuscripts were included in this analysis (n=30).

Table S6. Risk of bias of the studies included in Question 6 - *In adults with bronchiectasis, how should studies for ACTs be conducted to reduce the risk of bias, facilitate comparison of findings, as well as conducting future meta-analyses?*

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Morgan et al.[62] 1999, Australia ¥	?	?	?	?	?	?
De Oliveira et al.[63] 2001, Brazil	?	?	?	?	+	?
Thompson et al.[64] 2002, UK	?	?	?	?	+	?
Tsang et al.[65] 2003, Hong Kong	+	?	+	?	-	?
Patterson et al.[66] 2004, UK	+	?	?	?	+	?
Patterson et al.[67] 2005, UK	+	?	?	+	+	?
Eaton et al.[68] 2007, New Zealand	+	+	?	?	+	?
Patterson et al.[69] 2007, UK	+	?	?	?	+	?
Murray et al.[70] 2009, UK	+	?	?	?	+	+
Syed et al.[71] 2009, India	-	?	?	?	+	?
Naraparaju et al.[72] 2010, India	+	?	?	?	+	?
Shabari et al.[73] 2011, India	?	?	?	?	+	?

Tambascio et al.[74] 2011, Brazil	+	?	?	?	+	?
Paneroni et al.[75] 2011, Italy	+	?	?	?	+	?
Guimarães et al.[76] 2012, Brazil	+	+	?	?	+	+
Figueiredo et al.[77] 2012, Brazil	+	+	?	+	+	?
Amit et al.[78] 2012, India	+	-	?	?	+	?
Nicolini et al.[79] 2013, Italy	+	?	?	?	+	+
Anand et al.[80] 2014, India	?	?	?	?	?	?
Senthil et al.[81] 2015, India	?	?	?	?	?	?
Semwal et al.[82] 2015, India	?	?	?	?	+	?
Ramos et al.[83] 2015, Brazil	+	?	?	?	?	?
Herrero-Cortina et al.[84] 2016, Spain	+	?	+	?	+	+
AbdelHalim et al.[85] 2016, Egypt	?	?	?	?	+	?
Silva et al.[86] 2017, Australia	+	+	-	?	+	?
Tambascio et al.[87] 2017, Brazil	+	?	?	?	+	+
Üzmezoğlu et al.[88] 2018, Turkey	+	?	?	?	+	?

Muñoz et al.[89] 2018, Spain	+	+	+	+	+	+
Herrero-Cortina et al.[90] 2018, Spain ¥	?	+	+	+	+	?
Herrero-Cortina et al.[91] 2019, Spain ¥	?	?	?	?	+	?
de Souza et at.[53] 2019, Brazil	+	?	-	?	+	?
Santos et al.[92] 2020, Australia	+	+	-	+	+	?
Nicolini et al.[93] 2020, Italy ¥	+	+	?	?	+	+
Livnat et al.[94] 2021, Israel	+	?	?	+	+	+

+ low risk of bias; ? unclear risk of bias; - high risk of bias. Only randomised trials were included in the analysis. Multiple reports from the same study were also excluded. ¥ Abstracts.
Scoring based on the reviewer's judgement for each risk of bias category.

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ERS statement on airway clearance techniques in adults with bronchiectasis

Supplementary material 2 – Selection criteria and search strategies used for questions

Question 1 - What is the physiological rationale for the use for ACTs in adults with bronchiectasis?

Selection criteria

	Population	Disease	Clinical status	Study design	Active treatment	Comparison	Outcomes	Comments
Inclusion	Adults (≥18 y) Male or female Animal models In vitro Mathematical models	Bronchiectasis Overlaps (e.g, COPD, Asthma) Primary ciliary dyskinesia Kartagener syndrome Healthy people* Cystic fibrosis* COPD* Asthma*	Stable Exacerbation Hospital Admission	Systematic Review RCT (equivalence) Crossover Non-inferiority trial Superiority trial Quasi-experimental Cohort Case-control Cross-sectional Qualitative Narrative review	Not applicable	Not applicable	Airway surface layer Dehydrated ATP Mucus / cough transport Mucus / cough clearance CFTR Biophysical properties Ciliary movement /beat Mucin Solid content Sputum / expectoration Pressure Ventilation Oscillation Vibration Two-phases gas-liquid Flow Mechanical stress	* Panel agreed to include other muco-obstructive respiratory disease and healthy people in the second round.
	Population	**Disease**	**Clinical status**	**Study design**	**Active treatment**	**Comparison**	**Outcomes**	**Comments**
Exclusion	Children (<18y)	Non-muco obstructive respiratory diseases	Intensive Care	N/A	N/A	N/A	N/A	

COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis; ILD, interstitial lung disease; RCT, randomised controlled trial; ATP, adenosine triphosphate; CFTR, cystic fibrosis transmembrane conductance regulator; ACTs, airway clearance techniques; N/A, not applicable.

Question 2 - What is the physiological rationale of each one of the ACTs and what are the advantages and limitations of each technique?

Selection criteria

	Population	Disease	Clinical status	Study design	Active treatment	Comparison	Outcomes	Comments
Inclusion	Adults (≥18 y) Male or female Animal models In vitro Mathematical models	Bronchiectasis Overlaps (e.g, COPD, Asthma) Primary ciliary dyskinesia Kartagener syndrome Healthy people* Cystic fibrosis* COPD* Asthma*	Stable Exacerbation Hospital Admission	Systematic Review RCT (equivalence) Crossover Non-inferiority trial Superiority trial Quasi-experimental Cohort Case-control Cross-sectional Qualitative Narrative review	ACTs ¥	Not applicable	Pressure Airflow / Flow Oscillation / Frequency Vibration / Frequency Gas-liquid Ventilation ATP Airway diameter Interdependence Body posture Breath hold Advantage Disadvantage Limitation Adverse events Time consuming ACTs¥	* Panel agreed to include other muco-obstructive respiratory disease and healthy people in the second round. ¥ Name of the ACTs evaluated in bronchiectasis and obtained from Question 4 (effectiveness)
	Population	**Disease**	**Clinical status**	**Study design**	**Active treatment**	**Comparison**	**Outcomes**	**Comments**
Exclusion	Children (<18y)	Not applicable	Intensive Care	Not applicable	PR IMT Exercise NIV Muco-active drugs Invasive methods	Not applicable	Not applicable	

RCT, randomised controlled trial; ACTs, airway clearance techniques; ATP, adenosine triphosphate; PR, pulmonary rehabilitation; IMT, inspiratory muscle training; NIV, non-invasive ventilation; N/A, not applicable

Question 3 - Which are the ACTs that are used in the management of adults with bronchiectasis and are there any patterns according to geographical location?

Selection criteria

	Population	Disease	Clinical status	Study design	Active treatment	Comparison	Outcomes	Comments
Inclusion	Adults (≥18 y) Male or female Animal models In vitro	Bronchiectasis Overlaps (e.g, COPD, Asthma) Primary ciliary dyskinesia Kartagener syndrome	Stable Exacerbation Hospital Admission	RCT (equivalence) Crossover Non-inferiority trial Superiority trial Quasi-experimental Systematic Review Cross-sectional Cohort Case-control Qualitative Surveys, registers	ACTs	N/A	Region/Country	Studies recruiting more than one disease at the same time (e.g COPD and bronchiectasis) will be only included if specific data from bronchiectasis could be extracted (full text)
	Population	**Disease**	**Clinical status**	**Study design**	**Active treatment**	**Comparison**	**Outcomes**	**Comments**
Exclusion	Children (<18y)	CF COPD Asthma ILD Other respiratory diseases	Intensive Care	N/A	PR IMT Exercise NIV Muco-active drugs Invasive methods	N/A	N/A	

COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis; ILD, interstitial lung disease; RCT, randomised controlled trial; ACTs, airway clearance techniques; PR, pulmonary rehabilitation; IMT, inspiratory muscle training; NIV, non-invasive ventilation; N/A, not applicable

