Patient-managed interventions for adults with bronchiectasis: evidence, challenges and prospects

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Patient-managed interventions are key components of the bronchiectasis management. These include airway clearance techniques and hyperosmolar agents, pulmonary rehabilitation, nutrition, self-management programmes and potentially cough management. https://bit.ly/3XeNpwU

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Abstract

Bronchiectasis is a chronic lung condition which is characterised by recurrent chest infections, chronic sputum production and cough, and limited exercise tolerance. While bronchiectasis may be caused by various aetiologies, these features are shared by most patients with bronchiectasis regardless of the cause. This review consolidates the existing evidence on patient-managed interventions for adults with bronchiectasis, while also outlining areas for future research. Airway clearance techniques and hyperosmolar agents are key components of the bronchiectasis management and consistently recommended for clinical implementation. Questions around their prescription, such as optimal sequence of delivery, are still to be answered. Pulmonary rehabilitation and exercise are also recommended for patients with bronchiectasis. Relatively strong evidence underpins this recommendation during a clinically stable stage of the disease, although the role of pulmonary rehabilitation following an exacerbation is still unclear. Additionally, self-management programmes feature prominently in bronchiectasis treatment, yet the lack of consensus regarding their definition and outcomes presents hurdles to establishing a cohesive evidence base. Moreover, cough, a cardinal symptom of bronchiectasis, warrants closer examination. Although managing cough in bronchiectasis may initially appear risky, further research is necessary to ascertain whether strategies employed in other respiratory conditions can be safely and effectively adapted to bronchiectasis, particularly through identifying patient responder populations and criteria where cough may not enhance airway clearance efficacy and its control is needed. Overall, there is a growing recognition of the importance of patient-managed interventions in the bronchiectasis management. Efforts to improve research methodologies and increase research funding are needed to further advance our understanding of these interventions, and their role in optimising patient care and outcomes.

Introduction

Bronchiectasis is a common chronic respiratory disease, with important geographical variation in causes, severity and outcomes [1]. It is increasing in prevalence, reaching 0.25–0.50% of the adult population, and

making bronchiectasis the third airway disease in prevalence, following asthma and COPD [2–4]. Bronchiectasis leads to a considerable economic burden for healthcare systems and patients [5, 6]. Patients present frequent respiratory infections, high sputum volumes and sputum purulence, cough, fatigue, limited exercise tolerance and dyspnoea [7]. Various aetiologies can cause bronchiectasis, and at times the cause may be undetermined. However, these features are shared by most patients with bronchiectasis regardless of the cause. Quality of life and wellbeing of the patients with bronchiectasis is often impaired and related to disease symptoms and their severity [8, 9], particularly for symptoms such as cough, sputum and fatigue [9–12].

Treatment for bronchiectasis aims at managing symptoms, preventing complications and improving quality of life. International and national clinical guidelines for bronchiectasis recommend pharmacological and patient-managed interventions [13–15]. Pharmacological management of bronchiectasis includes antibiotics, bronchodilators and corticosteroids, often through inhaled administration [16]. Recommended patient-managed interventions that require active engagement and behavioural changes, often called nonpharmacological interventions, are airway clearance techniques (ACTs) and pulmonary rehabilitation [13–15, 17]. In alignment with the terminology argument from the *Thorax* editorial "Reclaiming the name 'bronchiectasis'" [18], we have opted to employ the term "patient-managed interventions" in lieu of "nonpharmacological interventions". This terminology shift aims to delineate interventions based on their intrinsic characteristics rather than their absence of pharmacological elements.

Patient-managed interventions have received less attention in research compared to pharmacological ones. The purpose of this review is to present the evidence of patient-managed interventions for bronchiectasis, including ACTs with or without the inhalation of hyperosmolar agents, pulmonary rehabilitation and self-management, considerations about their implementation, and areas of future research direction that can become part of a comprehensive health approach. We focus the review on adults with bronchiectasis not caused by cystic fibrosis, as there is a wide variability between children and adults, and as studies have traditionally differentiated these age and disease categories.

Patient-managed interventions

Airway clearance techniques

ACTs are patient-managed interventions specifically developed to generate greater mechanical airway stress, such as shear stress, compression or stretch, compared to normal breathing and its stimulating hydration on the mucus layer [17, 19]. Additionally, these techniques may aim to increase the peak expiratory flow and generate a flow bias between the two respiratory phases, thus breaking the adhesive bonds of the mucus layer and enhance mucociliary clearance and ventilation distribution [17, 19]. The breathing pattern of patients is changed using these techniques, generally by increasing the volume mobilised, including post-inhalation pauses, prolonging the expiratory phase, generating airway oscillations and using forced expiratory manoeuvres. Further information on the procedures of individual ACTs is available in online resources (https://impact-be.com/about-acts/, https://smr-b.com, [20]). Hyperosmolar agents, such as hypertonic saline and mannitol, produce an osmotic shock in the airways that acutely improves the biophysical properties and hydration of the mucus layer [21]. Alongside stimulating cough, this leads to accelerated mucus transportability [21].

International and national clinical guidelines for the management of adults with bronchiectasis recommend the routine use of ACTs, with and without hyperosmolar agents [13–15, 22, 23]. ACTs are considered essential strategies to improve the management of sputum-related symptoms and prevent the negative impact on health-related quality of life (HRQoL) and social interactions caused by these symptoms [13–15, 22, 23]. In addition to reducing the burden of symptoms, ACTs and hyperosmolar agents aim to reduce the risk of exacerbations and prevent hospitalisations by enhancing the clearance of inflammatory markers and modulating the bacterial load in the airways [17]. However, the level of recommendation reported in the guidelines for ACTs and hyperosmolar agents is variable, ranging from weak to strong, and is supported by low- to moderate-quality evidence [15, 24]. Reasons for this variability may be due to the paucity of long-term randomised trials, a heterogeneity of treatment responses [17], absence of clear evidence of superiority of one technique or hyperosmolar agent over others, or even the use of different methodological approaches to determine evidence [25, 26]. Furthermore, additional factors or patient characteristics which influence adherence to airway clearance therapy might influence treatment recommendation. Those with greater disease severity are more likely to engage in regular airway clearance therapy, so this may account for variations in treatment recommendations, particularly in the frequency of ACT prescription [25, 27]. Access to ACT specialists and use of airway clearance management are limited in people with bronchiectasis and differ across European countries. Data from the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) registry showed that ~48% of 16 723 patients do not

regularly perform any airway clearance intervention [25]. This rate was higher in central and eastern Europe compared to other European countries [25]. To date, the lack of concrete instructions on how to identify respondents to referral and uptake for these treatments, and how to implement them in clinical practice may be barriers that limit their accessibility and acceptability.

