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Early View

Task Force Report

European Respiratory Society Clinical Practice Guideline for the Management of Adult Bronchiectasis

James D. Chalmers, Charles S. Haworth, Patrick Flume, Merete B. Long, Pierre Régis Burgel, Katerina Dimakou, Francesco Blasi, Beatriz Herrero-Cortina, Raja Dhar, Sanjay H Chotirmall, Felix C. Ringshausen, Josje Altenburg, Lucy Morgan, Mattia Nigro, Megan L. Crichton, Chayenne Van Meel, Oriol Sibila, Alan Timothy, Eliza Kompatsiari, Tanja Hedberg, Thomas Vandendriessche, Pamela J. McShane, Thomy Tonia, Kevin Winthrop, Michael R. Loebinger, Natalie Lorent, Pieter Goeminne, Michal Shteinberg, Eva Polverino, Stefano Aliberti

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European Respiratory Society Clinical Practice Guideline for the Management of Adult Bronchiectasis

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Conflicts of interest summary

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Abstract

Background

Bronchiectasis is a common lung condition associated with wide range of infectious, immunological, autoimmune, allergic and genetic conditions. Exacerbations and daily symptoms have the largest impact on patients and healthcare systems, and they are the key focus of treatments. Current practice is heterogeneous globally, and bronchiectasis has historically been a neglected disease. Here, we present evidence-based international guidelines for the management of adults with bronchiectasis.

Methods

A European Respiratory Society (ERS) Task Force, comprising global experts, a methodologist, and patient representatives, developed clinical practice guidelines in accordance with ERS methodology and the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) approach. Systematic literature searches, data extraction, and meta-analysis were performed to generate evidence tables, and recommendations were formulated using the evidence-to-decision framework. A total of 8 PICO (Patient, Intervention, Comparator, Outcomes) questions and 3 narrative questions were developed.

Recommendations

The Task Force recommendations include strong recommendations in favour of airway clearance techniques for most patients with bronchiectasis and pulmonary rehabilitation for those with impaired exercise capacity. We issue a strong recommendation for the use of long-term macrolide treatment for patients at high risk of exacerbations and a strong recommendation in favour of long-term inhaled antibiotics in patients with chronic *Pseudomonas aeruginosa* infection at high risk of exacerbation. Conditional recommendations support the use of eradication treatment or mucoactive drugs in specific circumstances. We suggest not to routinely use long term oral, non-macrolide antibiotic treatment or inhaled corticosteroids. Additional guidance is also provided on testing for underlying causes, managing exacerbations, and managing the deteriorating patient.

Conclusion

The ERS bronchiectasis guidelines provide an evidence-based framework for optimal management of adults with bronchiectasis and serve as a benchmark for evaluating the quality of care.

Scope and objectives

The European Respiratory Society (ERS) guidelines for the management of bronchiectasis in adults provide evidence-based recommendations for the care of people with clinically significant bronchiectasis, defined by the presence of permanent dilatation of the bronchi evident on chest CT scan, along with characteristic clinical symptoms.[1] These guidelines are intended for all healthcare professionals involved in the care of adults with bronchiectasis, as well as for policymakers, regulatory authorities, and pharmaceutical companies. Bronchiectasis is a complex and heterogeneous disease; therefore, no guideline can be entirely comprehensive or replace clinical judgement. All guideline recommendations must be interpreted within the specific clinical context in which they are applied. Separate ERS guidelines for the management of bronchiectasis in children exist[2]. Bronchiectasis due to cystic fibrosis (CF) has a distinct evidence base; therefore, guidance for the management of CF is provided elsewhere.[3] Some bronchiectasis-associated conditions also have distinct guidelines for investigation and management, such as primary ciliary dyskinesia (PCD)[4], allergic bronchopulmonary aspergillosis (ABPA)[5] and non-tuberculous mycobacterial (NTM) pulmonary disease[6]. While the present guidelines apply for these conditions, they should be interpreted in conjunction with the relevant syndrome-specific recommendations.

Introduction

Bronchiectasis is a chronic inflammatory lung disease characterized by clinical symptoms such as cough, sputum production, and recurrent respiratory infections. Bronchiectasis is defined radiologically by the presence of bronchial dilation on chest CT scan.[1,7] The key goals of bronchiectasis management are to improve quality of life and symptoms, to prevent exacerbations and disease progression.[8,9] Bronchiectasis is caused by a wide variety of underlying conditions, including infectious, autoimmune, allergic, and genetic disorders.[10,11] Approximately 40% of cases have no identified cause.[12]

The disease pathophysiology is conceptualised through the “vicious vortex” concept, in which four interrelated components interact to drive disease progression.[13] These components are airway inflammation, impaired mucociliary clearance, airway infection and structural lung damage.[14–16] Management of bronchiectasis is therefore focused on addressing these four key components and treatments used can be thought of as primarily targeting one of these four components (figure 1).

Although bronchiectasis is common, it has historically been a neglected and under-researched condition.[17] The first international guidelines for bronchiectasis were published by the ERS in 2017; however, the majority of recommendations were conditional and based on low or very low certainty of evidence, largely due to a lack of high-quality randomized controlled trials.[18] In the past 8 years, there has been a notable increase in clinical trials and research activity in bronchiectasis, including extensive data from patient registries.[19–22] In this document we provide new recommendations for the management of bronchiectasis in adults.

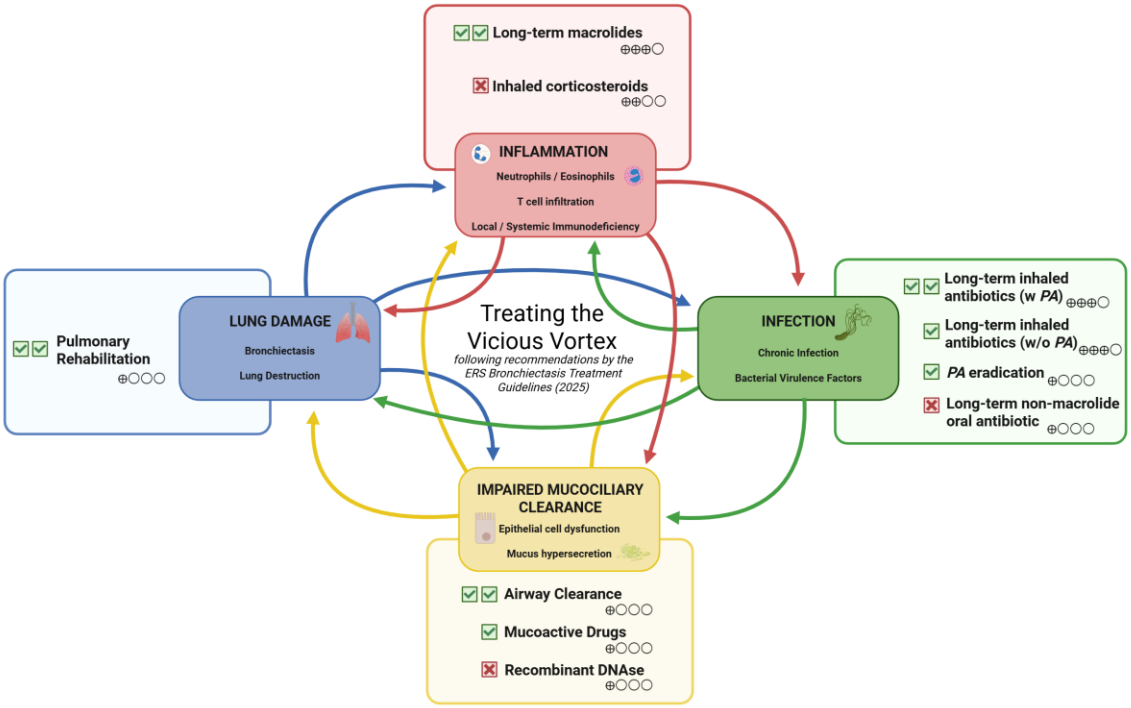

Figure 1. The vicious vortex of bronchiectasis with the treatments evaluated in the 2025 ERS bronchiectasis Guideline. Green indicates treatments that receive a recommendation in favour (Bold with two ticks indicates strong recommendation, non-bold with one tick indicates conditional recommendation for the intervention) Red indicates treatments that receive a recommendation against (the Red cross indicates a conditional recommendation against the intervention). The certainty of evidence is indicated by the crossed circles after each topic (1 cross= very low certainty, 2 crosses= low certainty of evidence, 3 crosses=moderate certainty of evidence, 4 crosses=high certainty of evidence).

Guideline methodology

The ERS guidelines for the management of bronchiectasis in adults were developed by an ERS Task Force in accordance with ERS rules for developing guidelines, which utilise the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach. The Task Force was chaired by Professor James D. Chalmers (Dundee, UK) and Professor Stefano Aliberti (Milan, Italy). The Task Force was international, representing 13 countries across 4 continents. Participants were selected by the chairs based on their expertise and experience, and the task force was constituted according to ERS rules. The Task Force also included professional information specialists who supported the literature searches, three patient representatives from the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) – European Lung Foundation (ELF) patient advisory group with lived experience of bronchiectasis,[23] and the ERS lead methodologist. Two members of the ERS guideline methodology network were assigned to the Task Force. Guideline development included virtual and face-to-face meetings, as well as extensive correspondence among voting panel members.

Questions and outcomes

The guideline includes 8 PICO (Patients, intervention, comparison, outcomes) questions and 3 narrative questions.[24] For PICO questions, formal systematic literature searches, meta-analysis and grading were performed. For narrative questions, formal systematic literature searches were also completed. Evidence-to-decision (EtD) frameworks were used to generate evidence to decision tables for both PICO and narrative questions. For each question, relevant outcomes were selected by panel members and patient representatives based on their clinical judgement. Outcomes were then rated on a 9-point scale and classified as critical, important, or of limited importance through a panel vote.[25] Only outcomes rated as critical or important based on the average panel score and subsequent discussion and consensus were included. Data for these outcomes were extracted for meta-analysis and considered in the evidence summaries.

Literature searches and systematic literature searches

Literature searches were designed by two independent information specialists in partnership with the chairs, the ERS methodologist, and a panel member experienced in methodology. Each question was supported by a systematic literature search of up to five databases (Pubmed, Embase, Web of Science Core Collection, Scopus and CENTRAL) and two clinical trial databases (Clinicaltrials.gov and ICTRP). Searches were performed from inception of the databases to between November 2023 and January 2024. (detailed search methodology is shown in the online supplement). All studies addressing the relevant question were considered, including randomized controlled trials (RCTs) and observational studies. Review articles (with the exception of existing systematic reviews), editorials, and other papers not containing original data were excluded. The study selection process for each question is presented in PRISMA flow charts in the supplement. Where RCTs addressing the question were identified, these were considered as the main body of evidence and analyses were limited to those studies. If no RCTs were identified, data from observational studies were extracted and considered as the main body of evidence.

We performed a search for all RCTs related to bronchiectasis (search terms presented in the online supplement). As no RCTs were identified addressing the PICO question on eradication, and limited data were identified for the PICO question on non-macrolide oral antibiotics, specific searches were performed for these two PICO questions (search terms are presented in the online supplement). The search strategy for Narrative question 1 and Narrative question 2 and 3 are also presented online. Data from studies that did not meet the criteria for inclusion in the evidence summaries could still be included in the “additional considerations” section of the EtD framework, if they were relevant and informative to the discussions.

The first stage of literature review involved independent screening of titles and abstracts by two reviewers using Rayyan. Discrepancies in inclusion/exclusion were resolved by an independent third reviewer followed by discussion and consensus among all reviewers. Following full text review, based on predefined inclusion and exclusion criteria (see the online supplement), outcomes of interest were extracted using a pre-developed data extraction form in Microsoft excel, Meta-analyses were performed using Reviewer Manager version 5 (Cochrane). All meta-analyses used random effects models in view of the heterogeneity of patient populations, interventions and study designs identified. Risk of bias

for RCTs was evaluated using the Cochrane risk-of-bias tool 2 (RoB-2) for randomized trials embedded within the Review Manager software.

Certainty of evidence and strength of recommendations

The certainty of evidence for each outcome was evaluated using GRADE methodology as very low, low, moderate or high, taking into account risk of bias, inconsistency, indirectness, imprecision, and publication bias for each outcome.[26] For imprecision, certainty of evidence was downgraded if the confidence intervals included the possibility of the lack of a clinically relevant effect using established minimum clinically important differences, where these are available[27–30], and discussion among the panel members where this was not available. GRADE evidence profiles were created in GradePro for each PICO question and are presented in the supplementary material.

Recommendations

EtD frameworks were prepared for each question and discussed during a series of panel meetings. For the PICO questions and narrative question 1, evidence was reviewed and new recommendations formulated. For narrative questions 2 and 3 which deal with what is already recommended elsewhere, the panel reviewed existing recommendations from clinical guidelines and statements, identified those recommendations with which they agreed, and endorsed those recommendations. For all questions consensus was achieved by considering not only the available evidence, but also patients' values and preferences, as well as practical considerations.[31] Formal voting was performed to agree the final recommendations, with a pre-specified threshold: 70% agreement was required to approve recommendations. Voting panel members declared their conflicts of interest and were disqualified from voting on recommendations where they declared a conflict. At least 50% of the panel had to be non-conflicted and eligible to vote for a valid recommendation in line with ERS rules. Recommendation meetings were held between July 2024 and January 2025. As recommendations were formulated within 12 months of the literature searches, the searches were not updated.

Recommendations are formulated as either strong or conditional. In line with GRADE terminology, we use "we recommend" for strong recommendations and "we suggest" for conditional recommendations.

Additional information to operationalize the recommendations is provided as remarks. The evidence supporting these remarks is discussed and reflects the clinical judgement of the guideline panel.

Summary of recommendations

Question	Recommendation(s)	Remarks
NQ1- **How can underlying causes of bronchiectasis be identified and how can the severity, comorbidities, and other treatable traits be**	1. Management of patients with bronchiectasis should include standardized testing to identify the underlying cause of bronchiectasis, to evaluate disease severity and activity as well as risk of poor outcome,	See the relevant section for the associated detailed investigation and management considerations

evaluated?	and to identify co-morbidities and associated treatable traits (Strong recommendation for the intervention, moderate certainty of evidence stemming from narrative review of the evidence)	
PQ1- **Should airway clearance techniques be used compared with no airway clearance techniques in adults with bronchiectasis?**	2. We recommend that patients with bronchiectasis should be taught airway clearance techniques (strong recommendation *for the intervention*, very low certainty of evidence)	• Airway clearance techniques (ACTs) are best taught by a respiratory physiotherapy with appropriate experience. • There is no evidence that one technique is superior to another and, therefore, treatment should be personalized. • Airway clearance devices may be used to support manual ACTs. • Previous ERS guidelines limited ACTs to patients with chronic productive cough. The current recommendation acknowledges that some patients with a dry cough, particularly those with mucus plugging on chest CT, may benefit from ACTs. Instruction in ACTs may also assist patients during periods of increased symptoms, such as exacerbations.
PQ2- **Should mucoactive drugs be used compared with no mucoactive drugs in adults with bronchiectasis?**	3. *We suggest to offer mucoactive treatments to patients with bronchiectasis where airway clearance has failed to control symptoms (conditional recommendation for the intervention, very low certainty of evidence)* 4. *We suggest not to offer recombinant DNAse to patients with bronchiectasis (conditional recommendation against the intervention, very low certainty of evidence)*	• The choice of mucoactive treatment should be guided by patient's co-morbidities and concerns around treatment burden and tolerability. • Mucoactive treatments are best delivered as part of a comprehensive airway clearance regimen, which includes personalized airway clearance instruction with or without devices, and regular physical exercise.
PQ3- **Should long term inhaled antibiotics be used compared with no inhaled antibiotics in adults with bronchiectasis?**	5. We recommend to offer long-term inhaled antibiotics to patients at high risk of exacerbations and chronic infection with *Pseudomonas aeruginosa* despite standard care (Strong recommendation *for the intervention*, moderate certainty of evidence)	• Patient at high risk of exacerbations include patients with a history of 2 or more exacerbations in the prior year OR 1 severe exacerbation OR 1 exacerbation plus severe daily symptoms. • Inhaled antibiotics should be prescribed for a defined period and

