Appendix 8: Summary of Research Recommendations in PICO format

Research Recommendation in Guideline	**Suggested Research Title:** (e.g. What is the clinical and cost effectiveness of…)	**Patient Group**	**Intervention**	**Comparator**	**Outcomes**	**Why would this research be important? (for the public, patients or the NHS)**
Consensus criteria for diagnosis of ABPA need to be validated in bronchiectasis cohorts.	Consensus criteria for diagnosis of ABPA need to be validated in bronchiectasis cohorts.					
Consensus criteria for definition of abnormal post pneumococcal test immunisation antibody responses need to be validated in bronchiectasis cohorts.	Consensus criteria for definition of abnormal post pneumococcal test immunisation antibody responses need to be validated in bronchiectasis cohorts.					
Randomised controlled trials using clinically important outcome measures are required to assess the effectiveness of airway clearance techniques in varying severities of bronchiectasis.	Does the effectiveness of airway clearance techniques differ according to the severity of bronchiectasis?	Patients with bronchiectasis and sputum production	Airway clearance techniques	Different severities of bronchiectasis (mild, moderate or severe) as assessed by severity scores	Sputum production, Leicester Cough Questionnaire (LCQ), quality of life (QOL), exercise capacity and exacerbation frequency	Physiotherapy is time-consuming and not always enjoyable – patients may wish to be assured that the regime advised for them is most appropriate for their severity and likely benefits
Randomised controlled trials are required to evaluate the effects of airway clearance techniques in patients who are undergoing an exacerbation.	Is airway clearance useful for patients who are undergoing an exacerbation?	Patients with bronchiectasis and sputum production during an exacerbation	Airway clearance	Usual care without airway clearance	Sputum production, LCQ, QOL, time to stable state, time to next exacerbation, complications	An increase or a change in airway clearance is often recommended during an exacerbation – is it useful or an unnecessary burden?
Randomised controlled trials are needed to assess the long term impact of muco-active therapies.	What is the long term impact of muco-active therapies?	Patients with bronchiectasis and sputum production	Various muco-active therapies (6 months or longer)	Usual care without muco-active therapies	Sputum production, LCQ, QOL, exercise capacity, BMI, side-effects, spirometry and exacerbation frequency	Is there long term benefit from treatments such as hypertonic saline, carbocisteine etc. – these medications have a financial cost to the health service and can require much patient time
Randomised controlled trials are needed to assess the long term impact of anti-inflammatory therapies.	What is the long term impact of anti-inflammatory therapies?	Patients with bronchiectasis	Anti-inflammatory treatment (6 months or longer)	Usual care	QOL, exercise capacity, BMI, side effects, serial spirometry and exacerbation frequency	It is important to understand if anti-inflammatory therapies provide benefit or are counter-productive
Long term randomised controlled trials of oral and inhaled antibiotics are needed to assess their efficacy and safety in patients with bronchiectasis who have frequent respiratory tract infections with recurrent P. aeruginosa infection or other potential pathogenic micro-organisms.	What is the efficacy and safety of long term prophylactic antibiotics in patients with bronchiectasis who have frequent respiratory tract infections with potentially pathogenic micro-organisms on sputum culture.	Patients with bronchiectasis and positive sputum cultures who exacerbate at least 3 times per year	Long term prophylactic antibiotic appropriate to results of sputum culture	Usual care without long term antibiotics	Serial sputum culture with antibiotic resistance testing, sputum colour and volume, QOL, severity scores, spirometry, exacerbation frequency, side-effects/ discontinuation rates/ impact on the use of other medication	Concern about antibiotic stewardship is felt by all parties; it is important to know if the benefit of long term antibiotic therapy outweighs the potential disadvantages

Appendix 8 (*Continued*)