According to the guidelines, regular use of ACTs is the first-line treatment for people with bronchiectasis and sputum-related symptoms, while hyperosmolar agents only complement this treatment when sputum expectoration remains difficult, or ACTs fail to reduce the burden of sputum symptoms [13, 14]. Specific details on how to implement ACTs are scarce in the guidelines, except for the British Thoracic Society (BTS) guideline [14]. This national guideline advises the provision of at least two sessions of teaching ACTs by a respiratory physiotherapist, followed by regular annual reviews and additional appointments when there is a clinical deterioration [14]. Moreover, during a hospital admission, the BTS guideline recommends daily ACTs sessions guided by a respiratory physiotherapist until ACTs are optimised [14]. The most recent systematic review evaluating the ACTs effects during an acute exacerbation in bronchiectasis showed that these interventions are safe during this clinical stage and patients seem to prefer the use of ACT devices, such as oscillating positive expiratory pressure devices [28]. The ACT devices are generally well accepted by the patients because they offer the possibility to perform the treatment independently and they are easy to teach and learn, as well as they can be used in combination with other techniques [17]. However, characteristics of the device (size, weight, noise), the time needed for cleaning and disinfection, and their cost are barriers to long-term adherence [17]. Although the optimal frequency and duration of ACTs sessions in a clinically stable stage or during exacerbations is unknown, decisions are tailored to the patients and aim to achieve a balance between clinical benefits and treatment burden [17].

Treatment duration and selection of participants for the ACT studies could further guide clinical management. To date, only three long-term trials (⩾3 months) have evaluated the benefits of ACTs in adults with bronchiectasis [29–31]. These studies show that regular use of ACTs reduces the impact of sputum-related symptoms, improves the HRQoL, and reduces the frequency of exacerbations [29–31]. Considering that the only selection criterion in two of these studies was the presence of sputum expectoration (table 1), it is likely that response to ACTs is potentially hindered by participants with limited sputum-related symptoms at baseline. Consequently, future studies evaluating the ACTs in bronchiectasis need to prioritise the selection of participants who are more likely to respond to these treatments. For instance, respondents to ACTs could be patients who report a negative impact on HRQoL due to the presence of sputum-related symptoms. The assessment of long-term effectiveness (⩾6 months) is also needed.

Hyperosmolar agents

Hyperosmolar agents are used in addition to ACTs to enhance mucociliary clearance in bronchiectasis. There is evidence supporting the role of hyperosmolar agents during clinically stable stages of bronchiectasis. Usually, they are prescribed twice daily and prior to ACTs, based on the benefits observed in a study for adults with cystic fibrosis [37]. When the hyperosmolar agents are part of the airway clearance management alongside ACTs, they can also be administered during the ACTs. However, the effects of the hyperosmolar agents on the acceleration of mucus clearance may be less and of shorter duration in people with bronchiectasis compared to adults with cystic fibrosis, due to presenting comparatively less mucus dehydration [38]. Therefore, the optimal prescription of hyperosmolar agents in bronchiectasis, including dosage and frequency, could be different. Although the timing of hyperosmolar agent administration, *i.e.* before, during or after ACTs, has rarely been explored in bronchiectasis, people with cystic fibrosis perceived greater efficacy and satisfaction when hypertonic saline was inhaled before or during ACTs [39]. The role of hyperosmolar agents during an acute exacerbation in bronchiectasis is unknown.

For the implementation of hyperosmolar agents, the guidelines recommend a tolerability test before starting therapy and using a bronchodilator prior to the inhalation of the hyperosmolar agents [13, 14, 22, 23]. In clinical practice, informing patients that they may experience increased coughing, salty sensation and throat irritation with this treatment may help the patient to better adapt to these minor adverse effects. For people who fail the tolerability test using hypertonic saline nebulisation, it is possible to add hyaluronic acid to the saline solutions to improve tolerance and pleasantness [40, 41]. The role of hyaluronic acid is to reduce bronchospasm and balance airway water homeostasis [42], and it allows approximately two-thirds of people who are intolerant to hypertonic saline to tolerate this treatment [41]. Although the implementation of long-term monitoring of this treatment is not usually mentioned in the guidelines, periodic reviews to monitor inhalation technique and assess the impact of minor adverse events may be appropriate.

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TABLE 1 Main characteristics of the long-term trials (⩾3 months) evaluating airway clearance management effects in people with bronchiectasis