	6. We suggest to offer long-term inhaled antibiotics for patients at high risk of exacerbations and chronic infection with pathogens other than *Pseudomonas aeruginosa* despite standard care (Conditional recommendation *for the intervention*, moderate certainty of evidence)	treatment response should be formally evaluated. If ineffective or poorly tolerated it should be discontinued • Inhaled antibiotics are drug and device combinations and, therefore, patients should be provided with an appropriate nebulizer along with the medication. • Many clinicians would perform a supervised test dose of inhaled antibiotics because of the risk of bronchospasm.
PQ4- **Should long-term macrolides be used compared with no long-term macrolides in adults with bronchiectasis?**	7. We recommend to offer long-term macrolides to patients at high risk of exacerbations despite standard care (Strong recommendation *for the intervention*, moderate certainty of evidence)	• Macrolides are effective in a broad group of patients with bronchiectasis at high risk of exacerbations including patients with chronic *P. aeruginosa* infection, patients with airway infection caused by other pathogens, and those without evidence of airway infection. • Macrolides should not be prescribed as monotherapy to patients with NTM infection. NTM should be excluded before initiating macrolide therapy. • The most widely used long-term macrolide is azithromycin, typically at a dose of 250 mg daily or three times per week, or 500 mg three times per week. • In view of the risk of adverse effects, patient education, baseline screening, and appropriate follow-up are important when prescribing macrolides.
PQ5- **Should long term non-macrolide oral antibiotic treatment be used compared with no long term oral antibiotic treatment in adults with bronchiectasis?**	8. The panel suggests NOT to offer long-term non-macrolide oral antibiotics as a first line treatment to adult patients with bronchiectasis and a high risk of exacerbations (conditional recommendation against the intervention, very low certainty of evidence).	• Long-term non-macrolide oral antibiotics may have a role in specific situations where patients are at high risk of frequent exacerbations and other options such as long-term macrolides are contraindicated or have proven ineffective.
PQ6- **Should eradication treatment be used for patients with isolation of a new pathogenic**	9. We suggest to offer eradication treatment to patients with a new isolation of Pseudomonas aeruginosa	• A new isolation of *P.aeruginosa* may refer to the first time a patient has *P. aeruginosa* isolated or a further isolation following a prolonged period

microorganism compared with no eradication treatment?	(conditional recommendation *for the intervention*, very low certainty of evidence)	during which *P. aeruginosa* was not detected. • Eradication practices vary both among panel members and globally. Some clinicians prescribe systemic antibiotics (e.g 2-week course) followed by a repeat sputum culture, discontinuing antibiotics if the sample is negative. Others would add inhaled antibiotics for 4 weeks to 3 months, without rechecking sputum cultures. The 2017 ERS guidelines provide examples of different antibiotic strategies.
PQ7- **Should Long term inhaled corticosteroids be used compared to no long term inhaled corticosteroids in adults with bronchiectasis?**	10. We suggest not to offer long term inhaled corticosteroids to patients with bronchiectasis who do not have coexisting COPD or asthma (conditional recommendation against the intervention, low certainty of evidence)	• Patients with bronchiectasis should be evaluated for the presence of co-existing asthma and COPD. The presence of bronchiectasis does not alter the recommendation to use inhaled corticosteroids (ICS) in patients with asthma or in a subset of patients with COPD. Suspected asthma or COPD should be appropriately investigated in patients with bronchiectasis. • There is limited evidence suggesting that ICS may be beneficial in a subgroup of patients with bronchiectasis with elevated blood eosinophil counts who do not have asthma or other eosinophilic conditions. However, no recommendation on ICS use based on blood eosinophils is currently possible, and we recommend further research in this group. • The use of ICS should be reevaluated in patients without a clear indication. Discontinuation of ICS may be appropriate in some patients.
PQ8- **Should pulmonary rehabilitation be used compared with no pulmonary rehabilitation in adults with bronchiectasis?**	11. We recommend that patients with breathlessness and/or impaired exercise capacity should be offered pulmonary rehabilitation (strong recommendation *for the intervention*, very low certainty of evidence)	• The educational component of pulmonary rehabilitation (PR) should ideally be bronchiectasis specific and include discussion of airway clearance strategies. • Patients with bronchiectasis should be encouraged to undertake regular physical activity, given its multiple

		health benefits.
NQ2- **What diagnostic tests and interventions are currently recommended/used for managing exacerbations?**	See relevant section for summary of 9 recommendations arising from narrative review of the evidence	See the relevant section for the associated detailed recommendations endorsed by the panel
NQ3- **What investigations and treatments are currently recommended in a patient with bronchiectasis who is rapidly deteriorating in terms of symptoms or exacerbations?**	See relevant section for summary of 11 recommendations arising from narrative review of the evidence	See the relevant section for the associated detailed recommendations endorsed by the panel

Table 1. Summary of recommendations in the 2025 ERS Bronchiectasis Guidelines.

Narrative question 1

How can underlying causes of bronchiectasis be identified, and how can severity, comorbidities, and other treatable traits be evaluated?

Recommendations

Management of patients with bronchiectasis should include standardized testing to identify the underlying cause of bronchiectasis, to evaluate disease severity and activity as well as risk of poor outcome, and to identify co-morbidities and associated treatable traits (Strong recommendation for the intervention, moderate certainty of evidence stemming from narrative review of the evidence)

Investigation and management considerations (the following is based on the evidence from systematic searches, panel discussions, the clinical experience and current practice of the panel and recommendations in other guidelines)

- All patients newly diagnosed with bronchiectasis should be screened for immunodeficiency by measurement of serum immunoglobulins (IgG, IgM, IgA), ABPA by measurement of total IgE, Aspergillus specific IgG and IgE, as well as blood eosinophils, and NTM by mycobacterial microscopy and culture.
- In patients at high risk of NTM infection based on clinical and radiological features a minimum of three sputum samples or a bronchoalveolar lavage should be obtained.
- Alpha-1 antitrypsin testing should not be performed routinely but should be considered in patients with suggestive clinical and radiological features such as basal emphysema or severe airflow obstruction.
- Patients with symptoms onset during childhood or with specific clinical or radiological features (independent of age of onset) should be screened for CF and PCD.
- Newly diagnosed patients with bronchiectasis should have a bronchiectasis severity index calculated to assess the risk of future complications (table

- Patients at higher risk of future complications should be identified. Such patients should be considered for more frequent follow-up and a lower threshold for treatment. High-risk groups include:
    - Patients with COPD, PCD, or rheumatoid arthritis (RA)-associated bronchiectasis
    - Patients with *Pseudomonas aeruginosa* or other enteric Gram-negative infections
    - Patients with 2 or more exacerbations per year or 1 severe exacerbation (defined as requiring hospitalization or intravenous antibiotics) in the previous year
    - Patients with severe symptoms including high volumes of daily sputum production and sputum purulence
    - Patients with NTM infection
    - Patients with ABPA
- Assessment of co-morbid illnesses should be part of the evaluation of all patients with bronchiectasis:
    - Patients at risk should be investigated for associated cardiovascular disease
    - Patients at risk should be investigated for associated osteoporosis
    - Patients should be screened for symptoms of anxiety and depression and appropriate management initiated
    - Rhinosinusitis and gastroesophageal reflux disease (GRD) are common co-morbidities of bronchiectasis that should be identified and managed appropriately.
    - Treatment burden and the impact on associated conditions should be considered as part of treatment decisions when managing bronchiectasis
    - The assessments described here including considering the underlying cause, co-morbidities, disease activity and treatable traits, should be considered at all patient visits and not just at diagnosis.

Summary of evidence

Evidence supports standardized testing for underlying causes of bronchiectasis, as it may reveal treatable conditions, particularly immunodeficiency, NTM infection, ABPA, and CF.[4,10,11,32–34] Identifying these conditions can significantly improve outcomes. Additionally, certain aetiologies, such as COPD, PCD, and RA, have treatment and prognostic implications and can influence follow-up and management strategies.[35–38] Patients themselves often express a strong desire to understand the cause of their bronchiectasis, and this was supported by the patient representatives in the guideline panel.[39] Identifying the underlying cause begins with a thorough history, including childhood history, reviewing HRCT findings, medications, pulmonary function tests, and supported by laboratory investigations. Resource implications exist for extensive testing, so the approach should balance benefit and cost. Therefore, testing for immunoglobulin deficiency, ABPA and NTM are reasonable as they are not prohibitively expensive, each are common (up to 10% depending on the series and even higher in certain populations) and they change management.[10,40] Studies have found alpha-1 antitrypsin screening in unselected bronchiectasis patient populations to have a low positive rate[41,42] and so routine screening is not recommended. Screening for rarer conditions like CF and PCD is important but carries significant cost and logistical challenges. The majority of patients with these genetic causes will have symptoms in childhood, but additional features that may suggest CF include upper

lobe bronchiectasis, gastrointestinal symptoms (malabsorption/pancreatitic insufficiency/pancreatitis, intestinal obstruction), chronic rhinosinusitis with or without nasal polyps, male infertility and infection with *S. aureus*, *P. aeruginosa* or NTM. Although not all patients with bronchiectasis require screening for CF, a low threshold for testing should be adopted in view of the availability of specific CFTR modulator treatments.[43–45] Diagnosis of PCD should follow the ERS/ATS guidelines.[46] No cost-effectiveness data were identified in the analysed studies. Bronchiectasis aetiology varies globally, with post-TB bronchiectasis more common in Asia, Africa, and some parts of Europe[47], CF is less prevalent in Asia, and ABPA is reported less common in Southern than Northern Europe.[11]

Bronchiectasis has a highly variable clinical course.[48,49] Severity assessment aims at identifying patients at risk of progression, exacerbations, and mortality. The bronchiectasis severity index (BSI) is the most widely used standardised severity assessment tool, although others exist.[48,50,51] Use of such tools may help to identify patients most likely to experience complications. Nonetheless, severity scores have limitations, and potential misclassification of patients could lead to under- or overtreatment; therefore, features such as frequent exacerbations[38], severe daily symptoms[52], *P. aeruginosa* infection[53] and some aetiologies and associated conditions[54] should guide clinicians toward more intensive monitoring and management.

The concept of severe daily symptoms and sputum purulence relies on clinical judgement and can be pragmatically defined as symptoms which have a severe impact on patients day to day functioning or quality of life.[55] Objective tools such as the quality of life bronchiectasis questionnaire respiratory symptom score or St Georges Respiratory Questionnaire score may support identification of severe symptoms and the Murray colour chart can identify sputum purulence.[27,56] In a recent study using the EMBARC registry is mean score in nearly 10,000 patients was QOL-RSS of 60 points and SGRQ >52 points.[57] An objective sputum colour chart is available to identify sputum purulence.[58]

Comorbidities are frequently observed in patients with bronchiectasis and are associated with increased mortality and reduced quality of life.[54] Cardiovascular diseases[59], osteoporosis, depression, anxiety[60], chronic rhinosinusitis[61] and low body weight and malnutrition[48] are common and have available treatment or preventive strategies that could yield desirable benefits.[62]

Figure 2. Investigation and management considerations for initial assessment and subsequent aetiological testing for adults with bronchiectasis. The central components (dark blue) are routine for all patients. This figure summarises the investigation and management considerations described above based on the systematic searches, panel discussions and current practices. These do not constitute separate recommendations. In a deteriorating bronchiectasis patient a comprehensive aetiological workup should be repeated and guided by clinical, radiological and demographic clues to identify any missed, evolving or newly relevant causes.

Justification of recommendation

The recommendation to test for underlying causes in bronchiectasis is justified by the potential benefits of identifying treatable conditions that can improve patient outcomes. Although such testing may increase healthcare costs and introduce diagnostic complexity, the prioritisation of diagnosing treatable etiologies outweighs these concerns. The recommendation to limit testing for alpha-1 antitrypsin deficiency (A1ATD), CF and PCD to patients with suggestive clinical features reflects a targeted diagnostic approach that balances the need for comprehensive evaluation while minimizing unnecessary testing, healthcare costs and patient burden.

Assessing disease severity is essential to ensure a standardised evaluation of bronchiectasis, facilitating appropriate management strategies. Additionally, the identification and management of comorbidities support a holistic approach to patient care, ultimately improving clinical outcomes.

The treatable traits concept emphasizes the importance of a personalized approach to bronchiectasis management. Effective treatment strategies targeting the underlying cause, associated co-morbidities, and key disease features (infection, impaired mucociliary clearance, inflammation, etc) depend on comprehensive patient assessment to identify treatable traits.

Implementation considerations

Implementing testing for underlying causes in bronchiectasis requires a structured approach to address several practical challenges, including regional disparities in diagnostic capacity, variability in disease aetiology across populations, and the lack of standardized follow-up and management protocols. Testing for certain underlying causes (particularly PCD) may be difficult to implement in many regions due to limited access to specialized diagnostic facilities. While evidence exists to support treatment of some treatable traits (e.g cardiovascular disease secondary prevention), other areas lack clear therapeutic data. It is important to note that the screening strategies described here are considered first-line investigations. In patients with strong clinical suspicion of a particular condition, additional testing may be appropriate. An example of this is immunodeficiency. For example, although low immunoglobulin levels and functional antibody testing (e.g measurement of pneumococcal antibody followed by pneumococcal vaccination if low and repeat antibody measurement 6 weeks later) can identify many immunodeficiencies, referral to an immunologist should be considered for patients with suggestive features, even when initial immunoglobulin levels are normal.

Monitoring/evaluation

Etiological testing is typically undertaken at the time of diagnosis; however, this should be viewed as an ongoing process. If patients' clinical features change in a way that raises suspicion for a new diagnosis, further testing should be undertaken. Although formal severity assessment is recommended at diagnosis, it should not be limited to that time point. Assessment of future risk should be a key part of every clinical review.

Future research

Large-scale studies performing genetic testing for PCD, CF and primary immunodeficiecies in adults with bronchiectasis, with appropriate downstream testing to confirm the diagnoses, are required to determine the true prevalence of these conditions and to inform the development of optimal screening strategies. Studies implementing comprehensive aetiological testing approaches across different regions/countries are required to determine if the recommended screening strategies are globally applicable and cost-effective.

Severity marker	Score
Age, yrs	
<50	0
50-69	2
70-79	4
80+	6
BMI, kg/m^2	
<18.5	2
18.5-25	0
26-29	0
30 or more	0
FEV_1, % predicted	
>80	0
50-80	1
30-49	2
<30	3
Previous hospital admission	
No	0
Yes	5

Severity marker	Score
Number of exacerbations in previous year	
0	0
1-2	0
3 or more	2
MRC breathlessness score	
1-3	0
4	2
5	3
Pseudomonas colonization	
No	0
Yes	3
Colonization with other organisms	
No	0
Yes	1
Radiological severity: ≥3 lobes involved or cystic bronchiectasis	
≥3 lobes involved or cystic bronchiectasis	1
<3 lobes involved	0

Table 2. The Bronchiectasis Severity Index. Patients receive a score out of a maximum of 24 points. 0-4 points is considered “mild”/low risk of mortality of hospitalization, 5-8 points is considered moderate or intermediate risk of mortality and hospitalization. ≥9 points is considered severe or high risk of mortality and hospitalization.

PICO QUESTION 1- AIRWAY CLEARANCE

Should airway clearance techniques be used (compared to no airway clearance techniques) in adults with bronchiectasis?

Recommendation

We recommend that patients with bronchiectasis should be taught airway clearance techniques (strong recommendation for the intervention, very low certainty of evidence)

Remarks

- Airway clearance techniques (ACTs) are best taught by a respiratory physiotherapy with appropriate experience.
- There is no evidence that one technique is superior to another and, therefore, treatment should be personalized.
- Airway clearance devices may be used to support manual ACTs.
- Previous ERS guidelines limited ACTs to patients with chronic productive cough. The current recommendation acknowledges that some patients with a dry cough, particularly those with mucus plugging on chest CT, may benefit from ACTs. Instruction in ACTs may also assist patients during periods of increased symptoms, such as exacerbations.

Summary of evidence

We included two RCTs (a 12-month RCT and a 3-month cross-over trial) that evaluated ACTs in 39 participants versus 40 receiving standard care or placebo exercises. These studies showed no significant difference overall in the percentage of participants with at least one exacerbation during follow-up (OR 0.58, 95% CI 0.21 – 1.58)[63,64], whilst the 12-month RCT by Munoz *et al.* showed a significant reduction in exacerbation rate over 12 months. Improvements in health related quality of life were clearly demonstrated with ACTs, with a statistically significant mean total Leicester Cough Questionnaire (LCQ) score improvement of 2.81 (95% CI 0.72 – 4.9) and a mean difference in St. George's Respiratory Questionnaire (SGRQ) score of -12.51 points (95% CI -22.39 – -2.62).[63,64] Both of these exceed the reported minimum clinically important difference (MCID) for these measures. Our meta-analysis also indicated a significant reduction in breathlessness with a mean difference in the modified medical research council (mMRC) dyspnoea scale of -1.36 points (95% CI -2.14 – -0.58) and significant increase in 24-hour sputum volume (MD 6.2 ml, 95% CI 0.46 – 11.95).