Search strategy

Ovid MEDLINE(R) ALL <1946 to November 18, 2021>

1	exp Bronchiectasis/	9670
2	(bronchiectasis or bronchiectases or kartageners syndrome).mp.	13918
3	1 or 2	14661
4	exp Physical Therapy Modalities/	166262
5	(physiotherap* or physical therap*).mp.	78124
6	4 or 5	199815
7	(airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp	6585
8	(bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp.	4484
9	(10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp.	279774
10	(IPPB or intermittent positive pressure breathing).mp.	1132
11	(IPV or intrapulmonary percussive ventilation).mp.	7488
12	(HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp.	22276
13	(autogenic drainage or AD).mp.	163112
14	(ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp.	80
15	(ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp.	50544
16	(thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp.	78270
17	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	789940
18	3 and 17	1619
19	limit 18 to yr="2020 - 2022"	195

Embase <1974 to November 2021>

1	exp bronchiectasis/	23111
2	(bronchiectasis or bronchiectases or kartageners syndrome).mp.	25314
3	1 or 2	25891
4	exp physiotherapy/	95360
5	(physiotherap* or physical therap*).mp.	137890
6	4 or 5	138990
7	(airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp.	14070
8	(bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp.	9247
9	(10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp.	370847
10	(IPPB or intermittent positive pressure breathing).mp.	555
11	(IPV or intrapulmonary percussive ventilation).mp.	8326
12	(HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp.	30064
13	(autogenic drainage or AD).mp.	668900
14	(ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp.	113
15	(ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp.	59060
16	(thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp.	176105
17	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	1438374
18	3 and 17	5365
19	Limit 18 to Embase	3586

AMED (Allied and Complementary Medicine) <1985 to November 2021>

1	bronchiectasis/	37
2	(bronchiectasis or bronchiectases or kartageners syndrome).mp.	52
3	1 or 2	52
4	exp physical therapy modalities/	30639
5	(physiotherap* or physical therap*).mp. [mp=abstract, heading words, title]	24343
6	4 or 5	44896
7	(airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp.	121
8	(bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp.	446
9	(10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp.	2840
10	(IPPB or intermittent positive pressure breathing).mp.	
11	(IPV or intrapulmonary percussive ventilation).mp.	16
12	(HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp.	173
13	(autogenic drainage or AD).mp.	930
14	(ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp.	6
15	(ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp.	1146
16	(thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp.	957
17	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	48924
18	3 and 17	28

CINAHL 1981 - 2021

S18	S3 AND S17	502
S17	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	378,799
S16	thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation	46,820
S15	ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration	7,463
S14	ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*	47
S13	autogenic drainage or AD	60,779
S12	HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*	3,868
S11	IPV or intrapulmonary percussive ventilation	10,477
S10	IPPB or intermittent positive pressure breathing	218
S9	10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP	67,809
S8	bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*	3,476
S7	airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance	1,744
S6	S4 OR S5	193,173
S5	physiotherap* or physical therap*	85,201
S4	(MH "Physical Therapy+")	153,140
S3	S1 OR S2	2,344

S2	bronchiectasis or bronchiectases or kartageners syndrome	2,344
S1	(MH "Bronchiectasis")	1,295

Cochrane CENTRAL 1947 -2021

#1	MeSH descriptor: [Bronchiectasis] explode all trees	359
#2	bronchiectasis or bronchiectases or kartageners syndrome	1387
#3	#1 or #2	1394
#4	MeSH descriptor: [Physical Therapy Modalities] explode all trees	28018
#5	physiotherap* or physical therap*	84111
#6	#4 or #5	99235
#7	airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance	3401
#8	bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*	6189
#9	10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP	34271
#10	IPPB or intermittent positive pressure breathing	553
#11	IPV or intrapulmonary percussive ventilation	1498
#12	HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*	3255
#13	autogenic drainage or AD	32275
#14	ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*	617
#15	ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration	9541

#16 thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation 59979

#17 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 219950

#18 #3 and #17 877

PEDro

bronchiectasis and physiotherapy* (24)

bronchiectasis and physical therap* (10)

bronchiectasis and oscillat* (18)

bronchiectasis and sputum* (42)

bronchiectasis and mucociliary clearance (4)

Bronchiectasis and High Frequency Chest Wall Oscillation (4)

Bronchiectasis and postural drainage (10)

Question 4 - What is the clinical evidence for the effectiveness of ACTs, in terms of function and disability (e.g. sputum expectoration), activity (e.g. physical activity) and participation (e.g. self-care), in adults with bronchiectasis?

Selection criteria

	Population	Disease	Clinical status	Study design	Active treatment	Comparison	Outcomes	Comments
Inclusion	Adults (≥18 y) Male or female	Bronchiectasis Overlaps (e.g, COPD, Asthma) Primary ciliary dyskinesia Kartagener syndrome	Stable Exacerbation Hospital Admission	RCT (equivalence) Crossover Non-inferiority trial Superiority trial	ACTs alone Combined ACTs	Placebo Sham intervention ACT alone Combined ACTs Usual care Other (PR, mucoactive) No treatment	Function and disability Activity Participation	i) Studies recruiting more than one disease at the same time (e.g COPD and bronchiectasis) will be only included if specific data from bronchiectasis could be extracted (full text) ii) Abstracts were excluded
	Population	**Disease**	**Clinical status**	**Study design**	**Active treatment**	**Comparison**	**Outcomes**	**Comments**
Exclusion	Children (<18y) Animal models In vitro	CF COPD Asthma ILD Other respiratory diseases	Intensive Care	Cross-sectional Cohort Case-control Qualitative Quasi-experimental Systematic review	PR IMT Exercise NIV Muco-active drugs Invasive methods	N/A	N/A	

COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis; ILD, interstitial lung disease, RCT, randomised controlled trial; PR, pulmonary rehabilitation; IMT, inspiratory muscle training; NIV, non-invasive ventilation; N/A, not applicable

Search strategy

Ovid MEDLINE(R) ALL <1946 to November 19, 2021>

1	exp Bronchiectasis/	9670
2	(bronchiectasis or bronchiectases or kartagener* syndrome*).mp.	14716
3	1 or 2	14716
4	exp Physical Therapy Modalities/	166287
5	(physiotherap* or physical therap*).mp	78134
6	4 or 5	199847
7	airway* clearance*.mp.	1027
8	(sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp.	5782
9	(bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp.	4486
10	(oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp.	279899
11	(intermittent positive pressure breath* or IPPB).mp.	1132
12	(IPV or intrapulmonary percussive ventilation).mp.	7491
13	(HFCWO or High Frequency Chest Wall Oscillation).mp.	96
14	(ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration or autogenic drainage or AD or ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp.	213637
15	(thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp.	78287
16	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15	769147
17	3 and 16	1584
18	exp Hospitals/ or exp Patient Readmission/ or exp Prognosis/ or exacerbation*.mp.	2119018
19	(hospit* or readmission or emergency attendance or disease prognos*).mp.	38670

20 (day* adj3 recovery).mp. 7865

21 18 or 19 or 20 2137956

22 exp Patient Reported Outcome Measures/ 10190

23 (BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*).mp. 313676

24 22 or 23 313731

25 exp "Quality of Life"/ 227009

26 (quality of life or QoL or HRQoL or health?related quality of life).mp. 393279

27 25 or 26 393279

28 exp Cough/ or cough*.mp. or pulmonary function*.mp. or lung function*.mp. 131864

29 exp Peak Expiratory Flow Rate/ or spirometry.mp. or forced expiratory volume.mp. or FEV1.mp. or forced vital capacity.mp. or FVC.mp. or forced expiratory flow FEF25-75.mp. or peak expiratory flow.mp. or lung volume*.mp. or air?trapping.mp. or residual volume.mp. or RV functional residual capacity FRC.mp. or lung hyperinflation.mp. or total lung capacity.mp. or TLC.mp. 109699

30 exp Plethysmography/ 21798

31 (plethysmography or airway resistance or airway reactance or airway impedance).mp. 38466