First author, year [reference] (country)	Study design	Participants n	Selection criteria related to sputum symptoms	Baseline clinical characteristics related to sputum symptoms	Hyperosmolar solution	ACTs	Frequency and duration
Nicolini, 2022 [31] (Italy)	Randomised controlled trial	79	None	LCQ (group 1): 10.2±1.2/LCQ (group 2): 10.0±1.4/LCQ (control): 10.4±1.2 BHQ (group 1): 44.0±2.9/BHQ (group 2): 39.0±3.3/BHQ (control): 49.2±3.2 BCSS (group 1): 6.0±0.7/BCSS (group 2): 5.5±0.9/BCSS (control): 5.2±1.0 CAT (group 1): 15.9±2.0/CAT (group 2): 15.0±1.9/CAT (control): 14.3±1.8	NA	HFCWO (SmartVest) *versus* HFCWO (RespIn) *versus* usual care	ACT session: 20 min Frequency: twice per day Treatment duration: 54 weeks
Muñoz, 2018 [30] (Spain)	Randomised controlled trial	44	⩾10 mL of daily expectoration	24-h sputum volume (exp): 20 (15–40) mL/24-h sputum volume (control): 15 (15–20) mL LCQ (exp): 14.5±3.4/LCQ (control): 15.7±1.9 SGRQ (exp): 40.2±13.7/SGRQ (control): 35.0±9.9 mMRC (exp): 1 (0–1.25)/mMRC (control): 1 (1–1.25)	NA	ELTGOL *versus* placebo intervention (stretching)	ACT session: 15 or 30 min Frequency: twice per day Treatment duration: 52 weeks
Bilton, 2014 [32] (USA, Europe, Australia, New Zealand, South America)	Randomised controlled trial	461	>10 mL of daily expectoration SGRQ ⩾30	24-h sputum volume (exp): 28.9±18.7 mL/24-h sputum volume (control): 29.0±19.9 mL SGRQ (exp): 53.0±14.6/SGRQ (control): 52.2±14.7	Mannitol (400 mg) *versus* low-dose mannitol (50 mg)	O-PEP (Acapella) Not monitored	Hyperosmolar session: dry power inhalation (20 capsules per day) ACT session: NR Frequency: twice per day Treatment duration: 54 weeks
Bilton, 2013 [33] (Australia, New Zealand and UK)	Randomised controlled trial	343	>10 mL of daily expectoration Persistent cough for the majority of days	24-h sputum volume (exp): 20.5±18.1 mL/24-h sputum volume (control): 21.7±27.1 mL SGRQ (exp): 37.0±15.8/SGRQ (control): 37.6±15.8	Mannitol (400 mg) *versus* placebo capsules	O-PEP (Acapella) Not monitored	Hyperosmolar session: dry power inhalation ACT session: NR Frequency: twice per day Treatment duration: 12 weeks + optional extension over 52 weeks

Continued

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TABLE 1 Continued

First author, year [reference] (country)	Study design	Participants n	Selection criteria related to sputum symptoms	Baseline clinical characteristics related to sputum symptoms	Hyperosmolar solution	ACTs	Frequency and duration
Murray, 2009 [29] (UK)	Randomised crossover trial	20	Daily expectoration	24-h sputum volume: 5 (1.25–15) mL LCQ: 16.3 (14.1–17.9) SGRQ: 41.1 (24.6–44.8)	NA	O-PEP (Acapella) *versus* usual care	ACT session: 20–30 min Frequency: twice per day Treatment duration: 12 weeks
Nicolson, 2012 [34] (Australia)	Randomised controlled trial	40	Daily sputum expectoration	SGRQ-Symptoms (exp): 64.3±14.2/ SGRQ-Symptoms (control): 64.1±16.1 SGRQ-Activity (exp): 50.1±24.4/ SGRQ-Activity (control): 39.4±22.2 SGRQ-Impact (exp): 35.6±16.9/ SGRQ-Impact (control): 33.5±17.0 LCQ-Physical (exp): 4.4±1.0/LCQ-Physical (control): 4.2±1.7 LCQ-Psychological (exp): 4.7±1.3/ LCQ-Psychological (control): 3.9±1.5 LCQ-Social (exp): 4.6±1.2/LCQ-Social (control): 4.4±1.4	HS at 6% *versus* IS at 0.9%	None	Hyperosmolar: NR Frequency: twice per day Treatment duration: 52 weeks
Kellet, 2011 [35] (UK)	Randomised crossover trial	28	None	NR	HS at 7% *versus* IS at 0.9%	None	Hyperosmolar: NR Frequency: once per day Treatment duration: 12 weeks

Data are presented as n, mean±SD or median (interquartile range). According to Gao *et al.* [36], a high symptom burden is identified if the St George's Respiratory Questionnaire (SGRQ) (symptoms domains) >70. ACT: airway clearance technique; LCQ: Leicester Cough Questionnaire; BHQ: Bronchiectasis Health Questionnaire; BCSS: Breathlessness Cough and Sputum Scale; CAT: COPD Assessment Test; NA: not applicable; HFCWO: high-frequency chest wall oscillation; exp: experimental group; mMRC: modified Medical Research Council; ELTGOL: slow expiration with glottis opened in lateral posture; O-PEP: oscillating positive expiratory pressure; NR: not reported; HS: hypertonic saline; IS: isotonic saline.

Globally, hyperosmolar agents are well tolerated by patients with bronchiectasis, but show inconsistent findings on exacerbation frequency [43, 44]. Furthermore, higher doses show small benefits on sputum-related symptoms compared to the same agent in a lower dose concentration [43, 44]. This modest improvement in clinical outcomes in bronchiectasis using hyperosmolar agents compared to isotonic solutions was also observed in young children with cystic fibrosis. This contrasts with the clear improvement in lung function and reduction in exacerbations observed in the initial studies conducted in adults with cystic fibrosis who had more advanced disease [37, 45]. These data support the hypothesis that hyperosmolar agents' effects are less intense and prolonged if the mucus layer is not severely dehydrated [46, 47]. Therefore, it is less likely to observe clinical differences between hypertonic saline *versus* isotonic saline and between high-dose (400 mg) *versus* low-dose mannitol (50 mg). Additionally, GAO *et al*. [36] demonstrated that participants with bronchiectasis and high respiratory symptom burden, present greater clinical benefits after the inhalation of a hyperosmolar agent compared to participants with moderate or low respiratory symptom burden. The clinical benefits demonstrated were longer time to first exacerbation, a trend towards reduced exacerbation frequency, and symptoms improvements that exceeded the minimal clinically important difference. Still, the use of biomarkers (*e.g.* sputum percentage solids) [48], symptoms scales and questionnaires to identify patients with mucociliary clearance impairment and high symptom burden has rarely been part of the selection criteria in studies evaluating hyperosmolar agents in bronchiectasis (table 1).