The overall certainty of evidence was rated as very low, primarily due to a high risk of bias, imprecision. No studies reported on hospitalisation rates, adverse effects, or treatment burden.

Justification of recommendations

ACTs are associated with improved quality of life and symptoms, and may reduce exacerbations.[63,64] Airway clearance is a key component of daily bronchiectasis management.[65] Despite the very low certainty of evidence, the panel issued a strong recommendation based on the following: i) ACTs are self-administered, low-cost, and

accessible; ii) Patients widely recognise their benefits; iii) The recommendation was strongly supported by patient representatives. Although adverse effects and harms were not systematically reported or collected, ACTs are widely believed to be safe and low risk of adverse events. These factors outweigh the limitations of the evidence base and highlight a need for broader implementation. Airway clearance is underutilized in clinical practice, and this recommendation should encourage increased uptake among healthcare professionals and policy.[66]

Implementation considerations

Patients should receive appropriate training and personalised guidance in selecting the most suitable ACTs for their individual needs by a specialist respiratory physiotherapist. It is acknowledged that not all patients will have access to a respiratory physiotherapist and other healthcare professionals may be involved in teaching airway clearance. Although direct comparative studies are lacking, clinical experience from the panel members suggest starting treatment with independent ACTs (defined as methods used to clear mucus and secretions from the airways that can be performed by an individual without the need for assistance from another person or specialized equipment). Adjuvant airway clearance devices may be considered to enhance sputum properties, facilitate consistent treatment, and increase adherence and tolerability.[65] These devices may not be equally accessible in low- and middle-income settings, and patients typically bear the costs due to limited coverage by health systems. Although the acceptability of remote delivery for this intervention is uncertain, it may offer an opportunity to enhance accessibility. Additionally, the panel supports implementing ACTs alongside an educational approach that identifies the benefits of this intervention and addresses barriers and facilitators to promote long-term adherence.[67] Finally, when inhaled mucoactive agents or bronchodilators are administered alongside ACTs, the timing of administration in relation to ACTs should be carefully managed to maximize treatment synergy.

There are no head-to-head studies comparing different ACTs, and the consensus is that no one technique is superior to others.[18,65] Therefore, techniques should be chosen based on individual preference and effectiveness.

Monitoring/evaluation

Patients trained in ACTs should be periodically reviewed to ensure the techniques are still performed correctly, are suitable to patient needs and/or to modify techniques if the disease changes.

Future research

Large RCTs of ACTs in bronchiectasis would be desirable, though controlled trials of ACTs are complex since ACT are standard of care and there are ethical considerations in withholding this treatment. Key research priorities in this area include: i) Long-term impact of ACTs on exacerbation frequency (e.g 12 months or greater); ii) Optimal strategies for delivering ACT training; iii) Effectiveness of virtual methods such as online training or video/remote training to deliver ACTs; iv) Additional benefits provided by airway clearance devices; v) Whether exercise alone is as effective as ACTs in improving respiratory symptoms, and whether patients performing regular exercise also require ACTs[68]; vi) The

role, effectiveness, and adaptability of ACTs during exacerbations, especially in relation to exacerbation severity and individual patient characteristics.

PICO QUESTION 2 - Mucoactive drugs

Should mucoactive drugs be used (compared with no mucoactive drugs) in adults with bronchiectasis?

Recommendation

We suggest to offer mucoactive treatments to patients with bronchiectasis where airway clearance has failed to control symptoms (conditional recommendation for the intervention, very low certainty of evidence)

We suggest not to offer recombinant DNAse to patients with bronchiectasis (conditional recommendation against the intervention, very low certainty of evidence)

Remarks

- The choice of mucoactive treatment should be guided by patient's co-morbidities and concerns around treatment burden and tolerability.
- Mucoactive treatments are best delivered as part of a comprehensive airway clearance regimen, which includes personalized airway clearance instruction with or without devices, and regular physical exercise.

Summary of evidence

We included nine randomised trials investigating mucoactive treatments, including 12-52 weeks of inhaled mannitol[69,70], 15 days of oral erdosteine[71], 2-24 weeks of aerosolised recombinant human DNAse I[72,73], 3-12 months of inhaled hypertonic saline (6% or 7%)[74–76], and 12 months of oral N-acetylcysteine[77]. In three randomised trials, testing mannitol, hypertonic saline and N-acetylcysteine, we found no significant difference overall in exacerbation frequency (MD -0.28, 95% CI -0.63 – 0.07). We found no difference in exacerbation frequency rate ratio (0.99, 95% CI 0.80 – 1.23) from 2 trials and no difference in the proportion of patients free of exacerbations during follow up (odds ratio [OR] 1.48, 95% CI 0.88 – 2.51) from 3 trials.[77–79] One study reported time to first exacerbation that was significantly prolonged with 400 mg inhaled mannitol compared with low-dose mannitol control twice daily for 52 weeks (hazard ratio [HR] 0.78, 95% CI 0.63 – 0.96).[69] There were no differences found in the odds of participants remaining free from hospitalisation during follow-up (OR 3.35, 95% CI 0.32 – 35.36). Regarding quality-of-life measurements, in three studies overall there was a two point improvement in total SGRQ with treatment (MD -2, 95% CI -3.6 – -0.4) and in one study a large improvement in the quality of life bronchiectasis respiratory symptom domain was observed MD 11.42 lower (20.38 lower to 2.46 lower)]. In one trial of 12-months of N-acetylcysteine, 24 hour sputum volume was significantly lower, with a mean difference of 11.82 ml (95% CI -19.31 – -4.33) between the treatment and placebo groups.[77] Across four studies, we found no significant differences in percentage of participants experiencing at least one adverse event related to study medication in the

treatment groups (OR 1.4, 95% CI 0.96 – 2.04). No studies reported on impact on activities of daily living.

Justification of recommendation

Mucus in bronchiectasis is typically hyperconcentrated and viscous, impairing mucociliary clearance.[80] Mucus plugging, a common radiological feature, is associated with exacerbation risk and disease severity.[15] Oral mucoactive agents, such as carbocisteine or N-acetylcysteine, reduce mucus viscosity though evidence is limited.[12] Nebulized hypertonic saline and inhaled mannitol hydrate mucus and stimulate cough to facilitate clearance. Mucoactive treatments may improve symptom burden and quality of life when used in addition to airway clearance and exercise. Despite limited evidence our recommendation prioritises improvements in quality of life and symptoms, and is supported by the lack of significantly increased adverse events. One study assessing inhaled mannitol suggests greater benefit in patients with more severe symptoms.[52] Highly symptomatic patients with poor quality of life could therefore be considered for mucoactive treatment. Inhaled mucoactive treatments may cause wheezing or bronchospasm. The use of pre-treatment bronchodilators can mitigate this risk. Notably, recombinant human DNase was ineffective and reduced FEV_1 in a previous trial. Therefore, its use is not recommended.[73]

Implementation considerations

An individualized approach should be adopted, taking into account symptom and treatment burden, feasibility, tolerability, and patient preferences. As nebulized hypertonic saline can cause bronchospasm, a test dose and pre-treatment with a bronchodilator, especially in patients with asthma or severe airflow limitation, are recommended. Issues related to device availability, cleaning requirements, and replacement costs may increase treatment burden of inhaled therapies, as emphasized by patient representatives among the Task Force.[81] In this regard, high-efficiency, easy-to-clean nebulizers may be advantageous in resource-rich setting, Importantly, ACTs should be introduced before mucoactive therapy to ensure maximum treatment effectiveness.[65]

Monitoring/evaluation

Mucoactive treatments are primarily prescribed to improve symptoms and quality of life. If no clinical benefit is evident after a reasonable trial period (e.g 3 months), treatment should be discontinued.

Future research

Large RCTs using precision medicine approaches to target mucoactive treatments based onsymptom burden and/or particular sputum characteristics (i.e abnormal mucins, mucus properties or DNA content) are needed. Although recombinant human DNase proved ineffective in a trial published in 1998[73], new insights into neutrophil extracellular traps and poor disease outcomes[82], as well as bronchiectasis endotypes[83], suggest that further research is needed to clarify whether specific subgroups of adults with bronchiectasis may

benefit from recombinant human DNase. Mucociliary clearance targeting treatments, in contrast to antibiotics and anti-inflammatory treatments, have been neglected and the development of novel mucoactive agents should be a research priority in future.

PICO QUESTION 3 - Inhaled antibiotics

Should long term inhaled antibiotics be used (compared with no long term inhaled antibiotics) in adults with bronchiectasis?

Recommendation

We recommend to offer long term inhaled antibiotics to patients at high risk of exacerbations and chronic infection with *Pseudomonas aeruginosa despite standard care* (Strong recommendation for the intervention, moderate certainty of evidence)

We suggest to offer long term inhaled antibiotics to patients at high risk of exacerbations and chronic infection with pathogens other than *Pseudomonas aeruginosa despite standard care* (Conditional recommendation for the intervention, moderate certainty of evidence)

Remarks

- Patient at high risk of exacerbations include patients with a history of 2 or more exacerbations in the prior year OR 1 severe exacerbation OR 1 exacerbation plus severe daily symptoms.
- Inhaled antibiotics should be prescribed for a defined period and treatment response should be formally evaluated. If ineffective or poorly tolerated it should be discontinued
- Inhaled antibiotics are drug and device combinations and, therefore, patients should be provided with an appropriate nebulizer along with the medication.
- Many clinicians would perform a supervised test dose of inhaled antibiotics because of the risk of bronchospasm.

Summary of evidence

We included 18 randomised trials for this question, noting that some manuscripts reported more than one trial within a single paper. Across 13 trials, inhaled antibiotics reduced exacerbation frequency by 20% compared to controls (rate ratio 0.80, 95% CI 0.70-0.92).[20,84–90] Across 18 studies, there was a significant 15% reduction in the number of patients with at least one exacerbation (risk ratio 0.85, 95% CI 0.76 – 0.94) [20,84,93–95,85–92], frequency of severe exacerbations was reduced by 43% in eight studies (rate ratio 0.57, 95% CI 0.35-0.94)[20,84,86,94,96,97], and time to first exacerbation was prolonged in pooled data from 14 studies (hazard ratio [HR] 0.81, 95% CI 0.71-0.93) in those receiving inhaled antibiotics. Regarding quality of life and symptoms, there was no significant improvement in QoL-B respiratory symptoms score (MD 2.14, 95% CI 0.28 – 4.57)[84–90] or total SGRQ score (MD 2.63, 95% CI -5.37 – 0.1)[20,87,88,93–96] with inhaled antibiotic treatment overall in 11 and eight studies, respectively. In 18 studies, an increase in antimicrobial resistance was found with a 1.96-fold higher risk of identifying bacterial isolates with antibiotic minimum inhibitory concentrations (MICs) indicative of resistance in those receiving antibiotics (RR 1.96, 95%

CI 1.55 – 2.48). There were no differences in numbers of participants reporting treatment-emergent adverse events (TEAEs) in 15 studies (OR 1.04, 95% CI 0.81 – 1.35)[20,84,95,96,85–88,90,91,93,94] and no differences in all-cause mortality (OR 1.04, 95% CI 0.57 – 1.89) from 15 studies.

The certainty of evidence was rated as moderate overall. The majority evidence comes from studies included patients infected with *P. aeruginosa* while evidence for patients without *P. aeruginosa* infection remains more limited.

Justification of recommendation:

A strong recommendation was made for patients chronically infected with *P. aeruginosa,* based on clinically relevant reduction in exacerbation frequency, including severe exacerbations. A conditional recommendation was made for patients with other chronic infections, given the predominance of *P. aeruginosa* in the available meta-analysis and the availability of effective treatments, including long term macrolides, in these patients. The recommendation prioritises the clinically relevant improvements in exacerbation outcomes, in the context of the poor outcomes experienced by patients with chronic *P. aeruginosa* infection, and is also informed by the lack of any significant increase in adverse events. The panel acknowledged the risk of antimicrobial resistance which is important at population level but is of uncertain significance for the individual patient in the context of inhaled antibiotics. Feedback from patients also supported a strong recommendation.

Previous guidelines recommended the use of long-term treatments such as inhaled antibiotics for patients with 3 or more exacerbations per year.[18] The current wording of the recommendation reflects the understanding that the number of exacerbations in the previous year is an important risk factor for future exacerbations but is not the only risk factor.[38,47,48,52,98] Patients with a high burden of daily symptoms are also at high risk of future exacerbations, and the threshold to commence long-term treatments may be lower in patients with other important prognostic features.[52,57] Clinical features associated with a higher risk of future exacerbations include *P. aeruginosa* infection, PCD, COPD, RA and sputum purulence.[35,36,53,58,99] The present recommendation, therefore, suggests that patients with 2 or more exacerbations are likely to be at high risk of future exacerbations, but that some patients with a lower number of exacerbations with a high symptom burden may also benefit from preventative treatment. The threshold to commence treatment should be individualised taking into account the key risk factors in each individual patient as well as considerations around the balance of risks and benefits, availability, cost and the burden of treatment.

Antimicrobial stewardship is a key consideration. Long-term antibiotic treatment should be used after other aspects of treatment have been optimised and, therefore, other options such as airway clearance, vaccination against respiratory pathogens, treatment of underlying causes and co-morbidities have been addressed.

Practical considerations:

Inhaled antibiotic treatments have historically been given one month on and one month off by some clinicians. There is some evidence that continuous use of antibiotics provides sustained symptomatic benefit compared to cyclical treatment and no evidence that resistance is different.[20,84,100,101] Some clinicians advocate continuous use of antibiotics on this basis but availability and cost considerations may also influence this.

Treatment burden is an important consideration for patients prescribed inhaled antibiotics, particularly in relation to administration time and cleaning of equipment, which may affect adherence.[102] In line with antimicrobial stewardship principles inhaled antibiotics should be used where other measures have been ineffective to prevent exacerbations. There should be clear evidence of chronic bacterial infection of the airways and that other potential drivers of frequent exacerbations have been considered and addressed. Other important practical considerations are included in the remarks above. In addition to be provided with an appropriate nebulizer patients and/or caregivers should be appropriately trained in their use and cleaning. Inhaled antibiotics are often taken alongside with other medications. The recommended sequence of treatments, as described in the 2017 ERS bronchiectasis guidelines, would be to take bronchodilators first, followed by nebulized/inhaled mucoactive drugs, followed by performing airway clearance, and then taking inhaled antibiotics to optimise deposition.[18]

Monitoring and evaluation

Treatment should be prescribed for a defined period and re-evaluated. If no clear benefit is observed, inhaled antibiotics should be discontinued, and alternative strategies should be considered to reduce exacerbations. If benefit is observed treatment may be continued with monitoring for adverse effects. Long term treatment is defined as a minimum of 3 months but most available data is over 12 months. The optimal period for evaluating response is not known, but as the primary benefit is on exacerbations many clinicians would re-evaluate efficacy after 1 year.

Research priorities

Although long term inhaled antibiotics show efficacy in studies, predicting individual response remains a challenge as reflected by inconsistent results across RCTs. The panel, therefore, recommends studies that should focus on precision approaches to optimize treatment selection. Key research questions include: i) Can inflammatory or microbial biomarkers predict patients' response to inhaled antibiotics?; ii) What is the best way of identifying patients at risk of future exacerbations? Iii) What is the impact of inhaled antibiotics on antimicrobial resistance and what, if any, are the clinical consequences of resistance on treatment efficacy and future outcomes.

PICO QUESTION 4 – Macrolides

Should long-term macrolides be used (compared with no long-term macrolides) in adults with bronchiectasis?

Recommendation

We recommend to offer long-term macrolides to patients at high risk of exacerbations despite standard care (Strong recommendation for the intervention, moderate certainty of evidence)

Remarks

- Macrolides are effective in a broad group of patients with bronchiectasis at high risk of exacerbations including patients with chronic *P. aeruginosa* infection, patients with airway infection caused by other pathogens, and those without evidence of airway infection.
- Macrolides should not be prescribed as monotherapy to patients with NTM infection. NTM infection should be excluded before initiating macrolide therapy.
- The most widely used long-term macrolide is azithromycin, typically at a dose of 250 mg daily or three times per week, or 500 mg three times per week.
- In view of the risk of adverse effects, patient education, baseline screening, and appropriate follow-up are important when prescribing macrolides.