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Further interventional/randomised controlled trials needed to establish the role of any alternative therapies in the management of bronchiectasis.	Is there a role for "alternative therapy" in the management of bronchiectasis?	Patients with bronchiectasis	"Alternative therapies"	Usual care	Depending on the nature of the therapy, may include sputum production, LCQ, QOL, spirometry, exercise capacity, BMI, exacerbation frequency, side-effects	These modes of treatment are not currently funded due to a lack of evidence but some patients would value them if such evidence can be found
Studies assessing the benefits of nutritional supplementation in patients with bronchiectasis should be undertaken.	Are there benefits to nutritional supplementation in patients with bronchiectasis?	Patients with bronchiectasis	Nutritional supplementation	Usual care without nutritional supplementation	BMI, severity scores, QOL, exacerbation frequency, exercise capacity, spirometry	Poor nutrition contributes to severity of disease – can this be addressed?
The role of education, self management plans and who delivers the pulmonary rehabilitation needs to be explored.	What are the educational needs of patients with bronchiectasis and how should this education be delivered?	Patients with bronchiectasis	Education on aspects of the disease and self-care, delivered in various ways e.g. face to face, online	Usual care without education	QOL, psychological wellbeing, use of medical services, exacerbation frequency.	Disease-specific education may improve QOL for these patients and potentially reduce use of healthcare resources
The role of education, self management plans and who delivers the pulmonary rehabilitation needs to be explored.	Are self management plans useful in the management of bronchiectasis exacerbations?	Patients with bronchiectasis who exacerbate	Personalised self-management plan delivered by a healthcare provider who is familiar with the patient's case	Usual care without a self-management plan	QOL, use of medical services, exacerbation frequency, hospital admissions	This is a simple tool to improve outcomes
The role of pulmonary rehabilitation after exacerbations requiring hospital admission needs to be explored.	Is there a benefit from early pulmonary rehabilitation after exacerbations of bronchiectasis requiring hospital admission?	Bronchiectasis patients admitted for an exacerbation	Post-discharge pulmonary rehabilitation commencing within 2 weeks	Usual care	QOL, exercise capacity, spirometry, time to full resolution, time to next exacerbation, readmission rate within 30 days and within 90 days	This has been demonstrated to be useful in patients with COPD. Although bronchiectasis patients don't admit at the same rate as COPD, the ones that require admission for exacerbations are most likely to be high consumers of healthcare resource
The incidence of cross-infection of respiratory pathogens in the group exercise setting should be investigated in the bronchiectasis population.	What is the incidence of cross-infection of respiratory pathogens in a group exercise setting?	Patients with bronchiectasis undergoing pulmonary rehabilitation	Those exercising in a group setting	Those exercising at home	Microbiological evidence of cross infection and/or rates of cross infection	In cystic fibrosis, cross-infection is known to occur, but it has not yet been reported in bronchiectasis patients. Theoretically a group exercise setting would be high risk as exercise would tend to encourage expectoration.
A randomised control trial of P. aeruginosa eradication therapy is needed to determine the microbiological and clinical outcomes of eradication therapy.	Does P. aeruginosa eradication therapy prevent long term colonisation or improve health outcomes?	Bronchiectasis patients with new P. aeruginosa infection	Eradication therapy according to the 2018 BTS bronchiectasis guideline	Placebo treatment	Microbiological outcomes, side effects/drop-out rates, symptom, QOL, LCQ, time to next exacerbation, spirometry, exercise capacity, hospital admissions/use of other healthcare resources	There is no direct evidence for this form of treatment but it is widely used, incurring expense and potential side-effects. If it is effective, it could make a significant difference to patient outcomes which are adversely affected by P. aeruginosa colonisation.

Appendix 8 (*Continued*)

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Randomised controlled trials are needed to assess which patients with bronchiectasis would benefit from long term Immunoglobulin G replacement therapy alone or as an adjunct to long term antibiotic therapy- assessing the optimal dose of IgG replacement and identification of ideal trough IgG level to prevent recurrent infections.	Should all bronchiectasis patients with specific antibody deficiency receive long term Immunoglobulin G replacement therapy?	Bronchiectasis patients with specfici antibody deficiency not severe enough to be classed as CVID	IgG replacement with prophylactic antibiotics stratifying according to dose given/trough level of IgG achieved	Prophylactic antibiotics alone	Exacerbation frequency, sputum microbiology, spirometry, exercise capacity, QOL, CT scan	IgG replacement is necessary in CVID but there is variation in clinical practice in patients with lesser deficiencies and the ideal treatment dose/trough level is not known
Large scale robust data that confirm or refute the transmissibility of key pathogens such as P. aeruginosa and non-tuberculous mycobacteria are needed.	Can cross-infection with key pathogens such as P. aeruginosa and non-tuberculous mycobacteria occur in patients with bronchiectasis not related to cystic fibrosis?	This research recommendation requires an observational study which is not well adapted to the PICO approach. However…	Patients with bronchiectasis under long term follow-up at hospital clinics which routinely practise segregation	Patients with bronchiectasis under follow-up in centres without cross-infection precautions	Microbiological outcomes including genetic studies of sputum	Routine segregation of patients colonised with such organisms would require a significant increase in funding, staffing and space but if cross-infection is possible, this may be cost-effective in the long term