Combining airway clearance techniques and hyperosmolar agents

A combination of hyperosmolar agents and ACTs should be targeted at patients with difficulties in controlling their sputum-related symptoms, which are persistent despite regularly performing ACTs with optimal performance, and those with frequent exacerbations [13, 14, 36]. Although recommended in guidelines, to date, the combination of both treatments in this population has not been tested in clinical trials. In fact, the inclusion of ACTs as standard care in long-term trials of hyperosmolar agents was a feature of very few studies examining the effects of mannitol in bronchiectasis [32, 33]. Even in these studies, data regarding how ACTs were used, including teaching, frequency, duration, timing and the adherence to this treatment over time were not fully described (table 1). Trials in bronchiectasis showed that a single session combining hyperosmolar agents followed by ACTs resulted in greater immediate sputum expectoration and reduction of expectorated sputum throughout the rest of the day compared to using ACTs only [40, 49]. However, it is unknown whether these short-term effects can ultimately translate into robust clinical benefits in the long term.

Other airway clearance adjuncts

Education, exercise, and humidification are adjuncts to enhance the benefits of airway clearance management in bronchiectasis. Relevant education includes self-management strategies to monitor respiratory symptoms and identify a clinical deterioration and worsening of symptoms, access of reliable information about the airway clearance management, awareness of the positive benefits from the daily implementation of this therapy (*e.g.* less social disruption) and facilitation of regular meetings for a group of peers that would increase adherence to these treatments [50].

Endurance exercise is another adjunct of airway clearance management to obtain greater benefits in the control of respiratory symptoms [51]. However, the optimal timing regimen is still unknown. Exercise prior to airway clearance management may enhance the sputum volume expectoration, but airway clearance management prior to exercise may enable the patients to reach higher intensities and/or improve their exercise tolerability.

Finally, warm air humification treatment has been demonstrated to improve short-term airway clearance in patients with bronchiectasis [52]. Recent studies in bronchiectasis demonstrated the likelihood of a reduction in exacerbations with long-term domiciliary use of high-flow nasal therapy [53, 54]. Consequently, the use of high-flow nasal therapy, with or without supplementary oxygen if needed, can be a potential substitute in patients with indication for hyperosmolar agents alongside ACTs, who fail the tolerability test, or during acute exacerbations if tolerability to ACTs is decreased during this clinical stage.

Pulmonary rehabilitation and exercise

Centre-based pulmonary rehabilitation programmes

Pulmonary rehabilitation is defined as "a comprehensive intervention which requires a thorough patient assessment followed by patient-tailored therapies which include but are not limited to, exercise training, education and behaviour change to improve the physical and psychological well-being of those with bronchiectasis and promote long term adherence to health-enhancing behaviours" [55]. Programmes are

often delivered in a hospital outpatient department or community-based setting, although telerehabilitation is increasing utilised as an alternative [56].

Multiple international clinical guidelines recommend the referral of patients with bronchiectasis to pulmonary rehabilitation [13, 15, 23, 57, 58], with recognition that it should be considered for those with reduced exercise tolerance and/or who experience frequent exacerbations [13, 23]. The rationale for pulmonary rehabilitation or exercise training as a key aspect of bronchiectasis management aligns with the clinical symptoms of dyspnoea and fatigue, which have a negative impact on functional exercise capacity and HRQoL [9, 12, 59, 60].

Aligning with the well-recognised and standard approach for pulmonary rehabilitation [55], the exercise training component in bronchiectasis consists of a combination of aerobic (endurance) exercise and resistance training for the upper and lower limbs [61, 62]. Most centre-based programmes have a duration of 6–8 weeks, implementing supervised exercise twice weekly and with at least one unsupervised session at home [61, 62]. The initial prescription for both types of training, as well as the rate of progression mirrors what is recommended for those with COPD, where initial training intensities are based on individualised functional walking test results and progression is according to clinical signs and symptoms [63]. In addition to exercise training, adjuncts such as education, which may include directions for self-management, airway clearance management and respiratory muscle training, have all been included within pulmonary rehabilitation programmes offered for those with bronchiectasis [64].

Consistently, research, audits and quality improvement projects for pulmonary rehabilitation in bronchiectasis demonstrate benefits on functional exercise capacity and HRQoL in the short term for those with stable disease [61, 65–67]. A Cochrane review [64] of exercise training, which included pulmonary rehabilitation for people with bronchiectasis, demonstrated mean improvement in incremental shuttle walking distance of 87 m on a pooled analysis of five studies including 161 individuals immediately following the completion of training compared to usual care. The magnitude of change was beyond the previously defined clinically important change for this outcome measure of 47–70 m [68]. Similarly, clinically significant improvement was evident for the 6-min walk distance, at 42 m, which is the most commonly applied outcome measure in clinical practice [64, 69].

Comparable benefits have been noted in HRQoL, with clinically meaningful improvements from pooled analyses in the St George's Respiratory Questionnaire total score following training, as well as symptoms of dyspnoea and fatigue [64, 70]. These clinical effects are similar to those observed among people with COPD [71]. However, benefits for cough-related quality of life or psychological symptoms have been inconclusive [67, 72, 73]. This suggests that the form of exercise training applied within pulmonary rehabilitation may not translate to additional benefits for cough-related symptoms, while changes in anxiety or depression may be dependent of the extent of these symptoms prior to commencing a programme.

The longevity of benefits from pulmonary rehabilitation appears to be short, with improvements not maintained at 3 or 12 months [65, 70]. Since most programmes recommend ongoing exercise following their completion, additional support structures seem necessary to maintain improvements. However, the exact nature of such support remains unclear. A study that examined the effect of pulmonary rehabilitation programmes on measures of morbidity reported a reduced rate of exacerbations at 12 months and a longer time to first exacerbation [70]. While these are promising findings, their physiological reason remains unclear. Examination of additional markers of morbidity and mortality among those with bronchiectasis who undertake pulmonary rehabilitation are necessary to understand any longer-term effects of this intervention.

To date, only one study has explored the effects of pulmonary rehabilitation immediately following medical treatment for an acute exacerbation [74]. After 14 days of antibiotic therapy, patients were randomised to an outpatient rehabilitation programme for 6 weeks or usual care [74]. Both groups improved in functional exercise capacity and health- and cough-related quality of life, with no difference in the study's primary outcome, which was time to next exacerbation [74]. While this contrasts with the clinical improvements following pulmonary rehabilitation delivered immediately following an acute exacerbation of other chronic respiratory conditions [75], it may be in part due to the process of natural recovery. Individuals in this study had their acute exacerbations managed within the community and the study was not designed to represent the spectrum of exacerbations of bronchiectasis, including those hospitalised. For this reason, further clarification of the role of pulmonary rehabilitation in the acutely unwell individual with bronchiectasis is necessary.