Summary of evidence

We included 9 randomized controlled trials. Meta-analysis found a significant and highly clinically relevant 52% reduction in exacerbation frequency/rate (HR 0.48, 95% CI 0.37 – 0.62) in those receiving macrolides compared with those who did not from four randomized trials.[103–107] In five randomised trials, a significant 36% lower risk of having exacerbations (risk ratio 0.64, 95% CI 0.46 – 0.89) was found [103–106,108,109], Two trials reported a significantly longer time to first exacerbation (HR 0.32, 95% CI 0.21 – 0.47)[104,105]. A clinically-meaningful, significant improvement in SGRQ total score was found in seven studies, with average improvement of 7.26 points (MD -7.26, 95% CI -10.94 – -3.59)[103–105,107,109–111] in participants receiving long term macrolides *versus* those in the comparator groups. There were no differences in the frequency of identification of antimicrobial resistant organisms between participant groups across two studies (OR 1.08, 95% CI 0.22 – 5.19) or in the odds of isolating a new pathogen (OR 0.82, 95% CI 0.41 – 1.63) within two trials. In data from six studies, there was no significant increase in adverse events in those receiving macrolides (OR 0.86, 95% CI 0.53 – 1.39).[103–105,108,110,111] In three smaller studies, reported mortality overall was low, with no differences between groups and one study also reported no differences in incidence of hospitalisation (OR 0.45, 95% CI 0.04 – 5.19).

Justification of recommendations

A strong recommendation is supported by a highly clinically relevant reduction in exacerbations and a highly meaningful improvement in quality of life with long-term macrolide treatment.[106] The trials show no major safety concerns, and in studies of 6 to 12 months duration, antimicrobial resistance was not identified as a significant issue. The largest studies included patients with at least 1 exacerbation per year, and benefit was demonstrated across multiple patient subgroups including those with low exacerbation frequency and the subgroup of patients with *P. aeruginosa* infection.[106]

While previous guidelines recommended the use of long-term treatments such as macrolides for patients with 3 or more exacerbations per year[18], the current wording of the recommendation reflects the recognition that past exacerbation frequency is a key, but not exclusive, predictor of future risk.[38,47,48,52,98] Patients with a high burden of daily symptoms are also at high risk of future exacerbations, and, in such cases, the threshold for initiating long-term treatments may be lower.[52,57] Clinical features associated with a higher risk of future exacerbations include *P. aeruginosa* infection, PCD, COPD, RA and sputum purulence.[35,36,53,58,99] The present recommendation therefore suggests that patients with >=2 exacerbations are likely to be at high risk of future exacerbations, but that some patients with

a lower number of exacerbations with a high symptom burden or other risk factors may also benefit from preventative treatment. The threshold to commence treatment should be individualised, based on patient-specific risk factors, risk-benefit balance, and treatment burden.

Practical considerations

Although no major safety concerns were identified in the trials, macrolides are not without risks and most studies carefully excluded patients at high risk of macrolide related adverse events.[103–105] Prior to starting macrolide maintenance therapy, patients should be screened for NTM infection, QT-time abnormalities, and liver/kidney function abnormalities.[112] Patients should be warned about the possibility of ototoxicity, which usually manifest as tinnitus, hearing loss and vestibular dysfunction. Treatment should be discontinued if these symptoms occur. Many clinicians will perform ECG, urea and electrolytes and LFTs 2-3 weeks after initiation of macrolide maintenance treatment to monitor QT interval and liver/ kidney function. However, the optimal monitoring strategy is not yet defined due to a lack of studies.

The optimal macrolide dosage has not been established. The largest trials used either azithromycin 250 mg daily or 500 mg three times per week, or erythromycin.[103–105] The observed efficacy of erythromycin suggests a class effect, although azithromycin is preferred due to better tolerability and the possibility of intermittent dosing.[12] Adverse effects appear larger in studies that use higher doses[104,113] and clinicians may consider starting at the lowest effective dose (e.g azithromycin 250 mg daily or three times per week, or 500 mg three times per week).[112]

Monitoring and evaluation

Patients on long term macrolide therapy should be reviewed on an individualized basis to assess efficacy (e.g. number of exacerbations, symptoms) and side effects. The optimal duration of macrolide therapy is unknown, with the longest studies being up to 12 months. Discontinuation may be considered after one year if no clear benefit is observed, or, alternatively, if remission of exacerbations and symptoms is reached. In such cases, a careful discussion about the risks and benefits of discontinuation is needed due to the risk of relapse.

Research priorities

Key research questions in the field of long-term macrolide use include: i) What is the long-term safety profile of macrolides beyond 12 months, including impacts on antimicrobial resistance, emergence of new pathogens, and adverse effects?; ii) Can macrolide treatment prescribed at early disease stage (e.g mild bronchiectasis with non-frequent exacerbations but risk-factors for progression) result in slowing disease progression or even in achieving remission?; iii) What is the optimal monitoring strategy for adverse events? Do all patients require ECGs before and after macrolide initiation? Is NTM screening required for all patients or only for patients with high-risk clinical features? What is the value of baseline or follow-up audiology screening?; iv) Can macrolides be safely discontinued in clinically stable patients with a low symptom and exacerbation burden?

PICO QUESTION 5- Oral antibiotics

Should long-term non-macrolide oral antibiotics be used (compared to no long-term non-macrolide oral antibiotics) in adults with bronchiectasis?

Recommendation

The panel suggests NOT to offer long-term non-macrolide oral antibiotics as a first line treatment to adult patients with bronchiectasis and a high risk of exacerbations (conditional recommendation against the intervention, very low certainty of evidence).

Remarks

- Long-term non-macrolide oral antibiotics may have a role in specific situations where patients are at high risk of frequent exacerbations and other options such as long-term macrolides are contraindicated or have proven ineffective.

Summary of evidence

Two trials were included, investigating the use of amoxicillin, penicillin and oxytetracycline in patients with bronchiectasis.[114,115] Meta-analysis was not possible and so the results of the individual studies are reported narratively. After adjusting for exacerbations frequency in the year before the study, no statistically significant difference in exacerbation rates was observed between the amoxicillin and placebo groups.[114] Furthermore, no clinically meaningful reduction in mortality was reported[115]. Some reductions in breathlessness and sputum volume were noted, although these effects were limited. Currie *et al*. showed a 58% reduction in sputum volume after 32 weeks in the amoxicillin group compared to 19% in the placebo group.[114] Scadding and colleagues found a 26% reduction in sputum volume in the penicillin group, 36% reduction in the oxytetracycline group and 24% reduction in the placebo group after one year. Finally, a slight increase in adverse events and the emergence of potentially pathogenic organisms, as well as a modest rise in antibiotic resistance, were observed in the treatment arms. However, meta-analyses were not feasible due to limited and inconsistently reported data. The trials are also hampered by small population size, questionable inclusion criteria, and, sometimes, a low number of outcome events, resulting in very low certainty of evidence.

Justification of recommendation

The overall risk-benefit balance of long-term non-macrolide oral antibiotics appears to be unfavorable, given the lack of a clear reduction in exacerbations and other clinically relevant outcomes. The available studies are, however, hampered by small populations, unclear reporting of data, questionable inclusion criteria and sometimes a low number of events, resulting in very low certainty of evidence. Therefore, routine use of non-macrolide oral antibiotics is not recommended, as there is limited evidence, a risk of adverse effects and more effective first-line alternatives exist.

There are exceptional circumstances where non-macrolide maintenance antibiotics may be an appropriate treatment for patients with bronchiectasis. This includes in patients at high

risk of NTM or regions with high NTM prevalence[16], or in patients unable to take macrolides due to adverse effects. Therefore, in cases where macrolides are contraindicated or ineffective, and there is clear evidence of infection in respiratory cultures, a trial of long-term, targeted non-macrolide antibiotic therapy may be justified.

Implementation considerations

Physicians and healthcare workers should be advised on the current lack of evidence supporting the use of non-macrolide, long-term antibiotics in bronchiectasis. These treatments should only be considered in patients unable to receive macrolides, with the understanding by healthcare professionals that current data only show limited reduction in shortness of breath and sputum volume.

Monitoring/evaluation

As with any long-term treatment, a formal evaluation of efficacy is recommended and therapy should be discontinued if ineffective.

Future research

RCTs on long-term, non-macrolide oral antibiotics are needed to establish if they reduce exacerbations and improve symptoms, and which patient populations are most likely to benefit.

Figure 3 shows an algorithm for long-term antibiotic use in patients with bronchiectasis. The algorithm first emphasizes antimicrobial stewardship, and that alternative treatments and optimization of management should occur before long-term treatments are considered. Identification of patients at high risk of exacerbations include those with frequent prior exacerbations, severe symptoms, as well as severe exacerbations, while also considering additional risk factors for poor outcomes. In view of the greater evidence for inhaled antibiotics in patients with *P. aeruginosa* we recommend a different approach for patients with and without *P. aeruginosa* infection. Patients with *P. aeruginosa* may receive either a long-term macrolide or long-term inhaled antibiotic as first line treatment, with the choice based on patient preference and an individualized assessment of risks. For patients without *P. aeruginosa* infection macrolides are a clear first line option. (figure 3).

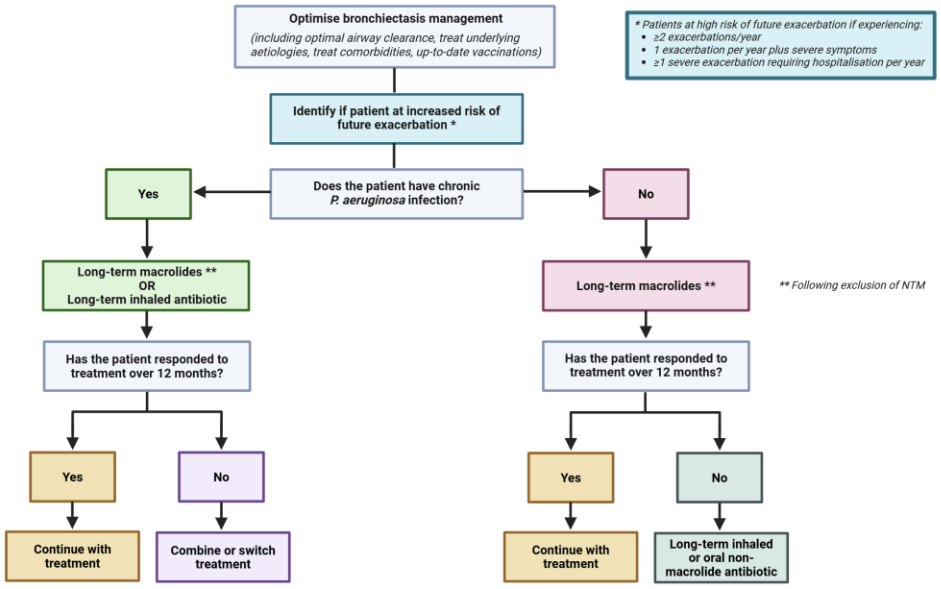

Figure 3. ERS algorithm for long-term antibiotic treatment in patients with bronchiectasis. The identification of high risk individuals is addressed in narrative question 1. Recommendations on long term inhaled antibiotics and macrolides are addressed in the respective PICO questions. Long term oral antibiotics are also addressed in the relevant PICO question. Note that while 12 month reevaluation is suggested as justified in the text, earlier reassessment is needed, particularly in the case of adverse events or clinical deterioration.

PICO QUESTION 6 - Eradication

Should eradication treatment be used for patients with isolation of a new pathogenic microorganism (compared to no eradication treatment)?

Recommendation

We suggest to offer eradication treatment to patients with a new isolation of *Pseudomonas aeruginosa* (conditional recommendation for the intervention, very low certainty of evidence)

Remarks

- A new isolation of *P.aeruginosa* may refer to the first time a patient has *P. aeruginosa* isolated or a further isolation following a prolonged period during which *P. aeruginosa* was not detected.
- Eradication practices vary both among panel members and globally. Some clinicians prescribe systemic antibiotics (e.g 2-week course) followed by a repeat sputum culture, discontinuing antibiotics if the sample is negative. Others would add inhaled antibiotics for 4 weeks to 3 months, without rechecking sputum cultures. The 2017 ERS guidelines provide examples of different antibiotic strategies.

Summary of the evidence

No randomized trials comparing eradication with no eradication treatment were identified. The only available evidence comes from before-and-after, observational studies assessing eradication success and clinical outcomes before and after the intervention. All studies examined *P. aeruginosa* eradication treatment. Six studies were identified, 5 observational studies and 1 randomized trial which evaluated two different eradication regimens. The randomized trial was treated as a before and after observational study for the purposes of analysis.[116–121] Pooled data from these studies indicate that eradication was achieved in approximately 40% of patients at 12 months.[122] Three studies reported a reduction in exacerbations and/or hospitalisations during the year following the eradication intervention.[116,120,121] The certainty of evidence is considered very low, due to the observational nature of the studies, the lack of a control group, and other limitations.

Justification of the recommendation

Despite limited available data, there is overwhelming evidence that chronic infection with *P. aeruginosa* is associated with increased mortality, exacerbations, hospitalisations and worse quality of life.[53,99,123,124] Preventing chronic *P. aeruginosa* infection is, therefore, of high benefit to patients, and this was confirmed by our panel members with lived experience. The conditional recommendation reflects both the very low certainty of evidence and the concern that while 40% achieve eradication with the current treatments, it is unknown how many patients would achieve spontaneous clearance due to the lack of control groups across studies. The eradication treatment carries burden, particularly if inhaled antibiotics are used, and antibiotic use is associated with a risk of antimicrobial resistance and side effects.

No evidence was identified for the eradication of organisms other than *P. aeruginosa* and implicit in the above recommendation is that eradication is not recommended routinely for pathogens other than *P. aeruginosa*

Implementation considerations

The 2017 ERS guidelines provides examples of antibiotic regimens for eradication which typically consist of 2 weeks of oral or IV antibiotics followed by 6 weeks to 3 months of inhaled antibiotics. Practice varies in terms of the antibiotics used, and whether some clinicians will check sputum cultures after the systemic antibiotic phase and discontinue treatment if sputum is negative, while some clinicians will use inhaled antibiotics regardless of whether initial culture conversion is achieved after systemic antibiotics.

Monitoring and evaluation

Patients undergoing eradication treatment should have sputum cultures performed after the completion of therapy and at 1 year to confirm whether eradication was successful. Patients in whom eradication is not achieved should be managed as having chronic *P. aeruginosa* infection.

Research priorities

An RCT comparing *P. aeruginosa* eradication therapy *versus* symptomatic treatment only is needed to establish the long-term efficacy and safety of this practice. Studies utilising molecular techniques to detect *P. aeruginosa* should be performed to identify if the organism is truly eradicated or merely suppressed following treatment.

PICO QUESTION 7– Inhaled corticosteroids

Should long-term inhaled corticosteroids be used (compared to no long-term inhaled corticosteroids) in adults with bronchiectasis?

Recommendation

We suggest not to offer long term inhaled corticosteroids to patients with bronchiectasis who do not have coexisting COPD or asthma (conditional recommendation against the intervention, low certainty of evidence)

Remarks

- Patients with bronchiectasisshould be evaluated for the presence of co-existing asthma and COPD. The presence of bronchiectasis does not alter the recommendation to use inhaled corticosteroids (ICS) in patients with asthma or in a subset of patients with COPD. Suspected asthma or COPD should be appropriately investigated in patients with bronchiectasis.
- There is limited evidence suggesting that ICS may be beneficial in a subgroup of patients with bronchiectasiswith elevated blood eosinophil counts who do not have asthma or other eosinophilic conditions. However, no recommendation on ICS use based on blood eosinophils is currently possible, and we recommend further research in this group.
- The use of ICS should be reevaluated in patients without a clear indication. Discontinuation of ICS may be appropriate in some patients.

Summary of evidence

Six randomised trials were identified, one cross-over study of beclomethasone diproprionate 1500 µg per daily[125] , RCTs of 400 µg budesonide twice daily, fluticasone 500 µg twice daily[126,127], beclomethasone-formoterol 200/12 µg twice daily[128], and a randomised trial of 250 µg or 500 µg fluticasone propionate[129]. Three studies reported no overall differences in average number of exacerbations or number of participants with an exacerbation in the groups receiving ICS compared to those receiving no treatment or placebo (MD -0.2, 95% CI -0.57 – 0.16; OR 0.89, 95% CI 0.24 – 3.26, respectively).[126,129,130] There were no significant differences in 24-hour sputum volume across three trials (MD -3.37, 95% CI -8.18 – 1.43)[125–

[127,129], or in FEV_1 in four trials (MD 0.03, 95% CI -0.19 – 0.12).[125,127,129,130] There were no significant effects identified for health-related quality of life: in two trials there were no differences in SGRQ total score (MD -3.54, 95% CI -8 – 0.92)[129,130] and in one study there was no change in QoL-B score (MD 3.7, 95% CI -9.59 – 16.99).[128] There was a significant increase AEs in four studies (OR 3.19, 95% CI 1.34 – 7.61) in those receiving ICS compared to the respective control groups. There was no significant impact on the incidence of hospitalisation in one study (OR 0.20, 95% CI 0.02 – 1.90) and no effect on mortality. No studies reported on occurrence of pneumonia or new NTM isolation.