32 30 or 31 42409

33 exp Magnetic Resonance Imaging/ 494505

34 exp Pulmonary Gas Exchange/ 20660

35 exp Ventilation/ 6090

36 (diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI).mp. 1103454

37 33 or 34 or 35 or 36 1120608

38 exp Sputum/ 22354

39 (sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration).mp. 77905

40 38 or 39 77905

41 exp Mucociliary Clearance/ or radioaerosol clearance.mp. or scintigraphy.mp. or cough clearance.mp. or cough transport.mp. or biophysical propert*.mp. 50304

42 exp Viscosity/ or exp Elasticity/ or exp Mucins/ or exp Mucus/ or surface propert*.mp. or tenacity.mp. or cohesivity.mp. or adhesivity.mp. or viscoelasticity.mp. or rheology*.mp. or rigidity transportability.mp. or ciliary movement.mp. or mucus hydration.mp. or solid content.mp. or solid percentage.mp. or mucin.mp. 282208

43 exp Bacterial Load/ or exp Osmotic Pressure/ or osmotic pressure.mp. or interfacial tension.mp. or bacterial load.mp. or bacterial density.mp. or bacterial eradication.mp. or pathogens.mp. or microbiology.mp. or inflammat*.mp. 2151731

44 exp Leukocyte Elastase/ or exp Peroxidase/ or exp Interleukins/ or exp Cell Count/ or marker*.mp. or neutrophil elastase.mp. or myeloperoxidase.mp. or interleukin*.mp. or cell count*.mp. 1473139

45 exp Respiratory Sounds/ or respiratory sound*.mp. or breath sound*.mp. or crackle*.mp. or wheeze*.mp. 18690

46 exp Exercise/ or exp Sleep/ or exp Anxiety/ or exp Depression/ or exp Dyspnea/ or exp Fatigue/ or exercise capacity.mp. or physical activity.mp. or sleep.mp. or anxiety.mp. or depression.mp. or symptom.mp. or dyspnea.mp. or breathlessness.mp. or fatigue.mp. or exacerbat*.mp. 1488792

47 (patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment).mp. 3683907

48 exp Patient Satisfaction/ or exp Patient Preference/ or exp Medication Adherence/ or exp Guideline Adherence/ or exp "Treatment Adherence and Compliance"/ or exp Self-Management/ or exp Self Efficacy/ or exp Anti-Bacterial Agents/ 1081177

49 exp Community Participation/ or participation.mp. or life role*.mp. or social role*.mp. or role function*.mp. or community engagement.mp. or integration.mp. or days of absence.mp. 412965

50 21 or 24 or 27 or 28 or 29 or 32 or 37 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 10999990

51 17 and 50 1470

Embase <1974 to 2021 November 17>

1 exp bronchiectasis/ 23111

2 (bronchiectasis or bronchiectases or kartageners syndrome).mp. 25314

3 1 or 2 25891

4 exp physiotherapy/ 95360

5 (physiotherap* or physical therap*).mp. 137890

6 4 or 5 138990

7 (airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp. 14070

8 (bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp. 9247

9 (10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp. 370847

10 (IPPB or intermittent positive pressure breathing).mp. 555

11 (IPV or intrapulmonary percussive ventilation).mp. 8326

12 (HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp. 30064

13 (autogenic drainage or AD).mp. 668900

14 (ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp. 113

15 (ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp. 59060

16 (thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp. 176105

17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 1462641

18 3 and 17 5471

19 exp hospital/ or exp hospital readmission/ or exp prognosis/ or exacerbation*.mp. 2309111

20 (hospit* or readmission or emergency attendance or disease prognos*).mp. 2968142

21 (day* adj3 recovery).mp. 12528

22 19 or 20 or 21 4097877

23 exp patient-reported outcome/ 39804

24 (BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*).mp. 494148

25 23 or 24 494852

26 exp "quality of life"/ 577730

27 (quality of life or QoL or HRQoL or health?related quality of life).mp. 710962

28 26 or 27 710962

29 exp coughing/ or cough*.mp. or pulmonary function*.mp. or lung function*.mp. 326350

30 exp peak expiratory flow/ or spirometry.mp. or forced expiratory volume.mp. or FEV1.mp. or forced vital capacity.mp. or FVC.mp. or forced expiratory flow FEF25-75.mp. or peak expiratory flow.mp. or lung volume*.mp. or air?trapping.mp. or residual volume.mp. or RV functional residual capacity FRC.mp. or lung hyperinflation.mp. or total lung capacity.mp. or TLC.mp. 201127

31 exp plethysmography/ 27475

32 (plethysmography or airway resistance or airway reactance or airway impedance).mp. 46361

33 31 or 32 46361

34 exp nuclear magnetic resonance imaging/ 1109244

35 exp lung gas exchange/ 13413

36 (diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI).mp. 1833235

37 34 or 35 or 36 1885023

38 exp sputum/ 26181

39 (sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration).mp. 121017

40 38 or 39 121017

41 exp mucociliary clearance/ or radioaerosol clearance.mp. or scintigraphy.mp. or cough clearance.mp. or cough transport.mp. or biophysical propert*.mp. 88499

42 exp viscosity/ or exp elasticity/ or exp mucins/ or exp mucus/ or surface propert*.mp. or tenacity.mp. or cohesivity.mp. or adhesivity.mp. or viscoelasticity.mp. or rheology*.mp. or rigidity transportability.mp. or ciliary movement.mp. or mucus hydration.mp. or solid content.mp. or solid percentage.mp. or mucin.mp. 425259

43 exp bacterial load/ or exp osmotic pressure/ or osmotic pressure.mp. or interfacial tension.mp. or bacterial load.mp. or bacterial density.mp. or bacterial eradication.mp. or pathogens.mp. or microbiology.mp. or inflammat*.mp. 2342191

44 exp leukocyte elastase/ or exp peroxidase/ or exp interleukins/ or exp cell count/ or marker*.mp. or neutrophil elastase.mp. or myeloperoxidase.mp. or interleukin*.mp. or cell count*.mp. 2752802

45 exp respiratory sounds/ or respiratory sound*.mp. or breath sound*.mp. or crackle*.mp. or wheeze*.mp. 72377

46 exp exercise/ or exp sleep/ or exp anxiety/ or exp depression/ or exp dyspnea/ or exp fatigue/ or exercise capacity.mp. or physical activity.mp. or sleep.mp. or anxiety.mp. or depression.mp. or symptom.mp. or dyspnea.mp. or breathlessness.mp. or fatigue.mp. or exacerbat*.mp. 2919077

47 (patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment).mp. 3865819

48 exp patient satisfaction/ or exp patient preference/ or exp medication compliance/ or exp protocol compliance/ or patient compliance/ or self-care/ or exp antiinfective agent/ 4314376

49 exp community participation/ or participation.mp. or life role*.mp. or social role*.mp. or role function*.mp. or community engagement.mp. or integration.mp. or days of absence.mp. 502392

50 22 or 25 or 28 or 29 or 30 or 33 or 37 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 16322829

51 18 and 50 5260

52 limit 51 to Embase 3522

AMED (Allied and Complementary Medicine) <1985 to November 2021>

1 bronchiectasis/ 37

2 (bronchiectasis or bronchiectases or kartageners syndrome).mp. [mp=abstract, heading words, title] 52

3 1 or 2 52

4 exp physical therapy modalities/ 30639

5 (physiotherap* or physical therap*).mp. [mp=abstract, heading words, title] 24343

6 4 or 5 44896

7 (airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp. [mp=abstract, heading words, title] 121

8 (bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp. [mp=abstract, heading words, title] 446

9 (10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp. [mp=abstract, heading words, title] 2840

10 (IPPB or intermittent positive pressure breathing).mp. [mp=abstract, heading words, title] 13

11 (IPV or intrapulmonary percussive ventilation).mp. [mp=abstract, heading words, title] 16

12 (HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp. [mp=abstract, heading words, title] 173

13 (autogenic drainage or AD).mp. [mp=abstract, heading words, title] 930

14 (ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp. [mp=abstract, heading words, title] 6