Identifying those who benefit most from pulmonary rehabilitation in bronchiectasis has not been extensively explored; however, some guidance may be derived from a mix of demographic features, symptom severity or degree of impact prior to commencing a rehabilitation programme. Similar outcomes in exercise capacity were evident in those classed as having mild (improvement of 49 m), moderate (improvement of 48 m) or severe (improvement of 60 m) bronchiectasis, according to the Bronchiectasis Severity Index (BSI) [76]. This suggests that people with all range of disease severity should be considered for referral to pulmonary rehabilitation. Improvements in quality of life and dyspnoea has been noted to be greater in those who were younger and had higher lung function, according to spirometry, while those who had poorer exercise capacity at the commencement of a programme derived greater improvement in quality life, functional exercise tolerance and anxiety levels [77]. The degree of exertional breathlessness prior to starting a programme varies in studies, ranging from $\geqslant$1 to $\geqslant$3 on Borg scale, with suggestions that those more impacted by breathlessness may benefit more from pulmonary rehabilitation. Given the finite resources, examination of the demographic and clinical characteristics of those with bronchiectasis who could benefit most from pulmonary rehabilitation would be clinically useful, even with the option of various models of care now available.

Telerehabilitation: home-based and virtual pulmonary rehabilitation programmes

Alternative models of centre-based pulmonary rehabilitation for those with bronchiectasis, *i.e.* home-based programmes and telerehabilitation, offer greater flexibility and convenience and can help to overcome the practical challenges related to access to centre-based programmes, including transport and geographic location. The composition of home-based programmes for people with bronchiectasis during a clinically stable state are outlined in table 2. Endurance exercise is commonly prescribed in the form of ground-based walking (possibly incorporating a pedometer) or step training (typically conducted in a centre-based setting or during a home visit), while resistance training typically consists of peripheral muscle exercises using free weights or elastic bands [78–82]. Supervision is variable, with some programmes offering weekly support through telephone calls, with or without motivational interviewing, and others no supervision.

Despite variations in structure, comparable clinical enhancements in functional exercise capacity, HRQoL, selected markers of physical activity, and peripheral muscle strength have been observed in home-based pulmonary rehabilitation for bronchiectasis, relative to centre-based programmes, when compared to standard care [79–82]. Supervision, even if distant, appears to be critical to progression of exercise, together with overcoming potential barriers to activity and enhancing engagement. While this is readily applied within a centre-based programme, it is important to incorporate supervision within a home-based programme to maximise benefits.

Telerehabilitation is an alternative method of offering pulmonary rehabilitation for those with bronchiectasis. A randomised controlled equivalence study that compared telerehabilitation to centre-based rehabilitation included a subset of people with bronchiectasis [83]. The telerehabilitation aerobic exercise training consisted of 30 min of home-based cycling (using a step-through exercise bike), with monitoring and supervision through using a tablet computer and a pulse oximeter [83]. Resistance training consisted of functional activities at an intensity which enabled achievement of eight to 12 repetitions for three sets of each exercise [83]. A home walking programme was encouraged on an additional 3 days per week. Participants with bronchiectasis achieved a similar degree of improvement in functional exercise capacity and HRQoL as those undergoing centre-based programmes [83].

With no adverse events recorded, and despite the small number of trials in people with bronchiectasis, telerehabilitation can be safely delivered and is clinically beneficial. This is further confirmed in similar telerehabilitation models for those with chronic respiratory conditions, some including patients with bronchiectasis [84, 85]. Other forms of web-based telerehabilitation including mobile phone and web applications are emerging [86]; future application of their effects in those with bronchiectasis will provide important insights into their role in delivering pulmonary rehabilitation.

Respiratory muscle training

Respiratory muscle weakness has been noted in those with bronchiectasis and is linked to dyspnoea and impaired coughing efficacy [87], which may limit secretion clearance. While the clinical application of respiratory muscle training does not appear to be widespread in bronchiectasis, it may play a role for those presenting with respiratory muscle weakness. Common approaches to respiratory muscle training have been undertaking in isolation or in conjunction with an exercise programme. For training undertaken in isolation, pressure thresholds of 30–70% maximal inspiratory pressure have demonstrated improvements in maximal inspiratory and expiratory pressures [88].

TABLE 2 Composition of home-based programmes in bronchiectasis

First author, year [reference]	Patient demographics	Programme duration and frequency	Programme components
Batzlaff, 2002 [78]	Clinically meaningful symptom burden; mean age 69 years, mean FEV_1 78.3% predicted	12 weeks	Flexibility and balance exercises, mindful breathing Weekly health coaching telephone calls
Pehlivan, 2019 [79]	Stable; median age 48 years, BSI 7, median mMRC 1	4 days per week for 2 months	Peripheral muscle strengthening training: targeting quadriceps, hamstrings, deltoid, biceps, free weights three times per week with 10 reps Self-walking: distance achieved from 6MWT, increased to 30 mins Breathing exercises for lung expansion and postural drainage, percussion and huffing, performed in seated position four times per day
Bondarenko, 2021 [80]	Stable; mixed respiratory disease (7 with bronchiectasis)	8-week programme, intensity and frequency individualised based on patient's goals	Walking programmes with pedometer for targeted step count or cycling at home or attending private gym with set programme Resistance training: mix of upper and lower limb large muscle group exercises, likely using home-made weights Supported by weekly telephone calls with motivational interviewing for 7 weeks
José, 2021 [81]	Clinically stable; mean age 47 years	3 sessions per week at home for 8 weeks	Step training for 20 mins, resistance training for quadriceps, hamstrings, deltoid and biceps brachii using elastic bands; and educational manual Weekly telephone call and home visit every 15 days
Cedeño de Jesús, 2022 [82]	Clinically stable; mean age 59–63 years; E-FACED score mild	3–5 sessions per week at home for 8 weeks	Intervention: 2×hospital sessions: educational workshop, with explanation of exercises at home and 1 h of exercise and 45–60 mins of education Home programme: UL and LL, weight progressively added with two sets of 6–8 reps, 3–5 days per week Walking or cycling for 20 mins, increasing duration weekly, 3–5 days per week Weekly motivational calls for 8 weeks

FEV_1: forced expiratory volume in 1 s; BSI: Bronchiectasis Severity Index; mMRC: modified Medical Research Council scale dyspnoea score; 6MWT: 6-min walk test; E-FACED: exacerbation, FEV_1, age, chronic colonisation, extension, dyspnoea score; LL: lower limb; UL: upper limb.