Certainty of evidence was low as most critical outcomes including exacerbations, quality of life and AEs, were rated as low due to downgrading for factors including imprecision and biases such as lack of blinding and premature trial termination.

Justification of the recommendation

The panel considered there is a lack of evidence of benefit of ICS and a risk of harms associated with this treatment. AEs of ICS are well known and include an increased risk of pneumonia and NTM infection as well as a small but significant increase in systemic adverse effects of corticosteroids.[131] 20-30% of people with bronchiectasis have comorbid asthma or COPD.[35,132] Treatment with ICS is recommended for most individuals with asthma and for a subset of people with COPD who have elevated blood eosinophils and frequent exacerbations.[133,134] There is no clear evidence that bronchiectasis should influence the decision to prescribe ICS in these groups.[135]

Blood eosinophils require further investigation in bronchiectasis as a predictor of ICS efficacy. Around 20% of patients with bronchiectasis have blood eosinophil counts >300cells/µl in the absence of asthma or other eosinophilic conditions.[136] There are reports suggesting that in a subset of individuals with elevated blood eosinophils, ICS may be beneficial in improving quality of life and reducing exacerbations but these data are from *post hoc* analyses and observational studies only and prospective trials are needed.[137]

Practical considerations

The use of ICS, with or without long-acting beta2 agonists (LABA), is widespread in patients with respiratory symptoms, and misdiagnosis of bronchiectasis as asthma or COPD is not uncommon.[35,132,138,139] Many newly diagnosed patients with bronchiectasis are already receiving ICS, and the decision to continue or withdraw ICS when bronchiectasis is diagnosed requires consideration.[140] Factors supporting ICS withdrawal include absence of asthma or COPD, supported by established criteria, and low blood eosinophils.[141] Conversely, every effort should be made to correctly identify asthma in patients with bronchiectasis as ICS have demonstrated benefit in this group.[132] Misdiagnosis of COPD is also common in bronchiectasis, and the ROSE criteria, which define COPD-Bronchiectasis associated in the presence of **R**adiological bronchiectasis, FEV1/FVC<0.7 (**O**bstruction), appropriate **S**ymptoms and appropriate **E**xposures (typically smoking) may support in appropriate diagnostic labelling. [141]

Monitoring and evaluation

If ICS are used, treatment effectiveness should be formally evaluated after a defined period of time, and ICS discontinued if ineffective or if AEs outweigh potential benefits.

Research priorities

A RCT of ICS in bronchiectasis is needed to establish if they can reduce exacerbation frequency and whether blood eosinophil counts predict treatment response. Since ICS is widely used in bronchiectasis, it may be possible to perform a randomized controlled trial of withdrawal of ICS. Further studies are required to understand the role of T2 inflammation in bronchiectasis (not exclusively limited to blood eosinophils) and whether T2 biomarkers can guide treatment.

PICO QUESTION 8 - Pulmonary rehabilitation

Should pulmonary rehabilitation be used (compared to no pulmonary rehabilitation) in adults with bronchiectasis?

Recommendation

We recommend that patients with breathlessness and/or impaired exercise capacity should be offered pulmonary rehabilitation (strong recommendation for the intervention, very low certainty of evidence)

Remarks

- The educational component of pulmonary rehabilitation (PR) should ideally be bronchiectasis specific and include discussion of airway clearance strategies.
- Patients with bronchiectasis should be encouraged to undertake regular physical activity, given its multiple health benefits.

Summary of evidence

We included 7 studies. Compared with usual care, the group of patients with bronchiectasis undergoing PR showed a significant improvement in exercise capacity after the intervention measured by distance (m) covered during 6 minute walking test (6MWT) in three studies (MD 41.13, 95% CI 28.74 – 53.53)[142–144], and measured by incremental shuttle walk test (ISWT) in four studies (MD 72.83, 95% CI 51.44 – 94.23).[144–147] These differences exceed the minimum clinically important difference. At follow-up, one study showed no difference in 6MWT distance (MD -6.74, 95% CI -29.61 – 16.13)[144] and two trials found no difference in ISWT distance (MD 39.41, 95% CI -33.02 – 111.83).[144,147] After the intervention, in two studies participants undergoing PR achieved significantly higher number of steps per day than those in the usual care groups (MD 1443, 95% CI 176 - 2709)[143,145], although in one study there was no difference in steps at the end of follow up (MD 18.1, 95% CI -2284.05 – 2320.25).[145] In two studies, breathlessness measured using the mMRC scale was significantly reduced after the intervention (MD -0.85, 95% CI -1.42 – -0.28).[142,143] Health-related quality of life measured by the SGRQ total score was significantly improved with PR; in two studies on average SGRQ score was 9.21 points lower (95% CI -13.2 – -5.22) after the intervention[142,147], and in one study 8.6 points lower (95% CI -14.34 – -2.86) in the

rehabilitation group compared with the usual care group at the end of follow up.[147] There was no differences in quality of life measured by LCQ in two studies after the intervention (MD 1.2, 95% CI -0.95 – 3.35) or at the end of follow-up (MD 0.98, 95% CI -0.32 – 2.29)[144,147], and no difference in QoL-B respiratory domain score in one study after the intervention (MD 3.6, 95% CI -3.18 – 10.38).[145] In one study, there was a significant 74% reduction in the odds of a participant experiencing at least one exacerbation during follow-up in the PR group compared to the usual care group (OR 0.26, 95% CI 0.08 – 0.81).[144] No significant impact on mortality was observed. No studies reported on occurrence of severe exacerbations.

Overall, there is a substantial benefit of PR in the short-term but most benefits are not sustained during follow-up distant from the intervention..

The certainty of evidence was rated very low due to downgrading based on risk of bias, inconsistency, and imprecision for many key outcomes.

Justification of recommendation

The recommendation is justified by consistent evidence of improvements in quality of life and exercise capacity. Despite the very low certainty of evidence, the strong recommendation is supported by the unequivocal improvement in functional capacity, and consistent results despite small sample sizes. Implementing PR requires substantial investment in resources and trained health professionals, which significantly increases the overall program costs.

Implementation considerations

Effective implementation of PR requires a multifaceted approach to tackle the many implementation pitfalls such as geographic inaccessibility, infrastructure, funding and standardization.[148,149] Many rehabilitation programs are designed primary for COPD, and the educational component may not be optimized for patients with bronchiectasis. As bronchiectasis becomes increasingly recognized, the feasibility of tailoring programs to patients with bronchiectasis is expected to improve. Previous guidelines address the delivery of PR.[150–152]

Monitoring/evaluation

In order to monitor rehabilitation quality and patient evolution, an official ATS/ERS policy statement advises that clinical outcomes must be measured for individual patients and include a standardized assessment of a patients' functional exercise capacity, dyspnea, and health status.[150,151] Additionally, evaluations of other outcomes are suggested, such as the impact PR has on psychological comorbidity and measurement of the patients' experience.

Future research

Future studies should explore how to individualize PR across different settings (home-based, outpatient clinics, hospital-based, community-based and tele-rehabilitation) as well as to evaluate digital tools that could replace face-to-face rehabilitation. Research should also try

to assess the impact of initiating PR during or immediately after an exacerbation. Finally, pragmatic strategies to sustain benefits of PR should also be a research priority.

Narrative question 2

What diagnostic tests and interventions are currently recommended/used for managing exacerbations?

We suggest the following diagnostic tests be performed during exacerbations (conditional recommendation for the intervention, very low certainty of evidence based on a narrative review of evidence):

Recommendations in current guidelines regarding diagnosis and treatment of exacerbations endorsed by the panel:

- An exacerbation is defined as a worsening of symptoms that exceeds day-to-day variability and requires a change in management. Core symptoms of exacerbation include a change in cough, sputum volume and/or consistency, sputum purulence, dyspnea and/or exercise intolerance, fatigue or malaise and haemoptysis.[153] Addition clinical features are fever, wheezing, general discomfort, anorexia, weight loss, pleuritic chest pain and changes on chest examination.[18,154,155]
- Features of a severe exacerbation (defined as requiring hospitalization or intravenous antibiotic treatment) may include tachypnoea, acute or acute on chronic respiratory failure, a significant decline in oxygen saturation or respiratory function, hypercapnia, hemoptysis, new onset of cyanosis, new signs of *cor pulmonale*, hemodynamic instability, and/or impaired cognitive function.[18,154,156]
- At the onset of an exacerbation, a sputum sample for microbiology should ideally be obtained before initiating antibiotic treatment.[18,154,156]
- Sputum culture should be repeated, where possible, if there is no response to the initial antibiotic treatment.[154,156,157]

We suggest the following interventions to be performed during exacerbations (conditional recommendation for the intervention, very low certainty of evidence based on a narrative review of evidence):

Recommendations in current guidelines regarding interventions endorsed by the panel:

- Antibiotics should be prescribed for an exacerbation, guided by previous microbiology results, local susceptibility patterns, and clinical severity.[18,154,156,157]
- An adult bronchiectasis self-management plan should include guidance on recognising exacerbations. Providing selected patients the ability to self-administer antibiotics at home with appropriate instruction and education, may allow more prompt treatment.[18,154,156,157]
- Patients not responding promptly to oral antibiotics or showing signs of a severe exacerbation, should be reviewed to determine if there is a need for a change in treatment, intravenous antibiotic treatment and/or hospitalization.[154]

- Airway clearance regimens may need to be adapted in frequency, intensity, and technique during an exacerbation.[65,154]
- In general, a 14-day antibiotic course is considered standard, especially in severe exacerbations or in patients with *P. aeruginosa infection.* Shorter courses may be appropriate in patients with mild bronchiectasis, those with infection due to pathogens more sensitive to antibiotics (e.g. *S. pneumoniae*), or patients with a rapid return to baseline symptoms during treatment.[18,154,156]

Summary of evidence

Exacerbations are a major cause of morbidity, diminished quality of life, and increased mortality in bronchiectasis, making their prevention and management a clinical priority.[153] The inherent complexity in defining an exacerbation complicates its diagnosis and management. Moreover, the evidence supporting diagnostic approaches and interventions in current guidelines is largely based on expert opinion and established clinical practice rather than high-quality trials, resulting in an overall low certainty of evidence.[18,153,157–159] Evidence suggests that In most exacerbations, there is no change in airway pathogens from stable state and antibiotic treatment is aimed to reduce symptoms, presumably by reducing the bacterial load rather than an attempt to eradicate the chronic infection.[83,160] Viruses are a common cause of bronchiectasis exacerbation.[83,161] Routinely screening for viruses in bronchiectasis has not been recommended by any guideline to date. Testing, particularly in inpatients presenting with acute respiratory tract infections is common and may influence management if SARS-CoV-2 or influenza are detected.[162,163] Table S1 lists documents that contributed to the review of the evidence.

Justification of recommendation

Despite the very low certainty of evidence, the recommendations are justified as many of the suggested practices are already routinely implemented in clinics and hospitals managing patients with bronchiectasis. While specific antibiotic regimens are not detailed due to variations in local practice and resistance patterns, general principles for management of exacerbations can still be established to guide clinical decision-making.

Implementation considerations

The implementation of these recommendations is expected to be straightforward, as they are generally inexpensive and already widely integrated into clinical practice. Given their broad acceptance and routine use in most settings, additional resource allocation or infrastructural changes are unlikely to be necessary for widespread adoption.

Monitoring/evaluation

Exacerbations are common and important events in the natural history of bronchiectasis. Monitoring and evaluation should prioritise assessing their frequency, severity, and response to interventions. Prevention of exacerbations is a major priority and therefore in addition to the acute management of exacerbations patients should be reviewed to determine if they are at high risk of future exacerbations, and preventative measures implemented to reduce future risk.

Future research

Future research should be focused on the following topics: i) Assessing the presence, severity, and evolution of bronchiectasis exacerbations; ii) Determining the optimal antibiotic management, especially regarding monotherapy *versus* dual antibiotics and evaluating the role of inhaled antibiotics during exacerbations; iii) Investigating the role of non-antibiotic treatments and identifying causes of exacerbations other than bacterial infection; iv) Establishing the optimal duration of antibiotic treatment particularly for outpatients v) identification of biomarkers that can allow shortening or individualising of antibiotic treatment duration.

Narrative Question 3

What investigations and treatments are currently recommended in a patient with bronchiectasis who is rapidly deteriorating in terms of symptoms or exacerbations?

We suggest the following investigations and management in a deteriorating patient (conditional recommendation for the intervention, very low certainty of evidence based on a narrative review of evidence):

Recommendations in guideline literature on investigations in the deteriorating patient endorsed by the panel:

- Clinical deterioration including increasing exacerbation frequency and/or severity, worsening of symptoms and/or rapid decline in lung function, should result in a comprehensive re-evaluation of the patients and their treatment.[18,154]
- Adherence to both airway clearance techniques and/or pharmacological treatment should be evaluated.[18,65,154]
- Underlying diseases other than bronchiectasis should be reviewed to ensure they are being adequately treated.[18,154]
- Investigation for specific conditions known to be associated with deterioration (e.g ABPA, NTM infection or infection with a new pathogen) should be considered.[5,18,154]
- Early diagnosis of bronchiectasis, accurate identification and treatment of its underlying cause, adequate management of chronic airway infection, and interventions to prevent exacerbations and control disease may delay disease progression.[2,18,154,156]
- Repeat chest CT imaging can help to identify several potential causes of deterioration.[154]
- Repeat testing for NTM should be performed when there are suggestive clinical or radiologic features of NTM infection, particularly in those who deteriorate despite appropriate antibiotics.[6,154]

Recommendations in guideline literature on treatments endorsed by the panel:

- Deteriorating patients who are not already under the care of a bronchiectasis specialist should be referred to a respiratory clinic with expertise in bronchiectasis.[154]

- Current treatment should be reviewed and optimised using a “treatable traits” approach. This includes, but is not limited, to treatment directed at the underlying aetiology of the patients bronchiectasis, airway clearance and mucoactive treatments, vaccination status, long-term (inhaled or oral) antibiotic treatment, *P. aeruginosa* eradication treatment, long-term inhaled bronchodilator and corticosteroid treatment, pulmonary rehabilitation, oxygen therapy and non-invasive ventilatory support where appropriate.[2,18,154,156,157]
- Lung resection may be considered in highly selected patients with localised disease whose symptoms are not controlled by medical treatment optimised by a bronchiectasis specialist.[18]
- Early referral for lung transplantation is essential in patients with progressive disease despite optimal medical management. This may include rapidly declining FEV1 or FEV1 <30%predicted, and/or PaCO2 >50mmHg.[18,154]

Summary of evidences

Deterioration in patients with bronchiectasis is a critical concern associated with substantial morbidity and mortality, making its management a high priority. While previous guidelines did not explicitly define or address rapidly deteriorating patients, they provided indirect guidance on managing patients with worsening symptoms.[18,98] Given the serious clinical implications, ensuring that these patients receive timely investigation, treatment adjustments, and specialist referrals is a fundamental aspect of care.

Current practice for deteriorating patients remains heterogeneous across healthcare providers, as no globally uniform definition of “deterioration” or “disease progression” exists. Typically, patients experiencing rapid worsening of symptoms are referred to a specialist clinic, where their treatment regimen is reevaluated and critically assessed. Key aspects of current care include baseline testing such as chest imaging, lung function and sputum microbiology, revaluation of aetiology, and adjustment of current treatments and preventive strategies. However, important gaps in current practice include treatment adherence assessment, which should be a routine component of patient evaluation, and a shared definition of “deterioration”, which is currently inconsistent and variable among healthcare providers.[18,98] Table S1 lists documents that contributed to the review of the evidence.

Justification of recommendations

Rapid deterioration in patients with bronchiectasis represents a critical aspect of the disease spectrum, necessitating timely recognition and appropriate management. While most current guideline literature, with the exception of the British Thoracic Society guidelines, do not provide specific guidance for the deteriorating patient, many existing recommendations are applicable to those experiencing increasing exacerbations or worsening symptoms and we therefore extracted these recommendations. These include guidance on follow-up strategies, treatment optimisation, and prevention measures to mitigate disease progression.[18,98,157]

The accumulated evidence supports early investigation and proactive treatment of patients who have deterioration. By applying these general principles from existing guidelines, clinicians can ensure that deteriorating patients receive timely and individualised management, potentially reducing morbidity and improving long-term outcomes.