15 (ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp. [mp=abstract, heading words, title] 1146

16 (thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp. [mp=abstract, heading words, title] 957

17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 48924

18 3 and 17 28

19 exp Hospitals/ or exp Hospitalization/ or exp Prognosis/ or exacerbation*.mp. [mp=abstract, heading words, title] 26356

20 (hospit* or readmission or emergency attendance or disease prognos*).mp. [mp=abstract, heading words, title] 15489

21 (day* adj3 recovery).mp. [mp=abstract, heading words, title] 104

22 19 or 20 or 21 36382

23 (BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*).mp. [mp=abstract, heading words, title] 2654

24 "quality of life"/ 10535

25 (quality of life or QoL or HRQoL or health?related quality of life).mp. [mp=abstract, heading words, title] 14890

26 24 or 25 14890

27 Cough/ or cough*.mp. or pulmonary function*.mp. or lung function*.mp. 1759

28 Peak Expiratory Flow Rate/ or spirometry.mp. or (forced adj2 expiratory adj2 volume).mp. or FEV1.mp. or (forced adj2 vital adj2 capacity).mp. or FVC.mp. or (forced adj2 expiratory adj2 flow).mp. or FEF25-75.mp. or (peak adj2 expiratory adj2 flow).mp. or (lung adj2 volume*).mp. or air?trapping.mp. or (residual adj2 volume).mp. or (RV adj2 functional adj2 residual adj2 capacity adj2 FRC).mp. or (lung adj2 hyperinflation).mp. or (total adj2 lung adj2 capacity).mp. or TLC.mp. [mp=abstract, heading words, title] 1563

29 plethysmography/ 26

30 (plethysmography or airway resistance or airway reactance or airway impedance).mp. [mp=abstract, heading words, title] 246

31 29 or 30 246

32 magnetic resonance imaging/ 1818

33 pulmonary gas exchange/ 60

34 (diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI).mp. [mp=abstract, heading words, title] 5707

35 32 or 33 or 34 5707

36 sputum/ 46

37 (sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration).mp. [mp=abstract, heading words, title] 421

38	36 or 37	421
39	Mucociliary Clearance/ or radioaerosol clearance.mp. or scintigraphy.mp. or cough clearance.mp. or cough transport.mp. or biophysical propert*.mp. [mp=abstract, heading words, title]	133
40	Elasticity/ or Viscosity/ or Mucus/	295
41	(surface propert* or tenacity or cohesivity or adhesivity or viscoelasticity or rheology* or rigidity transportability or ciliary movement or mucus hydration or solid content or solid percentage or mucin).mp.	158
42	(osmotic pressure or interfacial tension or bacterial load or bacterial density or bacterial eradication or pathogens or microbiology or inflammat*).mp. [mp=abstract, heading words, title]	9800
43	(marker* or neutrophil elastase or myeloperoxidase or interleukin* or cell count*).mp. [mp=abstract, heading words, title]	5030
44	respiratory sounds/ or respiratory sound*.mp. or breath sound*.mp. or crackle*.mp. or wheeze*.mp.	92
45	exp Exercise/ or exp Sleep/ or Anxiety/ or Depression/ or Dyspnea/ or exp Fatigue/ or exercise capacity.mp. or physical activity.mp. or sleep.mp. or anxiety.mp. or depression.mp. or symptom.mp. or dyspnea.mp. or breathlessness.mp. or fatigue.mp. or exacerbat*.mp.	36736
46	(patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment).mp. [mp=abstract, heading words, title]	39617
47	patient participation/ or exp "patient acceptance of health care"/ or self care/ or self efficacy/	9393
48	(participation or life role* or social role* or role function* or community engagement or integration or days of absence).mp.	9967
49	22 or 23 or 26 or 27 or 28 or 31 or 35 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48	122778
50	18 and 49	22

CINAHL 1981 - 2021

S36	S18 AND S35	473
S35	S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34	2,668,310
S34	Participation or life role* or social role* or role function* or community engagement or integration or days of absence	194,643
S33	patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment	1,429,152
S32	exercise capacity or physical activity or sleep or anxiety or depression or symptom or dyspnea or breathlessness or fatigue or exacerbat*.	795,076
S31	respiratory sound* or breath sound* or crackle* or wheeze*	4,390
S30	marker* or neutrophil elastase or myeloperoxidase or interleukin* or cell count*	217,039
S29	osmotic pressure or interfacial tension or bacterial load or bacterial density or bacterial eradication or pathogens or microbiology or inflammat*.	257,699
S28	surface propert* or tenacity or cohesivity or adhesivity or viscoelasticity or rheology* or rigidity transportability or ciliary movement or mucus hydration or solid content or solid percentage or mucin	8,646
S27	mucociliary clearance or radioaerosol clearance or scintigraphy or cough clearance or cough transport or biophysical propert*	7,452
S26	sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration	9,711

S25	diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI	262,176
S24	plethysmography or airway resistance or airway reactance or airway impedance	5,176
S23	spirometry or forced expiratory volume or FEV1 or forced vital capacity or FVC or forced expiratory flow FEF or peak expiratory flow or lung volume* or air trapping or residual volume or lung hyperinflation or total lung capacity or TLC	26,445
S22	cough* or pulmonary function* or lung function*	37,780
S21	quality of life or QoL or HRQoL or health?related quality of life	226,292
S20	BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*	74,079
S19	hospit * or readmission or emergency attendance or disease prognos* or (day N3 recovery)	37,883
S18	S3 AND S17	502
S17	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	378,799
S16	thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation	46,820
S15	ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration	7,463
S14	ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*	47
S13	autogenic drainage or AD	60,779
S12	HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*	3,868

S11	IPV or intrapulmonary percussive ventilation	10,477
S10	IPPB or intermittent positive pressure breathing	218
S9	10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP	67,809
S8	bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*	3,476
S7	airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance	1,744
S6	S4 OR S5	193,173
S5	physiotherap* or physical therap*	85,201
S4	(MH "Physical Therapy+")	153,140
S3	S1 OR S2	2,344
S2	bronchiectasis or bronchiectases or kartageners syndrome	2,344
S1	(MH "Bronchiectasis")	1,295

Cochrane CENTRAL 1947 – 2021

#1 MeSH descriptor: [Bronchiectasis] explode all trees 368

#2 bronchiectasis or bronchiectases or kartageners syndrome 1429

#3 #1 or #2 1436

#4 MeSH descriptor: [Physical Therapy Modalities] explode all trees 29256

#5 physiotherap* or physical therap* 86802

#6 #4 or #5 102651

#7 airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance 3478

#8 bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise* 6500

#9 10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP 35031

#10 IPPB or intermittent positive pressure breathing 567

#11 IPV or intrapulmonary percussive ventilation 1520

#12 HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall* 3337

#13 autogenic drainage or AD 32983

#14 ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory* 627

#15 ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration 9799

#16 thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation 61550

#17 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 226191

#18 #3 and #17 905

#19 hospit* or readmission or emergency attendance or disease prognos* or (day* adj3 recovery) 394341

#20	BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*	58688
#21	quality of life or QoL or HRQoL or health?related quality of life	145550
#22	cough* or pulmonary function* or lung function*	50754
#23	spirometry or forced expiratory volume or FEV1 or forced vital capacity or FVC or forced expiratory flow FEF or peak expiratory flow or lung volume* or air?trapping or residual volume or RV functional residual capacity FRC or lung hyperinflation or total lung capacity or TLC	94278
#24	plethysmography or airway resistance or airway reactance or airway impedance	6253
#25	diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI	89825
#26	sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration	9478
#27	mucociliary clearance or radioaerosol clearance or scintigraphy or cough clearance or cough transport or biophysical propert*	3795
#28	viscosity or elasticity or mucin* or mucus or surface propert* or tenacity or cohesivity or adhesivity or viscoelasticity or rheology* or rigidity transportability or ciliary movement or mucus hydration or solid content or solid percentage	28397
#29	osmotic pressure or interfacial tension or bacterial load or bacterial density or bacterial eradication or pathogens or microbiology or inflammat*	119691
#30	leukocyte elastase or exp peroxidase or exp interleukin* or cell count or marker* or neutrophil elastase or myeloperoxidase	77067
#31	respiratory sound* or breath sound* or crackle* or wheeze*	2692
#32	exercise capacity or physical activity or sleep or anxiety or depression or symptom or dyspnea or breathlessness or fatigue or exacerbat*	301024
#33	patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment or anti?bacterial agent*	713515
#34	patient satisfaction or medication adherence or guideline* adherence or treatment adherence or treatment compliance	94269
#35	community participation or life role* or social role* or role function* or community engagement or integration or days of absence	59108
#36	#19 and #20 and #21 and #22 and #23 and #24 and #25 and #26 and #27 and #28 and #29 and #30 and #31 and #32 and #33 and #34 and #35	7
#37	Limit to Cochrane CENTRAL	0