Importantly, higher-intensity protocols yield greater benefits in patient-reported outcomes, exercise capacity and HRQoL [89]. Performing respiratory muscle training twice daily for 15 mins, as part of an 8-week pulmonary rehabilitation programme, showed sustained improvement in functional exercise capacity at 3 months following completion of pulmonary rehabilitation, when compared to pulmonary rehabilitation only [65]. Although the underlying mechanism for this effect is unclear, it suggests that respiratory muscle training could support maintaining improvements in selected individuals with bronchiectasis. Confirmation of these translational effects and the optimal dosage for this therapy, particularly on symptoms of dyspnoea, are required to further inform bronchiectasis management.

Education as a core component of pulmonary rehabilitation

Among most studies of or within the clinical practice of delivering pulmonary rehabilitation in bronchiectasis, a package of care in the form of co-interventions is provided. Recommendations for pulmonary rehabilitation indicate that providers should offer education sessions tailored to the needs of individuals with bronchiectasis, such as the pathophysiology of bronchiectasis, ACTs and relevant inhaled therapy, as well as educating on the importance of an exercise training programme [14]. While it is probable that exercise training accounts for the majority of clinical benefits, possible contributions from adjuncts should be considered.

Given that airway clearance therapy is a core aspect of managing bronchiectasis [17], optimising this component of care concurrent to pulmonary rehabilitation is ideal. It may enhance the efficacy of exercise

training or an individual's airway clearance regimen, with the potential for greater benefit in respiratory symptoms. Although the role of education sessions in the context of pulmonary rehabilitation for bronchiectasis is unclear, reinforcement of key information and strategies following discussions related to nutrition, inhaler techniques, coping with dyspnoea, disease pathology, rationale for training, relaxation, smoking cessation and airway clearance therapy offers further opportunity to facilitate the development of self-management skills. Such education embeds aspects of self-management, knowledge and understanding, mastery of skills, problem solving, confidence, individual tailoring to patient needs and disease status, and partnerships between patients and healthcare professionals.

Nutrition

Evidence on other chronic respiratory conditions, such as COPD, indicate the importance of maintaining adequate nutritional status [90]. Data from the United States Bronchiectasis Nontuberculous Mycobacterial Research Registry showed that underweight patients (body mass index (BMI) <18.5 $kg \cdot m^{-2}$) had lower lung function than the normal, overweight and obese groups [91]. Low BMI has been associated with worse outcomes in people with bronchiectasis [92]. This correlation may reflect muscle wasting, but also increased inflammation in malnourished individuals with bronchiectasis [93]. However, specific studies about nutrition interventions and their impact on bronchiectasis management are scarce.

Self-management programmes

Self-management interventions are structured programmes that are designed to improve health behaviours and self-management skills [94]. In addition to medical optimisation, self-management encompasses the physical, psychological and social wellbeing aspects of a person's life [94]. Various definitions and terminologies have been reported, such as "supported self-management", "self-management education", "self-management action plans" and "self-health", but there is distinction between education and self-management education (supplementary material). However, there is no agreed definition of self-management or self-management interventions in bronchiectasis. While existing definitions and the principals of self-management and associated interventions can be applied to bronchiectasis, an agreed definition which is specific to bronchiectasis could support consistent application in clinical practice and meta-analysis of trials investigating the effectiveness of self-management interventions in this condition.

Existing guidelines for managing bronchiectasis do not have explicit evidence-informed recommendation on self-management, still, they clearly recommend interventions such as ACTs and pulmonary rehabilitation and their associated education [13, 14]. The BTS guideline suggests the inclusion of an individualised written self-management plan [14]. Choice, shared decision-making and individual values and preferences are also emphasised in another guideline [95].

Two reviews explored self-management interventions in bronchiectasis. A Cochrane review assessed the efficacy, cost effectiveness and adverse effects of self-management interventions in adults with bronchiectasis [96]. It included two studies where self-management included at least two elements from patient education, ACTs, adherence to medication, exercise or pulmonary rehabilitation, and action plans [96]. This first review concluded that insufficient evidence was available to determine whether self-management interventions benefit people with bronchiectasis. Another review extended this methodology to include a realist synthesis and included eight studies with at least two elements from patient education, symptom monitoring, ACTs, adherence to treatment including medication, exercise or physical activity and action planning (*i.e.* treatment-seeking support tools), and pulmonary rehabilitation explicitly containing self-management support interventions [97]. The results illustrate the mechanisms and theories of how self-management interventions might achieve improvements, reasons why some components might work, *e.g.* interactive sessions, patient education, as well as the contexts which could influence change in patient outcomes, *e.g.* patient characteristics, and the partnership between the healthcare professional and patient [97].

Research in bronchiectasis has also explored the views of patients and health professionals about self-management. Patients have indicated that they are receptive to self-management of their condition; they suggested topics to include and information relating to options for self-management delivery [96, 98]. Furthermore, patients and healthcare professionals reinforced the need for an individualised approach due to the impact of individual characteristics, psychosocial status, socioeconomic status and patients' behaviours [96, 98, 99]. Peer support could be included as a component of supported self-management (supplementary material), as bringing people together with similar conditions and experiences can help instil confidence and enable experiential learning. Other studies have discussed the opportunity for patient education and self-management to optimise health outcomes and highlight the prospect to advance this theme in research and practice [100, 101].