Implementation considerations

As with all aspects of bronchiectasis care, the approach to the deteriorating patient should be personalised and adapted based on the nature of the deterioration, the presenting signs and symptoms, and patients' treatable traits. The approach to deteriorating symptoms and reduced lung function may be different as will specific situations such as, a marked increase in haemoptysis, worsening shortness of breath requiring oxygen or non-invasive ventilation, and recurrent exacerbations due to chronic bacterial infections. Figure 4 shows a general approach to the deteriorating patient (the RAPID approach) which needs to be adapted to each individual patient's situation.

Monitoring/evaluation

Monitoring and evaluation should focus on early identification and timely intervention for patients experiencing disease deterioration, as this is a common feature of bronchiectasis. Regular clinical assessment, symptom tracking, and objective investigations should be prioritized to detect worsening conditions and guide appropriate treatment. Key aspects of monitoring include evaluating exacerbation frequency, response to treatment, microbiology, respiratory function decline and increased need for oxygen or ventilatory support.

Future research

Future research should focus on i) Improving diagnostic tools to enable faster identification, severity assessment, and objective follow-up of deteriorating patients with bronchiectasis; ii) Determining the optimal timepoint for hospitalisation referral, as well as referral for surgery or lung transplantation; ii) Establishing strategies for measure end-of-life care and palliative management in patients with advanced bronchiectasis.

R Recognize and Refer

- Recognize the deteriorating patient*
- Refer to or consult with a bronchiectasis specialist

A Assess

- History and physical examination
- Adherence to airway clearance and/or pharmacological treatment
- Newly developed or worsening comorbidity
- The presence of new or evolving treatable traits

P Perform

- A review of airway clearance by an experienced respiratory physiotherapist
- A high-resolution computed tomography (HRCT) scan of the chest
- Sputum culture for bacteria, fungi, mycobacteria, and acid-fast bacilli (AFB)
- Bronchoscopy if sputum cannot be obtained or culture results are inconclusive
- Tests to reassess underlying causes such as ABPA
- A full pulmonary function assessment

I Initiate

- Antibiotic treatment for infection
- Eradication therapy for Pseudomonas aeruginosa where appropriate
- Targeted treatment for non-tuberculous mycobacteria (NTM) or fungal lung infections
- Disease-specific therapy for newly diagnosed causes of bronchiectasis
- Updated strategies for airway clearance and exercise tolerance
- New Long-term maintenance treatments (e.g. inhaled antibiotics, macrolides) when indicated by the present guidelines

D Deal with complications

- Malnutrition: referral to a dietician; supplemental feeding
- Hemoptysis: bronchial artery embolization or surgical resection in selected cases, following multidisciplinary discussion with a thoracic surgeon experienced in bronchiectasis.
- Persistent or high-burden infections unresponsive to antibiotics: detailed imaging
- Respiratory Failure: supplemental oxygen; non-invasive ventilation; referral for lung transplantation

*persistent symptom worsening, increased frequency and/or severity of exacerbations/hospitalizations, progressive lung function decline, worsening radiological findings, and a substantial impairment in quality of life

Figure 4. The rapidly deteriorating patient treatment algorithm.[2,5,6,18,65,154–157]

Other treatments

At the time of writing, a novel anti-inflammatory treatment targeting neutrophilic inflammation, dipeptidyl peptidase-1 (DPP1) inhibition, has shown reduced exacerbations and reduced lung function decline in a 12-month phase 3 trial[164], building on the results of several positive phase 2 trials.[165–168] The phase 3 trial enrolled patients with bronchiectasis and a history of 2 or more exacerbations in the previous year. DPP1 inhibition is likely to have a role in future management of patients with bronchiectasis at high risk of exacerbations. As this therapy is not available and has not been approved by regulatory authorities at the time of writing, no recommendation is currently possible but this treatment is planned to be addressed in an update of the ERS bronchiectasis guidelines.

Discussion

Bronchiectasis remains a disease with a high unmet need. The evidence base has progressed significantly since the last ERS guidelines in 2017 facilitated a number of important changes in recommendations.[169] New recommendations are issued for the first time on severity of disease, co-morbidities and treatable traits and provide detailed summaries of existing guidance on exacerbation management and the deteriorating patient. Substantial changes are made to other aspects of management. Testing for underlying causes, airway clearance, macrolide antibiotics and inhaled antibiotics were all given a conditional recommendation in 2017 and are given a strong recommendation in the present guideline. This reflects a strengthened evidence base, and should result in changes in clinical practice to more proactively use these interventions. For patients with chronic *P. aeruginosa* infection, macrolides were a second line treatment after failure of an inhaled antibiotic in the 2017 guidelines but are a first line treatment alongside inhaled antibiotics in the 2025 guidelines as a result of improved evidence for both interventions.[100,106] A key change in the 2025 guideline is the introduction of individualised risk assessment of patients, where the previous guideline suggested initiating treatments in patients with 3 or more exacerbations per year. Registry data suggests that preventative treatments are generally underutilised in people with bronchiectasis.[12,21,140,170,171] The burden of disease is high, and many patients including those with <3 exacerbations per year are at high risk of exacerbation and deterioration. Although it is essential to avoid indiscriminate use of antibiotics, frequent exacerbations promote disease progression and place patients at risk of antimicrobial resistance due to frequent systemic antibiotic treatments. The present guideline promotes a more proactive, patient centred approach to preventative treatment based on identifying patients with high disease activity, and therefore at high risk of progression, and treating before severe deterioration occurs. Elements contributing to the perception and evaluation of disease activity—by both clinicians and patients—usually include the frequency, severity, and impact on quality of life of daily symptoms and exacerbations, the trajectory of lung function over time, as well as some clinical or radiological features such as sputum purulence and the presence of mucus plugs on imaging. Establishing clear definitions of disease activity and disease control will be helpful in future to guide treatment strategies.

Bronchiectasis is a rapidly developing field and it is hoped there will be effective new therapies in the next few years. At present, the 2025 guidelines emphasise the importance of "doing the simple things well" and focusing on identifying the underlying cause, airway clearance and appropriate pharmacotherapy. Adherence to these guideline recommendations should be evaluated in future through collecting data on the proportion of patients receiving appropriate testing and treatment[66], to achieve the ultimate goal of this

document which is to promote improved treatment for patients with bronchiectasis worldwide.

Summary

The ERS guidelines for the management of bronchiectasis in adults provides an evidence-based framework for the management of patients with bronchiectasis.

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Online supplementary materials

Methods search strategy

The Prisma for Searching (PRISMA-Search) was followed to report the searching methodology for this guideline. The search strategies were developed in collaboration with 2 biomedical information specialists (CVM and TV).

Given that for PICO 1, 2, 3, 4, 7 and 8, the goal was to only include randomized controlled trials (RCTs), it was decided to use one broad joint search string for these PICOs, aimed at retrieving all RCTs for bronchiectasis. For PICO 5 (nonmacrolide oral antibiotics) and 6 (pathogen eradication), and for the narrative questions, other study types apart from RCTs could be included. For that reason, more focused search strings were set up for these questions.

The following bibliographic databases were searched for all search questions: : Pubmed *(via NCBI, including MEDLINE - coverage from 1946 to date searched)*, Embase *(Embase.com - 1974 to date searched)*, Web of Science Core Collection *(webofscience.com; SCI-EXPANDED – 1955 to date searched, SSCI – 1956 to date searched, AHCI – 1975 to date searched, CPCI-S – 1990 to date searched, CPCI-SSH – 1990 to date searched, BKCI-S – 2005 to date searched, BKCI-SSH – 2005 to date searched, ESCI – 2018 to date searched)*, and Scopus *(Scopus.com - 1788 to date searched)*.

For PICO 1, 2, 3, 4, 7 and 8, the bibliographic database CENTRAL *(via Cochrane Library - unknown inception date to date searched)* and two clinical trial registers, namely Clinicaltrials.gov and the International Clinical Trials Registry Platform (ICTRP, WHO), were searched in addition to the databases listed above.

It was deemed unnecessary to search CENTRAL and the two clinical trial registers again for PICO 5 and 6 and the narrative questions, since all RCTs for bronchiectasis were already retrieved with the broad search for PICO 1, 2, 3, 4, 7 and 8. However, during screening for PICO 1,2,3,4,7 and 8 the other PICO's and narrative questions were kept in mind and relevant records were annotated towards them.

1) Database searches
    a) PICO 1, 2, 3, 4, 7 and 8

For PICO 1, 2, 3, 4, 7 and 8, a comprehensive database search was performed on the 30th of November 2023. Details of the search strings for each database can be found in the Supplementary Materials. Briefly, two concepts, namely 'Bronchiectasis' and 'Randomized Controlled Trials', were combined with the Boolean operator AND. Within each concept, index terms (where applicable) were combined with free text words (synonyms, related terms, …) to search in title, abstract and keywords with the Boolean operator OR.

    b) PICO 5

For PICO 5, a comprehensive database search was performed on the 11th of December 2023. Details of the search strings for each database can be found in the Supplementary Materials. Briefly, two concepts, namely 'Bronchiectasis' and 'Long term oral antibiotics', were combined with the Boolean operator AND. Within each concept, index terms (where applicable) were combined with free text words (synonyms, related terms, …) to search in title, abstract and keywords with the Boolean operator OR. The following antibiotic classes

and specific antibiotics were searched: fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin and moxifloxacin), penicillines (amoxicillin and flowacillin), tetracyclines (doxycycline and minocycline), sulfanilamides, trimethoprim/sulfamethoxazole, pyrimidines (trimethoprim) and cephalosporins (cefuroxime).

c) PICO 6

For PICO 6, a comprehensive database search was performed on the 11th of December 2023. Details of the search strings for each database can be found in the Supplementary Materials. Briefly, two concepts, namely 'Bronchiectasis' and 'Eradication', were combined with the Boolean operator AND. Within each concept, index terms (where applicable) were combined with free text words (synonyms, related terms, …) to search in title, abstract and keywords with the Boolean operator OR.

d) Narrative question 1

For Narrative Question 1, a comprehensive database search was performed on the 24th of January 2024. For this question we searched from the 1st of January 2014 onwards.Details of the search strings for each database can be found in the Supplementary Materials. Briefly, two concepts, namely 'Bronchiectasis' and 'Etiology/Severity/comorbidity', were combined with the Boolean operator AND. Within each concept, index terms (where applicable) were combined with free text words (synonyms, related terms, …) to search in title, abstract and keywords with the Boolean operator OR.

e) Narrative question 2 and 3

For Narrative questions 2 and 3, a comprehensive database search was performed on the 24th of January 2024. Details of the search strings for each database can be found in the Supplementary Materials. Briefly, three concepts, namely 'Bronchiectasis', 'Eradication' and 'Guideline', were combined with the Boolean operator AND. Within each concept, index terms (where applicable) were combined with free text words (synonyms, related terms, …) to search in title, abstract and keywords with the Boolean operator OR.

2) Screening

The retrieved references from each database search (PICO 1,2,3,4,7 and 8/ PICO 5/ PICO 6/ narrative question 1/ narrative questions 2 and 3) were imported into Endnote 20 (EndNote 20 /2013, Clarivate Analytics, Philadelphia, PA USA) and duplicates were removed according to the deduplication method as described by Jane Falconer. After deduplication, the records were imported into Rayyan for title/abstract screening and subsequent full text screening. For the title/abstract screening, each record was screened by at least two reviewers independently and blinded from each other. Conflicts were solved by a third reviewer that did not contribute to the initial title/abstract screening. The included records from the title/abstract screening were imported into Endnote for a full text retrieval. In case Endnote could not retrieve the full text, CVM and TV searched for the full text manually. All retrieved full texts were collected on OneDrive and access was granted to the reviewers. In addition, the bibliographic data of each record to be assessed for full text screening was imported into Rayyan. As such, the reviewers could easily keep track of inclusion/exclusion and annotate the reason for exclusion. Full text screening was performed in duplicate.

Inclusion and exclusion criteria for each individual PICO and narrative question are shown below

General inclusion criteria applicable to all questions

Inclusion

- Adult patients (age >=18 years)
- A confirmed diagnosis of bronchiectasis (typically by CT imaging but studies utilizing other methodologies will be included)
- Data is available for at least 1 pre-specified outcome for extraction

Exclusion criteria

- Studies limited to specific subtypes of bronchiectasis where the findings would not be applicable for the general population of patients with bronchiectasis (e.g studies exclusively conducted in specific populations of cystic fibrosis, NTM, ABPA or other individual aetiologies)
- Studies in broad patient populations e.g undifferentiated cough, unless data from patients with bronchiectasis can be identified and extracted
- Editorials
- Review articles (with the exception of systematic review and meta-analysis which can be included)
- Non-peer reviewed data such as abstracts

In general our PICO questions addressed intervention A vs absence of intervention A. Therefore this would generally exclude active comparator interventions (where intervention A is tested against intervention B).

Specific inclusion and exclusion criteria

Narrative 1: Studies were excluded if they contained data on less than 30 patients/participants.

PICO 1: airway clearance: We excluded studies with a treatment duration of less than 3 months. We excluded studies comparing two techniques (as the PICO question addresses airway clearance vs no airway clearance).

PICO 2: Mucoactive drugs: Inclusion criteria: for this question we allowed active comparators where the active comparator is not known to have definitive mucoactive properties (isotonic saline as a comparator for hypertonic saline and low dose mannitol as a comparator for standard dose mannitol). We also allowed studies with <3 months duration and studies on specific subtypes of bronchiectasis only for this question.

PICO 3: Inhaled antibiotics: Inclusion criteria: use of inhaled antibiotics during stable state Exclusion criteria: administration of inhaled antibiotics exclusively during an acute exacerbation.

PICO 4: Macrolides: Inclusion criteria: use of macrolides during stable state Exclusion criteria: administration of macrolides exclusively during an acute exacerbation.

PICO 5: Oral antibiotics: Inclusion criteria: use of oral antibiotics during stable state Exclusion criteria: follow-up of <3 months, administration of oral antibiotics exclusively during an acute exacerbation.

PICO 6: Eradication: Inclusion criteria: Use of a formalized antibiotic regimen with the specific objective to eradicate a pathogenic microorganism. Exclusion criteria: treatment with oral or inhaled antibiotics for long term use without a formal eradication regimen.

PICO 7: Inhaled corticosteroids: Inclusion criteria: use of an inhaled regimen containing an inhaled corticosteroid (with or without other drugs such as bronchodilators) with a

comparator that allows the efficacy of the inhaled corticosteroid to be evaluated i.e a bronchodilator comparator would be permitted.

PICO 8: Pulmonary rehabilitation: Inclusion criteria: Use of a formal rehabilitation, exercise training or similar intervention which contains an exercise component and incorporates a formal evaluation of efficacy.

Narrative 2 and 3: Inclusion criteria: Guidelines or related documents (consensus statements) issued from scientific societies or organisations and containing recommendations relevant to Narrative 2 or Narrative 3 on exacerbations and the deteriorating patient. Exclusion criteria: Commentaries, review articles, original research articles or other documents which do not include explicit evidence based recommendations.