PEDro

bronchiectasis and physiotherapy* (24)

bronchiectasis and physical therap* (10)

bronchiectasis and oscillat* (18)

bronchiectasis and sputum* (42)

bronchiectasis and mucociliary clearance (4)

Bronchiectasis and High Frequency Chest Wall Oscillation (4)

Bronchiectasis and postural drainage (10)

Question 5 – (a) What are the experiences and perceived impact of ACTs on adults with bronchiectasis? ; (b) What are the perceived barriers to and enablers of ACTs in adults with bronchiectasis?

Selection criteria

	Population	Disease	Clinical status	Study design	Active treatment	Comparison	Outcomes	Comments
Inclusion	Adults (≥18 y) Male or female	Bronchiectasis Overlaps (e.g, COPD, Asthma) Primary ciliary dyskinesia Kartagener syndrome	Stable Exacerbation Hospital Admission	RCT (equivalence) Crossover Non-inferiority trial Superiority trial Systematic Review Cross-sectional Cohort Case-control Qualitative Quasi-experimental	ACTs	Not applicable	Barriers Enablers Social impact Preference Feedback Adherence Opinion Experience Satisfaction PROs /PREMs Patient-centered care Qualitative Adherence Perspective Attitude Help Support Difficult Hinder Belief	Studies recruiting more than one disease at the same time (e.g COPD and bronchiectasis) will be only included if specific data from bronchiectasis could be extracted (full-text)
	Population	**Disease**	**Clinical status**	**Study design**	**Active treatment**	**Comparison**	**Outcomes**	**Comments**
Exclusion	Children (<18y) Animal models In vitro	CF COPD Asthma ILD Other respiratory diseases	Intensive Care	N/A	PR IMT Exercise NIV Muco-active drugs Invase methods	N/A	N/A	

COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis; ILD, interstitial lung disease; RCTs, randomised controlled trial; ACTs, airway clearance techniques; PR, pulmonary rehabilitation; IMT, inspiratory muscle training; NIV, non-invasive ventilation; PROs, patient reported outcomes; PREMs, patient reported experience measures; N/A, not applicable

Search strategy (a)

Ovid MEDLINE(R) ALL <1946 to November 19, 2021>

1	exp Bronchiectasis/	9670
2	(bronchiectasis or bronchiectases or kartagener* syndrome*).mp.	14716
3	1 or 2	14716
4	exp Physical Therapy Modalities/	166287
5	(physiotherap* or physical therap*).mp.	78134
6	4 or 5	199847
7	airway* clearance*.mp.	1027
8	(sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp.	5782
9	(bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp.	4486
10	(oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp.	279899
11	(intermittent positive pressure breath* or IPPB).mp.	1132
12	(IPV or intrapulmonary percussive ventilation).mp.	7491
13	(HFCWO or High Frequency Chest Wall Oscillation).mp.	96
14	(ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration or autogenic drainage or AD or ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp.	213637
15	(thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp.	78287
16	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15	769147
17	3 and 16	1584
18	exp Hospitals/ or exp Patient Readmission/ or exp Prognosis/ or exacerbation*.mp.	2119018

19 (hospit * or readmission or emergency attendance or disease prognos*).mp. 38670

20 (day* adj3 recovery).mp. 7865

21 18 or 19 or 20 2137956

22 exp Patient Reported Outcome Measures/ 10190

23 (BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*).mp. 313676

24 22 or 23 313731

25 exp "Quality of Life"/ 227009

26 (quality of life or QoL or HRQoL or health?related quality of life).mp. 393279

27 25 or 26 393279

28 exp Cough/ or cough* or pulmonary function* or lung function* 131864

29 exp Peak Expiratory Flow Rate/ or spirometry or forced expiratory volume or FEV1 or forced vital capacity or FVC or forced expiratory flow FEF25-75 or peak expiratory flow or lung volume* or air?trapping or residual volume or RV functional residual capacity FRC or lung hyperinflation or total lung capacity or TLC.mp. 109699

30 exp Plethysmography/ 21798

31 (plethysmography or airway resistance or airway reactance or airway impedance).mp. 38466

32 30 or 31 42409

33 exp Magnetic Resonance Imaging/ 494505

34 exp Pulmonary Gas Exchange/ 20660

35 exp Ventilation/ 6090

36 (diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI).mp. 1103454

37 33 or 34 or 35 or 36 1120608

38 exp Sputum/ 22354

39 (sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration).mp. 77905

40 38 or 39 77905

41 exp Mucociliary Clearance/ or radioaerosol clearance.mp. or scintigraphy.mp. or cough clearance.mp. or cough transport.mp. or biophysical propert*.mp. 50304

42 exp Viscosity/ or exp Elasticity/ or exp Mucins/ or exp Mucus/ or surface propert*.mp. or tenacity.mp. or cohesivity.mp. or adhesivity.mp. or viscoelasticity.mp. or rheology*.mp. or rigidity transportability.mp. or ciliary movement.mp. or mucus hydration.mp. or solid content.mp. or solid percentage.mp. or mucin.mp. 282208

43 exp Bacterial Load/ or exp Osmotic Pressure/ or osmotic pressure.mp. or interfacial tension.mp. or bacterial load.mp. or bacterial density.mp. or bacterial eradication.mp. or pathogens.mp. or microbiology.mp. or inflammat*.mp. 2151731

44 exp Leukocyte Elastase/ or exp Peroxidase/ or exp Interleukins/ or exp Cell Count/ or marker*.mp. or neutrophil elastase.mp. or myeloperoxidase.mp. or interleukin*.mp. or cell count*.mp. 1473139

45 exp Respiratory Sounds/ or respiratory sound*.mp. or breath sound*.mp. or crackle*.mp. or wheeze*.mp. 18690

46 exp Exercise/ or exp Sleep/ or exp Anxiety/ or exp Depression/ or exp Dyspnea/ or exp Fatigue/ or exercise capacity.mp. or physical activity.mp. or sleep.mp. or anxiety.mp. or depression.mp. or symptom.mp. or dyspnea.mp. or breathlessness.mp. or fatigue.mp. or exacerbat*.mp. 1488792

47 (patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment).mp. 3683907

48 exp Patient Satisfaction/ or exp Patient Preference/ or exp Medication Adherence/ or exp Guideline Adherence/ or exp "Treatment Adherence and Compliance"/ or exp Self-Management/ or exp Self Efficacy/ or exp Anti-Bacterial Agents/ 1081177

49 exp Community Participation/ or participation.mp. or life role*.mp. or social role*.mp. or role function*.mp. or community engagement.mp. or integration.mp. or days of absence.mp. 412965

50 21 or 24 or 27 or 28 or 29 or 32 or 37 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 10999990

51 17 and 50 1470

52 (methodology or qualitative or quantitative or measure* or study or studies or review*).mp. 16760006