Education can optimise implementation of specific supportive interventions by helping patients to understand their use and importance in managing their individual symptoms. Nonetheless, further consensus on what constitutes a holistic self-management intervention in bronchiectasis could be helpful to inform future guidelines, and research about the role of education and self-management plans [14].

Implementation and challenges

Despite recommendations for ACTs and hyperosmolar agents in bronchiectasis, these are poorly utilised [15, 16, 25, 102]. Two key barriers to clinical benefits from the regular use of airway clearance management are adherence and quality of performance (*e.g.* inhalation technique for hyperosmolar agents and breathing instructions for ACTs) [17, 50]. Current literature does not support that a specific ACTs is superior to another one; thus, the selection of ACTs is tailored to patients' characteristics (*e.g.* clinical stage, disease severity, age, body habitus, comorbidities and location of bronchiectasis), considering the advantages and disadvantages of each ACT, the option of combining and trialling new techniques, and identifying the main enablers and barriers to these interventions (*e.g.* self-management techniques, family support, and lack of time, motivation, lack of access to techniques and/or devices due to financial constraints, feeling ashamed of sputum-related symptoms) [51, 103]. As these factors can change over time, close monitoring and optimising ACTs when necessary are essential strategies to enhance long-term adherence [14].

In respect to key barriers for long-term hyperosmolar agents' use in bronchiectasis, these are the treatment burden and need to clean the devices [13]. Due to reducing the overall treatment time, the simultaneous use of hyperosmolar agents with ACTs, especially hypertonic saline, has gained interest in clinical practice. Although studies in cystic fibrosis suggest that this timing regimen is not inferior to the traditional use of hyperosmolar agents followed by ACTs [39], some aspects need to be considered: 1) if the clinical benefits are dose-dependent, there is a risk of receiving lower doses of the hyperosmolar agent using the simultaneous regime due to expectoration of the inhaled solution; 2) breathing patterns during ACTs modify inhalation and may affect the deposition rate within the lung; 3) the complexity of the overall session increases; therefore, the optimal performance on both interventions is more difficult to maintain over time; and 4) for ACTs that involve positive expiratory pressure devices, modified equipment for the nebulisation is required [39]. Nevertheless, simultaneous use of hyperosmolar agents with ACTs could not only improve adherence by reducing the treatment burden, but also increase the tolerability of hyperosmolar agents, particularly if a nebuliser with a positive expiratory pressure device is standard part of the treatment [39].

Similarly, despite the benefits of pulmonary rehabilitation, both referral rates and attendance rates amongst those with bronchiectasis are less than ideal [104], while the utilisation of structured self-management programmes in bronchiectasis is largely unknown. Reasons for low attendance rates for pulmonary rehabilitation are likely to align in part with those described for people with COPD, including lack of perceived benefit, particularly if individuals are already engaged in exercise for related purposes; challenges related to access, including transport and cost of travel; as well as competing demands for time, programme timing and lack of support [105]. Any of these practical features, particularly in the younger cohort of those with bronchiectasis, may influence referral rates and uptake.

For some people with bronchiectasis, an individually tailored physical activity or exercise routine, which they are sufficiently engaged with, may be a suitable alternative to pulmonary rehabilitation. A pilot study for people with bronchiectasis monitored and encouraged exercise and physical activity over an 8-week study period using a web-based programme called ActivOnline [106]. This study found that ActivOnline was feasible and acceptable for encouraging engagement and was associated with participant perception of benefit [106]. A review of data from the Australian Bronchiectasis Registry found that adults with bronchiectasis do engage in a mix of physical activities for fitness, such as walking, aerobics or gym sessions, swimming, cycling or jogging [107]. While the precise clinical effects of these activities are yet to be determined, the frequency of engagement of at least once per week for 79% within the population implies that benefit is likely to be perceived on an individual basis. Given that enjoyable and motivating activities are linked to greater engagement [108], further exploration of pragmatic approaches to exercise and physical activity in this population will provide more guidance.

Self-management is a dynamic process and should focus on addressing the patients' problems and concerns, including an individual needs assessment. Needs assessments tools are available in other populations to guide this discussion with patients and to enhance a patient-centred approach to self-management [109–112], but not for people with bronchiectasis. Lorig and Holman [94] defined key self-management skills as problem solving, decision-making, resource utilisation, forming a patient/healthcare provider partnership, action planning and self-tailoring. Challenges to successful

self-management can stem from individuals' socioeconomic status, comorbidities, past knowledge and experiences, treatment burden time and healthcare systems [96, 113]. The context and healthcare systems in which patients receive self-management interventions can vary, including aspects of delivery in primary care, specialist centres or pulmonary rehabilitation, use of digital forums, individual or group-based delivery, peer-led or healthcare-professional-led, nature and type of resources and materials. Lower levels of patient activation, health literacy and confidence to self-manage can contribute to patients feeling overwhelmed and lacking the confidence to make decisions to support their health, resulting in poorer health outcomes [114, 115]. Therefore, regardless of the setting, an awareness of health literacy, accessibility, choice and individual tailoring is essential when developing a self-management intervention.

Recognising the differences between self-management behaviours and the success of self-management interventions is important when considering the best way to assess the impact of self-management interventions and there are challenges in the measurement and quantification of health outcomes specific to self-management. Studies exploring self-management interventions in bronchiectasis used the Chronic Disease Self-Efficacy Scale (CDSES), health-related quality of life, exercise capacity, Borg scale for dyspnoea and service use [97]. Assessment of self-management could also be achieved in the context of measuring confidence, self-efficacy, knowledge, goal achievement and behaviour change. For example, the Patient Activation Measure can help to identify factors associated with patient activation and help clinicians to better understand patients' capability for self-management and tailor their intervention to their patients' needs. The CDSES can help the assessment of patients' confidence and self-efficacy to self-manage a range of specific activities, ranging from exercise and managing symptoms to communication with health professionals [116, 117].

The Self-Management Abilities Test is a tool that is available to identify the self-management abilities of adults with bronchiectasis [118]. A Delphi process was used to inform items for 20 multiple-choice questions within domains of general health knowledge, bronchiectasis-specific knowledge, symptom management, communication and addressing deterioration. This tool is not intended to test knowledge and skills or provide a score, but rather to identify specific gaps in patients' understanding and abilities, so that the provision of education can be tailored to the needs of each patient.