Methodological references

Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, Koffel JB; PRISMA-S Group. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev. 2021;10(1):39. doi: 10.1186/s13643-020-01542-z

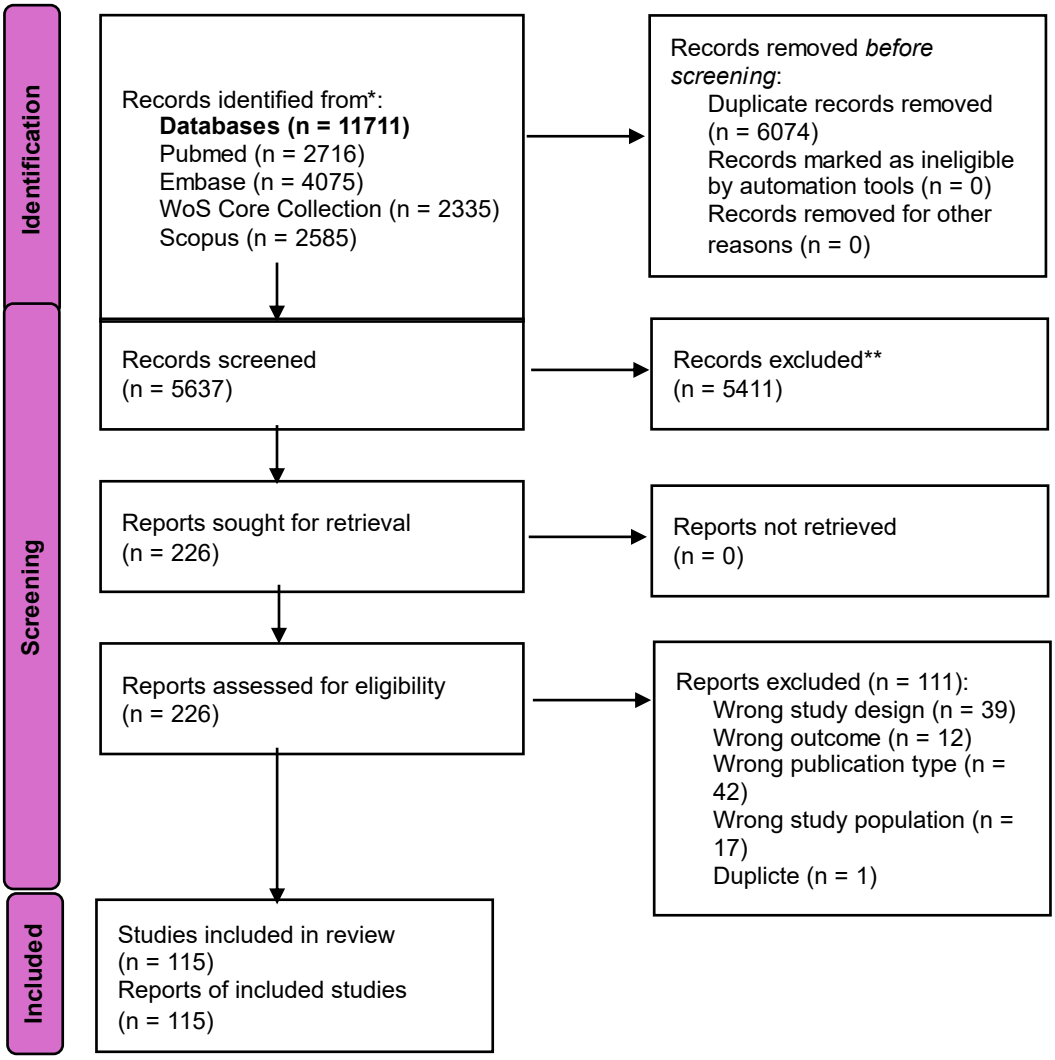
Mourad Ouzzani, Hossam Hammady, Zbys Fedorowicz, and Ahmed Elmagarmid. Rayyan — a web and mobile app for systematic reviews. Systematic Reviews (2016) 5:210, DOI: 10.1186/s13643-016-0384-4.

Table S1. Guidelines and consensus statements included in the narrative 2 and 3 literature review

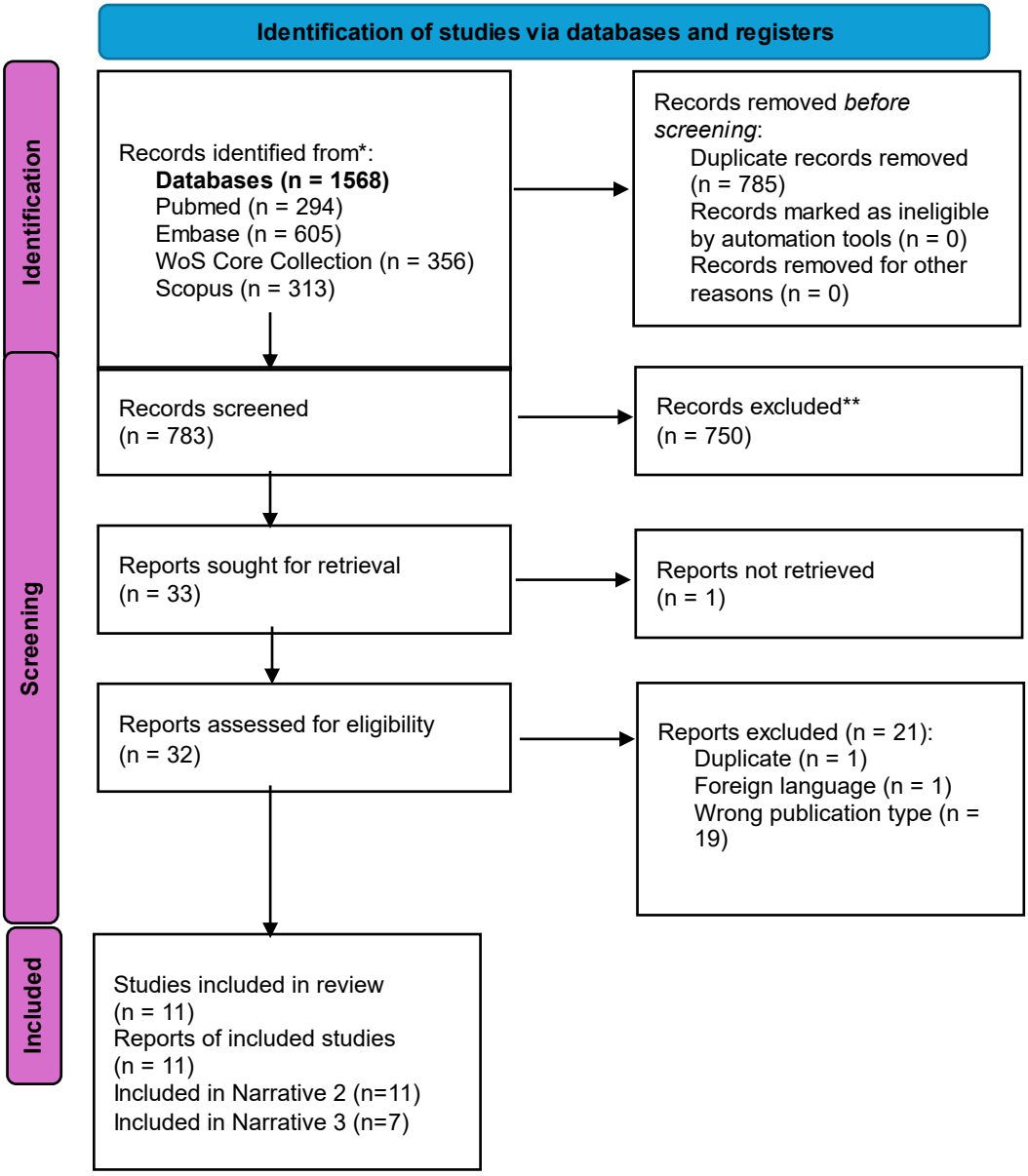
Name of guideline or statement	**Publication year**	**Reference**
British Thoracic Society guideline for non-CF bronchiectasis.	2008	Thorax. 2010 Jul;65 Suppl 1:i1-58. doi: 10.1136/thx.2010.136119.
Diagnosis and treatment of bronchiectasis. Spanish Society of Pneumology and Thoracic Surgery	2008	Arch Bronconeumol. 2008 Nov;44(11):629-40. doi: 10.1157/13128330.
Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand Thoracic Society of Australia and New Zealand guidelines	2015	Med J Aust. 2015 Jan 19;202(1):21-3. doi: 10.5694/mja14.00287
The Saudi Thoracic Society guidelines for diagnosis and management of noncystic fibrosis bronchiectasis.	2017	Ann Thorac Med. 2017 Jul-Sep;12(3):135-161. doi: 10.4103/atm.ATM_171_17
Pulmonary exacerbation in adults with bronchiectasis: a consensus definition for clinical research	2017	Eur Respir J. 2017 Jun 8;49(6):1700051. doi: 10.1183/13993003.00051-2017. Print 2017 Jun.
European Respiratory Society guidelines for the	2017	Eur Respir J. 2017 Sep 9;50(3):1700629.

management of adult bronchiectasis.		doi: 10.1183/13993003.00629-2017. Print 2017 Sep.
Spanish Guidelines on Treatment of Bronchiectasis in Adults.	2018	Arch Bronconeumol (Engl Ed). 2018 Feb;54(2):88-98. doi: 10.1016/j.arbres.2017.07.016. Epub 2017 Nov 9
Spanish Guidelines on the Evaluation and Diagnosis of Bronchiectasis in Adults	2018	Arch Bronconeumol (Engl Ed). 2018 Feb;54(2):79-87. doi: 10.1016/j.arbres.2017.07.015. Epub 2017 Nov 9.
British Thoracic Society Guideline for bronchiectasis in adults.	2019	Thorax. 2019 Jan;74(Suppl 1):1-69. doi: 10.1136/thoraxjnl-2018-212463.
British Thoracic Society guideline for the use of long-term macrolides in adults with respiratory disease	2020	Thorax 2020;75:370–404
Thoracic Society of Australia and New Zealand (TSANZ) position statement on chronic suppurative lung disease and bronchiectasis in children, adolescents and adults in Australia and New Zealand	2023	Respirology. 2023 Apr;28(4):339-349. doi: 10.1111/resp.14479. Epub 2023 Mar 2