53 qualitative research/ 69671

54 exp Research Design/ 471736

55 52 or 53 or 54 16851487

56 51 and 55 1196

Embase <1974 to November 2021>

1 exp bronchiectasis/ 23558

2 (bronchiectasis or bronchiectases or kartageners syndrome).mp. 25789

3 1 or 2 26373

4 exp physiotherapy/ 97558

5 (physiotherap* or physical therap*).mp. 141191

6 4 or 5 142318

7 (airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp. 14312

8 (bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp. 9466

9 (10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp. 379529

10 (IPPB or intermittent positive pressure breathing).mp. 555

11 (IPV or intrapulmonary percussive ventilation).mp. 8788

12 (HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp. 30540

13 (autogenic drainage or AD).mp. 675962

14 (ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp. 114

15 (ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp. 60328

16 (thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp. 179334

17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 1462641

18 3 and 17 5471

19 exp hospital/ or exp hospital readmission/ or exp prognosis/ or exacerbation*.mp. 2309111

20 (hospit* or readmission or emergency attendance or disease prognos*).mp. 2968142

21 (day* adj3 recovery).mp. 12528

22 19 or 20 or 21 4097877

23 exp patient-reported outcome/ 39804

24 (BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*).mp. 494148

25 23 or 24 494852

26 exp "quality of life"/ 577730

27 (quality of life or QoL or HRQoL or health?related quality of life).mp. 710962

28 26 or 27 710962

29 exp coughing/ or cough*.mp. or pulmonary function*.mp. or lung function*.mp. 326350

30 exp peak expiratory flow/ or spirometry.mp. or forced expiratory volume.mp. or FEV1.mp. or forced vital capacity.mp. or FVC.mp. or forced expiratory flow FEF25-75.mp. or peak expiratory flow.mp. or lung volume*.mp. or air?trapping.mp. or residual volume.mp. or RV functional residual capacity FRC.mp. or lung hyperinflation.mp. or total lung capacity.mp. or TLC.mp. 201127

31 exp plethysmography/ 27475

32 (plethysmography or airway resistance or airway reactance or airway impedance).mp. 46361

33 31 or 32 46361

34 exp nuclear magnetic resonance imaging/ 1109244

35 exp lung gas exchange/ 13413

36 (diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI).mp. 1833235

37 34 or 35 or 36 1885023

38 exp sputum/ 26181

39 (sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration).mp. 121017

40 38 or 39 121017

41 exp mucociliary clearance/ or radioaerosol clearance.mp. or scintigraphy.mp. or cough clearance.mp. or cough transport.mp. or biophysical propert*.mp. 88499

42 exp viscosity/ or exp elasticity/ or exp mucins/ or exp mucus/ or surface propert*.mp. or tenacity.mp. or cohesivity.mp. or adhesivity.mp. or viscoelasticity.mp. or rheology*.mp. or rigidity transportability.mp. or ciliary movement.mp. or mucus hydration.mp. or solid content.mp. or solid percentage.mp. or mucin.mp. 425259

43 exp bacterial load/ or exp osmotic pressure/ or osmotic pressure.mp. or interfacial tension.mp. or bacterial load.mp. or bacterial density.mp. or bacterial eradication.mp. or pathogens.mp. or microbiology.mp. or inflammat*.mp. 2342191

44 exp leukocyte elastase/ or exp peroxidase/ or exp interleukins/ or exp cell count/ or marker*.mp. or neutrophil elastase.mp. or myeloperoxidase.mp. or interleukin*.mp. or cell count*.mp. 2752802

45 exp respiratory sounds/ or respiratory sound*.mp. or breath sound*.mp. or crackle*.mp. or wheeze*.mp. 72377

46 exp exercise/ or exp sleep/ or exp anxiety/ or exp depression/ or exp dyspnea/ or exp fatigue/ or exercise capacity.mp. or physical activity.mp. or sleep.mp. or anxiety.mp. or depression.mp. or symptom.mp. or dyspnea.mp. or breathlessness.mp. or fatigue.mp. or exacerbat*.mp. 2919077

47 (patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment).mp. 3865819

48 exp patient satisfaction/ or exp patient preference/ or exp medication compliance/ or exp protocol compliance/ or patient compliance/ or self-care/ or exp antiinfective agent/ 4314376

49 exp community participation/ or participation.mp. or life role*.mp. or social role*.mp. or role function*.mp. or community engagement.mp. or integration.mp. or days of absence.mp. 502392

50 22 or 25 or 28 or 29 or 30 or 33 or 37 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 16322829

51 18 and 50 5366

52 limit 51 to yr="1883 - 2021" 5260

53 (methodology or qualitative or quantitative or measure* or study or studies or review*).mp. 24290083

54 exp qualitative research/ 95231

55 exp methodology/ 6666989

56 53 or 54 or 55 24888340

57 52 and 56 4130

58 Limit to Embase 2680

AMED (Allied and Complementary Medicine) <1985 to November 2021>

1 bronchiectasis/ 37

2 (bronchiectasis or bronchiectases or kartageners syndrome).mp. [mp=abstract, heading words, title] 52

3 1 or 2 52

4 exp physical therapy modalities/ 30639

5 (physiotherap* or physical therap*).mp. [mp=abstract, heading words, title] 24343

6 4 or 5 44896

7 (airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp. [mp=abstract, heading words, title] 121

8 (bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp. [mp=abstract, heading words, title] 446

9 (10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp. [mp=abstract, heading words, title] 2840

10 (IPPB or intermittent positive pressure breathing).mp. [mp=abstract, heading words, title] 13

11 (IPV or intrapulmonary percussive ventilation).mp. [mp=abstract, heading words, title] 16

12 (HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp. [mp=abstract, heading words, title] 173

13 (autogenic drainage or AD).mp. [mp=abstract, heading words, title] 930

14 (ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp. [mp=abstract, heading words, title] 6

15 (ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp. [mp=abstract, heading words, title] 1146

16 (thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp. [mp=abstract, heading words, title] 957

17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 48924

18 3 and 17 28

19 exp Hospitals/ or exp Hospitalization/ or exp Prognosis/ or exacerbation*.mp. [mp=abstract, heading words, title] 26356

20 (hospit* or readmission or emergency attendance or disease prognos*).mp. [mp=abstract, heading words, title] 15489

21 (day* adj3 recovery).mp. [mp=abstract, heading words, title] 104

22 19 or 20 or 21 36382

23 (BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*).mp. [mp=abstract, heading words, title] 2654

24 "quality of life"/ 10535

25 (quality of life or QoL or HRQoL or health?related quality of life).mp. [mp=abstract, heading words, title] 14890

26 24 or 25 14890

27 Cough/ or cough*.mp. or pulmonary function*.mp. or lung function*.mp. 1759

28 Peak Expiratory Flow Rate/ or spirometry.mp. or (forced adj2 expiratory adj2 volume).mp. or FEV1.mp. or (forced adj2 vital adj2 capacity).mp. or FVC.mp. or (forced adj2 expiratory adj2 flow).mp. or FEF25-75.mp. or (peak adj2 expiratory adj2 flow).mp. or (lung adj2 volume*).mp. or air?trapping.mp. or (residual adj2 volume).mp. or (RV adj2 functional adj2 residual adj2 capacity adj2 FRC).mp. or (lung adj2 hyperinflation).mp. or (total adj2 lung adj2 capacity).mp. or TLC.mp. [mp=abstract, heading words, title] 1563

29 plethysmography/ 26

30 (plethysmography or airway resistance or airway reactance or airway impedance).mp. [mp=abstract, heading words, title] 246

31 29 or 30 246

32 magnetic resonance imaging/ 1818

33 pulmonary gas exchange/ 60

34 (diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI).mp. [mp=abstract, heading words, title] 5707

35 32 or 33 or 34 5707

36 sputum/ 46

37 (sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration).mp. [mp=abstract, heading words, title] 421

38 36 or 37 421

39 Mucociliary Clearance/ or radioaerosol clearance.mp. or scintigraphy.mp. or cough clearance.mp. or cough transport.mp. or biophysical propert*.mp. [mp=abstract, heading words, title] 133

40 Elasticity/ or Viscosity/ or Mucus/ 295

41 (surface propert* or tenacity or cohesivity or adhesivity or viscoelasticity or rheology* or rigidity transportability or ciliary movement or mucus hydration or solid content or solid percentage or mucin).mp. 158