There is a dearth of research exploring self-management interventions in bronchiectasis. Self-management interventions have demonstrated improvements in HRQoL, and a lower probability of respiratory-related hospital admissions in COPD [119], as well as a reduction in hospital visits and unscheduled consultations and improving control in asthma [120]. To advance this theme in bronchiectasis, there is a need to clearly define self-management, agree what interventions, single or multi-component, and behaviours constitute a self-management intervention, agree how to deliver the specific components and what training is needed for healthcare professionals in order to support patients for maximum effectiveness and cost effectiveness, and finally agree on methods to assess the outcome of self-management interventions.

Further research prospects

Cough in bronchiectasis

Although cough is a cardinal and debilitating disease symptom in bronchiectasis, it has received little attention in research. A meta-analysis has shown that cough in bronchiectasis has the highest correlation with poor HRQoL compared to all other clinical symptoms or measures [9, 12]. The symptom of cough can be assessed using standardised outcome measures [121], but very few studies have included its assessment outside the Leicester Cough Questionnaire (LCQ), which measures cough-related quality of life [122]. These studies have investigated cough in bronchiectasis through cough frequency and cough reflex sensitivity using the capsaicin challenge, which is a cough provocation test, *i.e.* capsaicin sensitivity is based on the lowest capsaicin concentration eliciting at least two and five coughs (C2 and C5, respectively) [10, 123, 124]. One prospective observational study assessed the cough frequency in 54 patients with bronchiectasis during a clinically stable stage and showed that 24-h cough frequency in patients with bronchiectasis was higher compared to healthy age-matched individuals [10]. Ambulatory objective cough frequency was also associated with higher sputum production, exacerbations and age [10].

Despite overlap on capsaicin cough sensitivity between healthy participants and people with bronchiectasis, those with bronchiectasis present significantly higher sensitivity to capsaicin compared to healthy controls [123, 124]. The scores of cough sensitivity also correlated with the LCQ total score and the total cough symptom score [123], but not with the presence of infected sputum [124]. The relationship between cough sensitivity and severity of bronchiectasis is unclear, as one study did not identify a correlation between capsaicin sensitivity and extent of disease [123], whilst another one showed a significant association between higher capsaicin sensitivity and more severe scores in the BSI [124].

Similar to these results in bronchiectasis, recent work has shown that patients with COPD and chronic cough have heightened cough reflex sensitivity, while cough sensitivity is associated with objective 24-h cough frequency in this population [125]. Patients with COPD were able to suppress their cough during a capsaicin challenge test [125], but there are no published data on cough reflex suppression during capsaicin challenge in bronchiectasis.

Cough management

Despite a paucity of physiological studies that are focused on bronchiectasis, sputum volume and consistency are most likely the primary mechanistic causes of cough in this condition [126]. Thus, an absolute suppression of cough in bronchiectasis is not recommended. However, the severity of cough in some patients with bronchiectasis may not always facilitate airway clearance and theoretically, it could be attributed to higher cough reflex sensitivity. Finding a balance between managing an effective cough for airway clearance and addressing cough as a debilitating symptom is crucial [127]. Incorrectly applied cough management is risky, as it can potentially increase respiratory infections [14, 127] and be associated with poorer quality of life, as shown in a meta-analysis conducted with participants with cystic fibrosis [128].

Cough management utilises patient-managed interventions, including education and breathing exercises aiming at cough control or reduction [129]. These interventions encompass a variety of techniques such as education strategies to reduce cough, cough control or suppression, laryngeal hygiene hydration strategies, continuous positive airway pressure, psychoeducational counselling and mindfulness [129].

Few studies have shown the safety and feasibility of cough management interventions in participants with chronic refractory cough and interstitial lung disease [130–132]. Two randomised placebo-controlled trials conducted with participants with refractory chronic cough demonstrated improvements in various symptom scores, including the score for cough [132], the LCQ and cough frequency compared to the control group, sustained up to 3 months, although there was no difference in the capsaicin reflex sensitivity between groups [130]. An observational study in 98 patients, including participants with chronic refractory cough and bronchiectasis, showed that cough suppression therapy improved symptoms in 51% of patients, with a mean LCQ score change of 3.76. Among these, 16 patients with bronchiectasis showed a mean improvement of 2.41 [128, 133]. Although these results are promising, further research with a particular focus on selection criteria, safety and balance between airway clearance and cough management is necessary for bronchiectasis.

Conclusion

Patient-managed interventions can be individualised and tailored to patient needs and include a spectrum of intervention strategies integrated into the lifelong management of bronchiectasis. Complexity and variability make it challenging to standardise these interventions for research. Studies for patient-managed interventions need innovative ways to generate high-quality evidence, since they can be challenging to study in traditional placebo-controlled randomised controlled trials (RCTs). In addition to efficacy and effectiveness, exploration of alternative outcomes such as structural airways abnormalities (*e.g.* mucus plugs), airway inflammatory markers, airway microbiota and patient-reported outcomes evaluating social impact are desirable. Further work for the economic evaluation of these interventions is also required, and their implementation in resource-limited settings and low- and middle-income countries needs consideration. It is possible that due to the resources required and their nature, patient-managed interventions could be particularly useful and applicable to multiple healthcare systems, providing that they are culturally and socially adapted. Despite challenges in research and clinical implementation, there is a growing recognition of the importance of patient-managed interventions in the bronchiectasis management. Efforts to improve research methodologies and increase research funding are needed to further advance our understanding for these interventions, and their role in optimising patient care and outcomes.

Questions for future research

- What is the optimal prescription for airway clearance techniques and hyperosmolar agents in bronchiectasis?
- What is the role of pulmonary rehabilitation in the management of patients with bronchiectasis following an exacerbation that requires hospitalisation?
- What is the most appropriate definition and outcome measures for self-management interventions in bronchiectasis?
- Is cough management both safe and efficacious in addressing persistent cough which does not aid airway clearance, in carefully selected patients diagnosed with bronchiectasis and experiencing significant cough burden?

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