42 (osmotic pressure or interfacial tension or bacterial load or bacterial density or bacterial eradication or pathogens or microbiology or inflammat*).mp. [mp=abstract, heading words, title] 9800

43 (marker* or neutrophil elastase or myeloperoxidase or interleukin* or cell count*).mp. [mp=abstract, heading words, title] 5030

44 respiratory sounds/ or respiratory sound*.mp. or breath sound*.mp. or crackle*.mp. or wheeze*.mp. 92

45 exp Exercise/ or exp Sleep/ or Anxiety/ or Depression/ or Dyspnea/ or exp Fatigue/ or exercise capacity.mp. or physical activity.mp. or sleep.mp. or anxiety.mp. or depression.mp. or symptom.mp. or dyspnea.mp. or breathlessness.mp. or fatigue.mp. or exacerbat*.mp. 36736

46 (patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment).mp. [mp=abstract, heading words, title] 39617

47 patient participation/ or exp "patient acceptance of health care"/ or self care/ or self efficacy/ 9393

48 (participation or life role* or social role* or role function* or community engagement or integration or days of absence).mp. 9967

49 22 or 23 or 26 or 27 or 28 or 31 or 35 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 122778

50 18 and 49 22

51 (methodology or qualitative or quantitative or measure* or study or studies or review*).mp. [mp=abstract, heading words, title] 153414

52 research design/ 2290

53 51 or 52 154425

54 50 and 53 13

CINAHL

S39	S36 AND S38	66
S38	methodology or qualitative or quantitative or measure* or study or studies or review*	3,419,562
S36	S18 AND S35	473
S35	S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34	2,668,310
S34	Participation or life role* or social role* or role function* or community engagement or integration or days of absence	194,643
S33	patient* feedback or patient* preference* or patient* experience* or patient view* or patient perspective* or patient accept* or scale* or visual analogical scale* or tolerability or feasibility or adherence or self-management or self-efficacy or side effect* or adverse effect* or adverse event* or extra medication or antibiotic us* or burden of treatment	1,429,152
S32	exercise capacity or physical activity or sleep or anxiety or depression or symptom or dyspnea or breathlessness or fatigue or exacerbat*.	795,076
S31	respiratory sound* or breath sound* or crackle* or wheeze*	4,390
S30	marker* or neutrophil elastase or myeloperoxidase or interleukin* or cell count*	217,039
S29	osmotic pressure or interfacial tension or bacterial load or bacterial density or bacterial eradication or pathogens or microbiology or inflammat*.	257,699
S28	surface propert* or tenacity or cohesivity or adhesivity or viscoelasticity or rheology* or rigidity transportability or ciliary movement or mucus hydration or solid content or solid percentage or mucin	8,646
S27	mucociliary clearance or radioaerosol clearance or scintigraphy or cough clearance or cough transport or biophysical propert*	7,452

S26	sputum or sputum weight or sputum volume or sputum quantity* or sputum colo?r or sputum purulence or sputum propert* or sputum cytology or expectoration or mucociliary transport or mucus* or mucociliary clearance or ease of expectoration	9,711
S25	diffusion or DLCO or gas exchange or HRCT or high?resolution computed tomography or saturation or lung clearance index or multiple breath washout or ventilation inhomogeneity or ventilation or magnetic resonance imag* or MRI	262,176
S24	plethysmography or airway resistance or airway reactance or airway impedance	5,176
S23	spirometry or forced expiratory volume or FEV1 or forced vital capacity or FVC or forced expiratory flow FEF or peak expiratory flow or lung volume* or air trapping or residual volume or lung hyperinflation or total lung capacity or TLC	26,445
S22	cough* or pulmonary function* or lung function*	37,780
S21	quality of life or QoL or HRQoL or health?related quality of life	226,292
S20	BSI or FACED or E-FACED or patient-reported outcome* or PRO or Patient Reported Experience* or PREM or patient?reported experience measure*	74,079
S19	hospit * or readmission or emergency attendance or disease prognos* or (day N3 recovery)	37,883
S18	S3 AND S17	502
S17	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	378,799
S16	thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation	46,820
S15	ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration	7,463
S14	ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*	47

S13	autogenic drainage or AD	60,779
S12	HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*	3,868
S11	IPV or intrapulmonary percussive ventilation	10,477
S10	IPPB or intermittent positive pressure breathing	218
S9	10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP	67,809
S8	bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*	3,476
S7	airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance	1,744
S6	S4 OR S5	193,173
S5	physiotherap* or physical therap*	85,201
S4	(MH "Physical Therapy+")	153,140
S3	S1 OR S2	2,344
S2	bronchiectasis or bronchiectases or kartageners syndrome	2,344
S1	(MH "Bronchiectasis")	1,295

Cochrane CENTRAL

There were no records retrieved in Cochrane CENTRAL

PEDro

There were no records retrieved in PEDro

Search strategy (b)

Database: Ovid MEDLINE® ALL <1946 to November 2021>

1	exp Respiratory Tract Infections/ or exp Respiratory Tract Diseases/	1557604
2	limit 1 to (“young adult (19 to 24 years)” or “adult (19 to 44 years)” or “young adult and adult (19-24 and 19-44)” or “middle age (45 to 64 years)” or “middle aged (45 plus years)” or “all aged (65 and over)” or “aged (80 and over)”)	654517
3	exp Physical Therapy Modalities/	166262
4	(hysiotherapy* or physical therap*).mp.	78124
5	4 or 5	199815
6	(airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp	6585
7	(bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp.	4484
8	(10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp.	279774
9	(IPPB or intermittent positive pressure breathing).mp.	1132
10	(IPV or intrapulmonary percussive ventilation).mp.	7488
11	(HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp.	22276
12	(autogenic drainage or AD).mp.	163112
13	(ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp.	80
14	(ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp.	50544
15	(thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp.	78270
16	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	789940
17	exp Feedback/	31702
18	exp Culture/	172636

19 exp Attitude to Health/ or exp Attitude/ 634144

20 exp Perception/ or exp Social Perception/ 463601

21 exp Patient Reported Outcome Measures/ 10872

22 exp Patient-Centered Care/ 22837

23 (PREM or patient?reported experience* or patient?reported outcome* or patient?centred or patient?centered).ti,ab. 305

24 (barrier* or enabler* or belief* or social impact* or burden impact* or perspective* or feedback or qualitative or adherence or core themes* or attitude* or perception* or opinion* or experience* or hysiother* or help or support or hinder or difficult or satisfaction or preference or acceptance or voice or benefit).ti,ab. 5170748

25 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 5844237

26 16 and 25 205027

27 2 and 26 7725

28 27 not (covid or coronavirus or knee or liver or kidney or diabetes or pregnan* or child or children or p?ediatric).mp. 1092

Embase <1974 to November 2021>

1 respiratory tract infection/ or respiratory tract disease/ 124256

2 limit 1 to (adult <18 to 64 years> or aged <65+ years>) 39614

3 exp physiotherapy/ 95401

4 (hysiotherapy* or physical therap*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 137949

5 3 or 4 139050

6 (airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).ti,ab. 8847

7 (bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).ti,ab. 2037

8 (10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).ti,ab. 327980

9 (IPPB or intermittent positive pressure breathing).ti,ab. 515

10 (IPV or intrapulmonary percussive ventilation).ti,ab. 8126

11 (HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).ti,ab. 29258

12 (autogenic drainage or AD).ti,ab. 225160

13 (ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).ti,ab. 110

14 (ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).ti,ab. 38203

15 (thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).ti,ab. 68835

16 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 831523

17 exp feedback system/ 125559

18 exp cultural anthropology/ 54184

19 attitude to health/ or attitude/ 188253

20 perception/ 135619

21 exp patient-reported outcome/ 36700

22 patient care/ 323082

23 (PREM or patient?reported experience* or patient?reported outcome* or patient?centred or patient?centered).ti,ab. 2315

24 (barrier* or enabler* or belief* or social impact* or burden impact* or perspective* or feedback or qualitative or adherence or core themes* or attitude* or perception* or opinion* or experience* or hysiother* or help or support or hinder or difficult or satisfaction or preference or acceptance or voice or benefit).ti,ab. 6751743

25 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 7119942

26 16 and 25 238048

27 2 and 26 534

28 27 not (covid or coronavirus or knee or liver or kidney or diabetes or pregnan* or child or children or p?ediatric).mp. 351

29 Limit to Embase 233

AMED (Allied and Complementary Medicine) <1985 to November 2021>

1 exp respiratory tract infections/ or exp respiratory tract disease/ 9187

2 (respiratory tract* adj2 (disease* or infection*)).mp. [mp=abstract, heading words, title] 943

3 1 or 2 9257

4 exp physical therapy modalities/ 30639

5 (hysiotherapy* or physical therap*).mp. [mp=abstract, heading words, title] 24343

6 4 or 5 44896

7 (airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance).mp. [mp=abstract, heading words, title] 121

8 (bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*).mp. [mp=abstract, heading words, title] 446

9 (10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP).mp. [mp=abstract, heading words, title] 2840

10 (IPPB or intermittent positive pressure breathing).mp. [mp=abstract, heading words, title] 13

11 (IPV or intrapulmonary percussive ventilation).mp. [mp=abstract, heading words, title] 16

12 (HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*).mp. [mp=abstract, heading words, title] 173

13 (autogenic drainage or AD).mp. [mp=abstract, heading words, title] 930

14 (ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*).mp. [mp=abstract, heading words, title] 6

15 (ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration).mp. [mp=abstract, heading words, title] 1146

16 (thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation).mp. [mp=abstract, heading words, title] 957

17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 48924

18 feedback/ 506

19 exp culture/ 3921

20 attitude to health/ or attitude/ 4638

21 exp perception/ 4624

22 patient centered care/ 551

23 (PREM or patient?reported experience* or patient?reported outcome* or patient?centred or patient?centered).mp. 3

24 (barrier* or enabler* or belief* or social impact* or burden impact* or perspective* or feedback or qualitative or adherence or core themes* or attitude* or perception* or opinion* or experience* or hysiother* or help or support or hinder or difficult or satisfaction or preference or acceptance or voice or benefit).ti,ab. 77504

25 18 or 19 or 20 or 21 or 22 or 23 or 24 83869

26 17 and 25 12076

27 3 and 26 439

28 27 not (covid or coronavirus or knee or liver or kidney or diabetes or pregnan* or child or children or p?ediatric).mp. 380

CINAHL

S27	S25 not S26	8,418
S26	covid or coronavirus or knee or liver or kidney or diabetes or pregnan* or child or children or p?ediatric	1,533,434
S25	S1 AND S24	10,888
S24	S15 AND S23	125,028
S23	S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22	2,106,499
S22	barrier* or enabler* or belief* or social impact* or burden impact* or perspective* or feedback or qualitative or adherence or core themes* or attitude* or perception* or opinion* or experience* or hysiother* or help or support or hinder or difficult or satisfaction or preference or acceptance or voice or benefit	2,092,838
S21	PREM or patient?reported experience* or patient?reported outcome* or patient?centred or patient?centered)	3,119
S20	(MH “Patient-Reported Outcomes”)	3,956
S19	(MH “Perception”)	30,838
S18	(MH “Attitude to Health”)	47,346
S17	(MH “Culture”)	30,664
S16	(MH “Feedback”)	16,999
S15	S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	382,225
S14	thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation	47,201
S13	ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration	7,473

S12	ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*	48
S11	autogenic drainage or AD	62,286
S10	HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*	3,923
S9	IPV or intrapulmonary percussive ventilation	10,567
S8	IPPB or intermittent positive pressure breathing	221
S7	10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP	68,300
S6	bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*	3,512
S5	airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance	1,756
S4	S2 OR S3	194,094
S3	hysiotherapy* or physical therap*	86,119
S2	(MH “Physical Therapy+”)	153,538
S1	(MH “Respiratory Tract Diseases+”) OR (MH “Respiratory Tract Infections+”)	321,335

Cochrane CENTRAL 1947 – 2021

**This iteration of the strategy is truncated due to the large numbers of results retrieved for the full search.*

#1	MeSH descriptor: [Respiratory Tract Infections] explode all trees	17796
#2	MeSH descriptor: [Respiratory Tract Diseases] explode all trees	67532

#3 #1 or #2 67532

#4 MeSH descriptor: [Physical Therapy Modalities] explode all trees 29256

#5 (physiotherap* or physical therap*) 86806

#6 #4 or #5 102655

#7 (airway* clearance or sputum clearance or mucus clearance or lung clearance or tracheobronchial clearance or mucociliary clearance) 3478

#8 (bronchopulmonary hygiene or pulmonary hygiene or lung hygiene or breathing exercise*) 6500

#9 (10 oscilat* or PEP or positive expiratory pressure or Flutter or Acapella or Cornet or Quake or Aerobika or Threshold or TheraPEP) 35034

#10 (IPPB or intermittent positive pressure breathing) 567

#11 (IPV or intrapulmonary percussive ventilation) 1520

#12 (HFCWO or High Frequency Chest Wall Oscillation or chest wall* or thoracic wall*) 3337

#13 (autogenic drainage or AD) 32984

#14 (ELTGOL or Expiration Lente Totale Glotte Ouverte or slow expiration* or glottis opened or slow expiratory*) 627

#15 (ACBT or active cycle* or postural drainage or gravity?assisted drainage or percussion or clapping or vibration) 9799

#16 (thoracic expansion or FET or forced expirat* or huff* or inspiratory muscle training or respiratory therapy or mechanical stress or shaker or shaking or non?invasive ventilation) 61552

#17 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 226196

#18 (PREM or "patient-reported experience*" or "patient reported outcome*" or "patient-centred" or "patient centered") 12491

#19 #17 and #18 3420

#20 #3 and #19 262

#21 (covid or coronavirus or knee or liver or kidney or diabetes or pregnan* or child or children or p?ediatric) 471603

#22 #20 not #21 151

#23 Cochrane CENTRAL 1947-2021 128

PEDro

Respiratory tract infection* (34)

Respiratory tract disease* (10)

Question 5 - In adults with bronchiectasis, how should studies for ACTs be conducted to reduce the risk of bias, facilitate comparison of findings, as well as conducting future meta-analyses?

Selection criteria

	Population	Disease	Clinical status	Study design	Active treatment	Comparison	Outcomes	Comments
Inclusion	Adults (≥18 y) Male or female	Bronchiectasis Overlaps (COPD, Asthma) Primary ciliary dyskinesia Kartagener syndrome	Stable Exacerbation Hospital Admission	RCT (equivalence) Crossover Non-inferiority trial Superiority trial	ACTs Combined ACTs	Placebo Sham intervention ACT alone Combined ACTs Usual care Other (PR, mucoactive) No treatment	Random sequence Allocation concealment Blinding of participants Blinding of assessors Blinding of researchers in charge of intervention Incomplete data Selective reporting	i) Studies recruiting more than one disease at the same time (e.g COPD and bronchiectasis) will be only included if specific data from bronchiectasis could be extracted ii) Abstracts are included
	Population	**Disease**	**Clinical status**	**Study design**	**Active treatment**	**Comparison**	**Outcomes**	**Comments**
Exclusion	Children (<18y) Animal models In vitro	CF COPD Asthma ILD Other respiratory disease	Intensive Care	Quasi-experimental Cross-sectional Cohort Case-control Qualitative Systematic Review Narrative review	PR IMT Exercise NIV Muco-active drugs Invasive methods	N/A	N/A	

COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis; ILD, interstitial lung disease; RCT, randomised controlled trial; ACTs, airway clearance techniques; PROs, patient reported outcomes; PR, pulmonary rehabilitation; IMT, inspiratory muscle training; NIV, non-invasive ventilation N/A, not applicable

Search strategy

The same search strategy was used as in question 4.