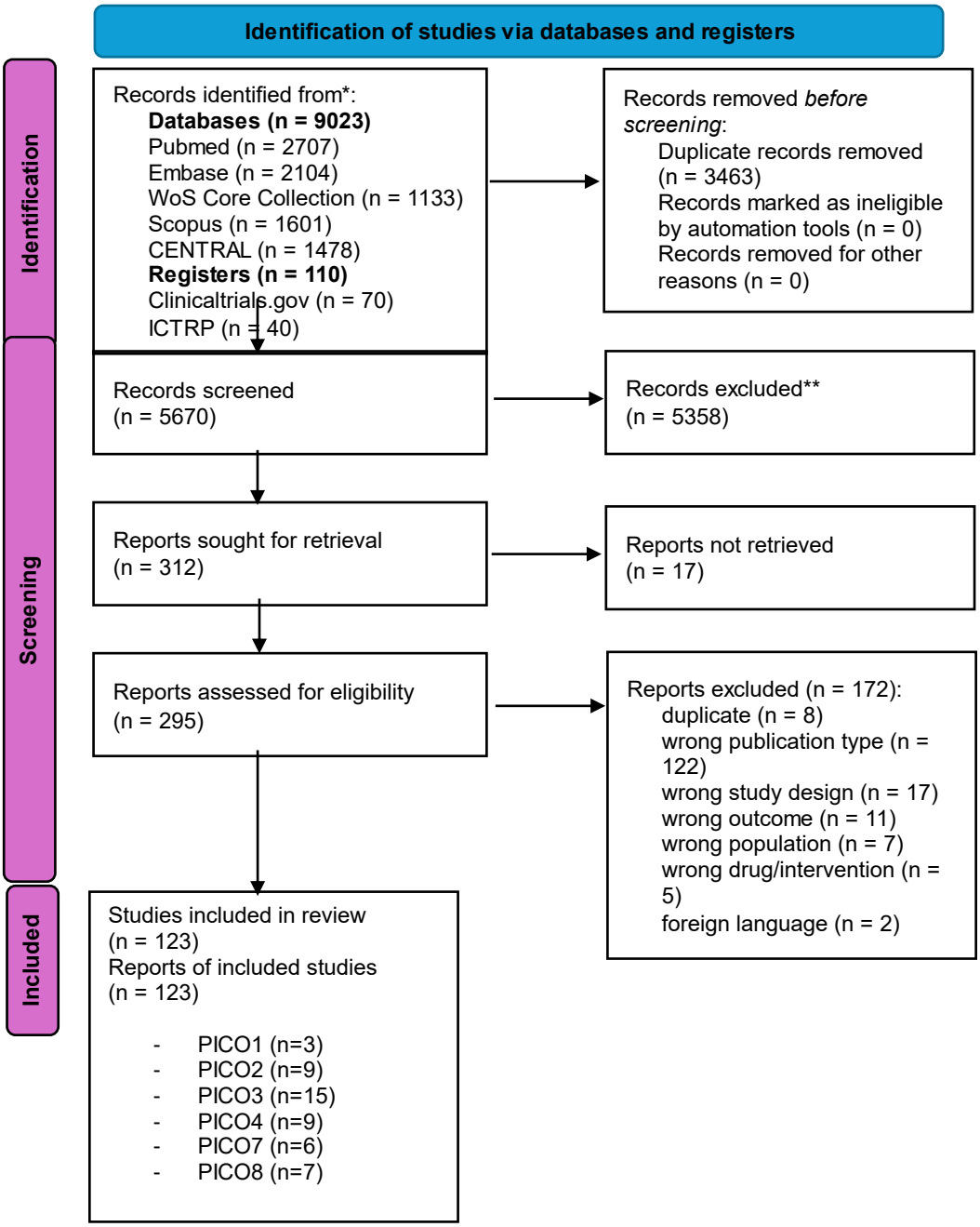
Flow Chart, Narrative Question 1



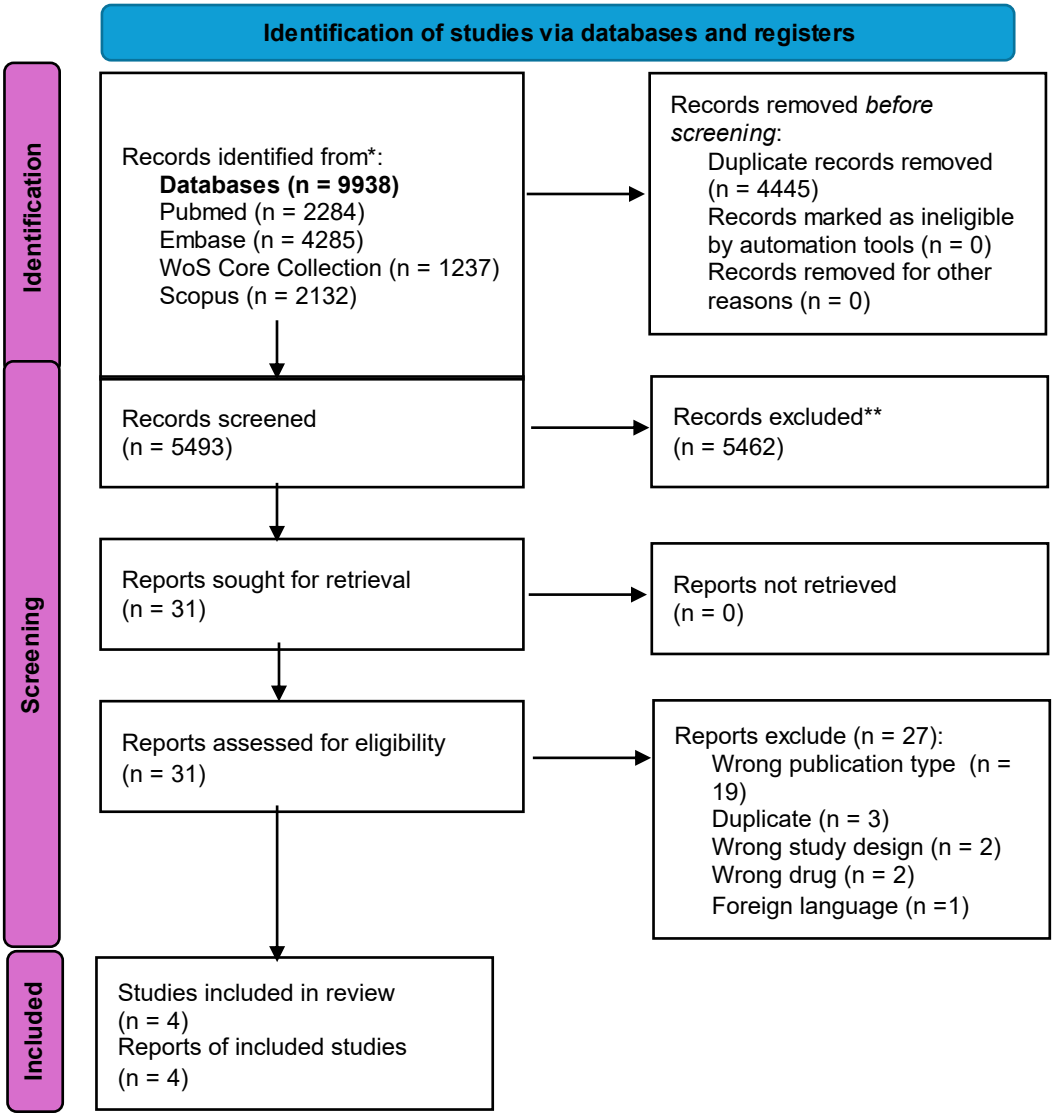
Flow Chart- Narrative questions 2 and 3



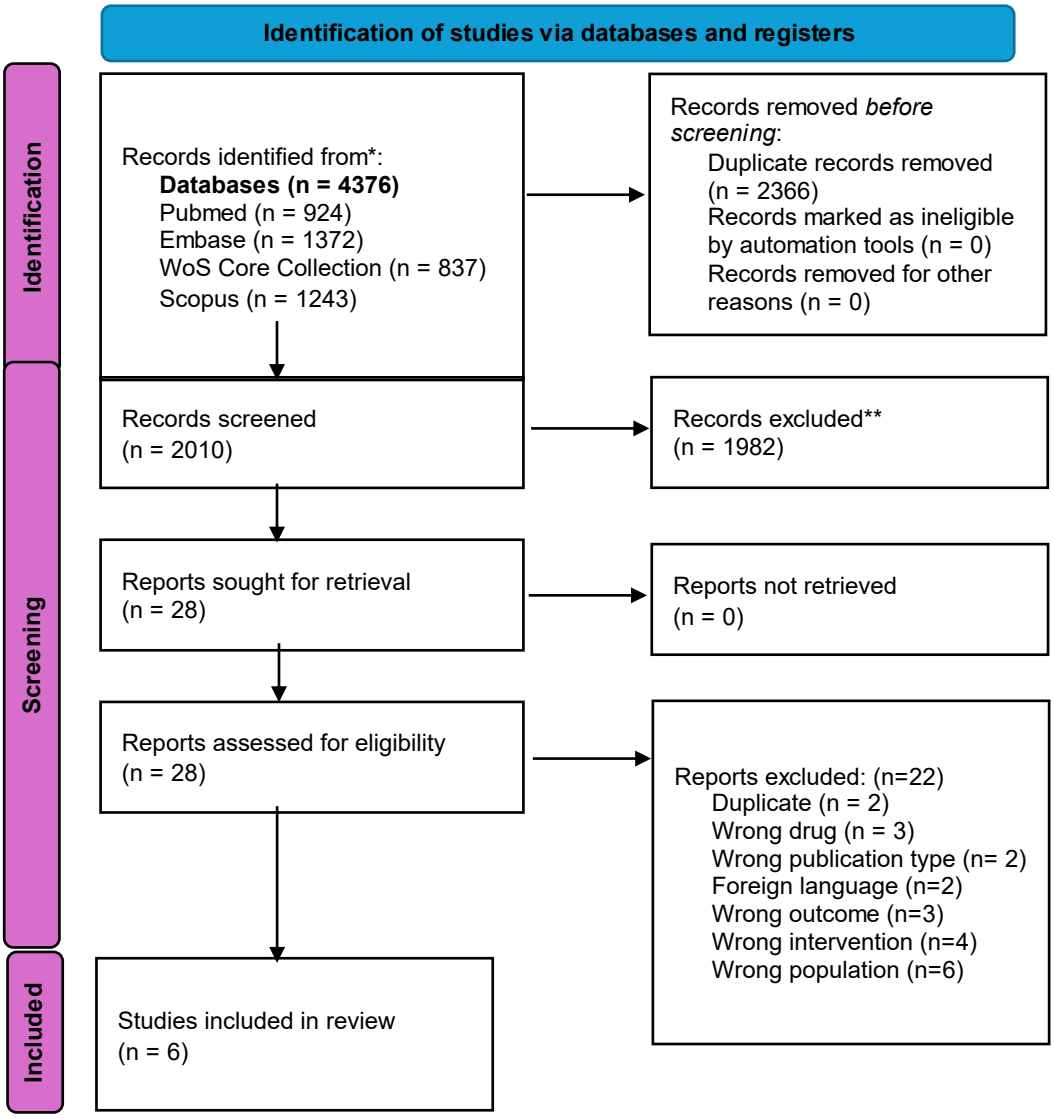
Flow Chart PICO questions 1,2,3,4,7,8



Flow Chart PICO Question 5



Flow Chart PICO 6



The following section outlines the search terms used and detailed search strategy Search terms used

PICOs 1,2,3,4,7,8

Pubmed (including Medline) 30112023 => 1 + 2 = 2707 results

1. Bronchiectasis

"Bronchiectasis"[Mesh] OR "bronchiectas*"[tiab] OR "bronchoectasia"[tiab]

2. RCT

("Clinical Trial"[pt] OR "placebo"[tiab] OR "drug therapy"[sh] OR "random*"[tiab] OR "RCT"[tiab] OR "trial"[tiab] OR "phase 1"[tiab] OR "phase 2"[tiab] OR "phase 3"[tiab] OR "phase 4"[tiab] OR "phase I"[tiab] OR "phase II"[tiab] OR "phase III"[tiab] OR "phase IV"[tiab] OR "clinical study"[tiab] OR "controlled study"[tiab] OR "controlled design"[tiab] OR "open label"[tiab] OR "double blind*"[tiab] OR "single blind*"[tiab])

NOT ("Animals"[Mesh] NOT "Humans"[Mesh])

Test:

Pico3: (checked and approved)

PMID:

32097051[uid] OR 30975143[uid] OR 28397992[uid] OR 25246664[uid]

Pico2: (checked and approved)

PMID

34760994[uid] OR 29326318[uid] OR 23556995[uid]

Pico1: **(checked and approved)**

PMID

24625200[uid] OR 30658914[uid] OR 31405826[uid]

Pico4: (checked and approved)

PMID

31405828[uid] OR 23532241[uid]

Pico7: (checked and approved)

PMID

22684355[uid] OR 15741443[uid]

Pico8: (checked and approved)

PMID

24731015[uid] OR 22947443[uid]

Embase (Embase.com) 30112023 => 1+2 = 2104 results

3. Bronchiectasis

'bronchiectasis'/exp OR 'bronchiectas*':ti,ab,kw OR 'bronchoectasia':ti,ab,kw

4. RCT

('clinical trial'/exp OR 'placebo':ti,ab,kw OR 'random*':ti,ab,kw OR 'RCT':ti,ab,kw OR 'trial':ti,ab,kw OR 'phase 1':ti,ab,kw OR 'phase 2':ti,ab,kw OR 'phase 3':ti,ab,kw OR 'phase 4':ti,ab,kw OR 'phase I':ti,ab,kw OR 'phase II':ti,ab,kw OR 'phase III':ti,ab,kw OR 'phase IV':ti,ab,kw OR 'clinical study':ti,ab,kw OR 'controlled study':ti,ab,kw OR 'controlled design':ti,ab,kw OR 'open label':ti,ab,kw OR 'double blind*':ti,ab,kw OR 'single blind*':ti,ab,kw)

NOT 'conference abstract':it

Scopus 30112023 => 1 + 2 = 1601 results

1. Bronchiectasis

TITLE-ABS("bronchiectas*"OR "bronchoectasia") OR AUTHKEY("bronchiectas*"OR "bronchoectasia")

2. RCT

TITLE-ABS("placebo" OR "random*" OR "RCT" OR "trial" OR "phase 1" OR "phase 2" OR "phase 3" OR "phase 4" OR "phase I" OR "phase II" OR "phase III" OR "phase IV" OR "clinical study" OR "controlled study" OR "controlled design" OR "open label" OR "double blind*" OR "single blind*") OR AUTHKEY("placebo" OR "random*" OR "RCT" OR "trial" OR "phase 1" OR "phase 2" OR "phase 3" OR "phase 4" OR "phase I" OR "phase II" OR "phase III" OR "phase IV" OR "clinical study" OR "controlled study" OR "controlled design" OR "open label" OR "double blind*" OR "single blind*")

WoS Core Collection 30112023 => 1 + 2 = 1133 results

1. Bronchiectasis

TS=("bronchiectas*"OR "bronchoectasia")

2. RCT

TS=("placebo" OR "random*" OR "RCT" OR "trial" OR "phase 1" OR "phase 2" OR "phase 3" OR "phase 4" OR "phase I" OR "phase II" OR "phase III" OR "phase IV" OR "clinical study" OR "controlled study" OR "controlled design" OR "open label" OR "double blind*" OR "single blind*")

NOT DT=("meeting abstract")

Clinical Trial Registers

3. Clinicaltrials.gov (using the classic website: https://classic.clinicaltrials.gov/)

Bronchiectasis in field 'Condition or disease' and filter "with results" = 27 results on 30/11/2023

Bronchiectasis in field 'Other terms' and filter "with results" = 43 results on 30/11/2023

4. ICTRP

bronchiectas* with results only = 58 results on 40 trials on 30/11/2023

Cochrane CENTRAL 30112023 => 1 = 1478 results (trials)

1. Bronchiectasis

[mh "Bronchiectasis"] OR (bronchiectas* OR "bronchoectasia"):ti,ab,kw

PICO 5

Pubmed (including Medline) 11122023 => 1 + 2 = 2284 results

2. Bronchiectasis

"Bronchiectasis"[Mesh] OR "bronchiectas*"[tiab] OR "bronchoectasia"[tiab]

3. Long term oral antibiotic treatment (excluding long-term macrolides)

"Anti-Bacterial Agents"[Mesh] OR "anti-bacterial"[tiab] OR "antibacterial"[tiab] OR "Bacteriocid*"[tiab] OR "anti-mycobacterial"[tiab] OR "antimycobacterial"[tiab] OR "antibiotic*"[tiab] OR "Anti-Bacterial Agents"[Pharmacological Action] OR

"Fluoroquinolones"[Mesh] OR fluoroquinolon*[tiab] OR ("Quinolones"[Mesh:NoExp] AND "1987":"2001"[mhda]) OR quinolon*[tiab] OR chinolon*[tiab] OR quinolin*[tiab] OR chinolin*[tiab] OR

"Ciprofloxacin"[Mesh:NoExp] OR "cipro*"[tiab] OR "ciprinol"[tiab] OR "aceoto"[tiab] OR "acire"[tiab] OR "alcon cilox"[tiab] OR "apulmiq"[tiab] OR "araxacina"[tiab] OR "aristin-c"[tiab] OR "auripro"[tiab] OR "bacquinor"[tiab] OR "bactiflox"[tiab] OR "baflox"[tiab] OR "basemar"[tiab] OR "battizer"[tiab] OR "baycip"[tiab] OR "bernoflox"[tiab] OR "bivorilan"[tiab] OR "bosix"[tiab] OR "c-flox"[tiab] OR "c-floxacin"[tiab] OR "catex"[tiab] OR "cetraflux"[tiab] OR "cetraxal"[tiab] OR "chinocid"[tiab] OR "cidroxal"[tiab] OR "cifin"[tiab] OR "ciflan"[tiab] OR "ciflo"[tiab] OR "ciflosin"[tiab] OR "ciflot"[tiab] OR "ciflox"[tiab] OR "cifloxin"[tiab] OR "cifox"[tiab] OR "cifran"[tiab] OR "cilab"[tiab] OR "ciloquin"[tiab] OR "ciloxan"[tiab] OR "ciloxin"[tiab] OR "cimogal"[tiab] OR "cinaflox"[tiab] OR "cipad"[tiab] OR "ciperus"[tiab] OR "cipflox"[tiab] OR "ciphin"[tiab] OR "cipide"[tiab] OR "cipio"[tiab] OR "ciplox"[tiab] OR "ciplus"[tiab] OR "cipocin"[tiab] OR "ciprecu"[tiab] OR "ciriax"[tiab] OR "cirok"[tiab] OR

"cirokan"[tiab] OR "cirox"[tiab] OR "ciroxin"[tiab] OR "citopcin"[tiab] OR "citrovenot"[tiab] OR "cobay"[tiab] OR "corsacin"[tiab] OR "cosflox"[tiab] OR "cuminol"[tiab] OR "cuspis"[tiab] OR "cycin"[tiab] OR "cyfloxin"[tiab] OR "cypral"[tiab] OR "cyprobay"[tiab] OR "cysfec"[tiab] OR "doriman"[tiab] OR "droll"[tiab] OR "eoxin"[tiab] OR "eprocin"[tiab] OR "estecina"[tiab] OR "felixene"[tiab] OR "fimoflox"[tiab] OR "flociprin"[tiab] OR "flontalexin"[tiab] OR "floroxin"[tiab] OR "floxager"[tiab] OR "floxantina"[tiab] OR "floxbio"[tiab] OR "fonterra"[tiab] OR "generflon"[tiab] OR "gerbat"[tiab] OR "ginorectol"[tiab] OR "giroflox"[tiab] OR "gonning"[tiab] OR "grifociprox"[tiab] OR "h-next"[tiab] OR "holdestin"[tiab] OR "ibixacin"[tiab] OR "inciflox"[tiab] OR "infectocipro"[tiab] OR "inkamil"[tiab] OR "iprolan"[tiab] OR "isotic"[tiab] OR "jayacin"[tiab] OR "k-sacin"[tiab] OR "kenzoflex"[tiab] OR "kinoves"[tiab] OR "kinox"[tiab] OR "kipocin"[tiab] OR "labentrol"[tiab] OR "ladinin"[tiab] OR "limox"[tiab] OR "linhaliq"[tiab] OR "lipoquin"[tiab] OR "lofucin"[tiab] OR "loxan"[tiab] OR "macar"[tiab] OR "medociprin"[tiab] OR "mitroken"[tiab] OR "nafloxin"[tiab] OR "neofloxin"[tiab] OR "nivoflox"[tiab] OR "novidat"[tiab] OR "novoquin"[tiab] OR "oftacilox"[tiab] OR "opthaflox"[tiab] OR "otanol"[tiab] OR "otiprio"[tiab] OR "otociprin"[tiab] OR "otosec"[tiab] OR "phaproxin"[tiab] OR "pharcina"[tiab] OR "poncoflox"[tiab] OR "probiox"[tiab] OR "prociflor"[tiab] OR "procin"[tiab] OR "proflaxin"[tiab] OR "profloxin"[tiab] OR "proksi 250"[tiab] OR "proksi 500"[tiab] OR "proquin"[tiab] OR "proxacin"[tiab] OR "pulmaquin"[tiab] OR "qilaflox"[tiab] OR "qinosyn"[tiab] OR "quilox"[tiab] OR "quinobiotic"[tiab] OR "quinoflox"[tiab] OR "quinolide"[tiab] OR "quinox"[tiab] OR "quintor"[tiab] OR "qupron"[tiab] OR "rancif"[tiab] OR "ravalton"[tiab] OR "revionorm"[tiab] OR "rigoran"[tiab] OR "rofcin"[tiab] OR "roflazin"[tiab] OR "rosacin eye drop"[tiab] OR "samper"[tiab] OR "sarf"[tiab] OR "sepcen"[tiab] OR "septicide"[tiab] OR "septocipro"[tiab] OR "sifloks"[tiab] OR "siprogut"[tiab] OR "siprox"[tiab] OR "sophixin ofteno"[tiab] OR "spitacin"[tiab] OR "strox"[tiab] OR "suiflox"[tiab] OR "superocin"[tiab] OR "syntoflox"[tiab] OR "topistin"[tiab] OR "truoxin"[tiab] OR "ufexil"[tiab] OR "ullax"[tiab] OR "unex"[tiab] OR "unicexal"[tiab] OR "uniflox"[tiab] OR "urodixin"[tiab] OR "uroxin"[tiab] OR "viprolox"[tiab] OR "zindolin"[tiab] OR "zipra"[tiab] OR "zumaflox"[tiab] OR

"Levofloxacin*"[tiab] OR "(S)-isomer Ofloxacin"[tiab:~2] OR Quixin[tiab] OR Levaquin[tiab] OR "aeroquin"[tiab] OR "cravit"[tiab] OR "elequine"[tiab] OR "eyflox"[tiab] OR "floxacin"[tiab] OR "floxel"[tiab] OR "iquix"[tiab] OR "leroxacin"[tiab] OR "lesacin"[tiab] OR "levokacin"[tiab] OR "levox"[tiab] OR "levoxacin"[tiab] OR "mosardal"[tiab] OR "nofaxin"[tiab] OR "oftaquix"[tiab] OR "oxalux"[tiab] OR "prixar"[tiab] OR "quinsair"[tiab] OR "reskuin"[tiab] OR "supraflox"[tiab] OR "tavanic"[tiab] OR "unibiotic"[tiab] OR "venaxan"[tiab] OR "volequin"[tiab] OR

"Ofloxacin"[Mesh] OR "ofloxacin*"[tiab] OR "tarivid"[tiab] OR "akilen"[tiab] OR "audret"[tiab] OR "bactocin"[tiab] OR "bioquil"[tiab] OR "danoflox"[tiab] OR "effexin"[tiab] OR "eukinoft"[tiab] OR "exocin"[tiab] OR "exocine"[tiab] OR "flobacin"[tiab] OR "flodemex"[tiab] OR "flotavid"[tiab] OR "flovid"[tiab] OR "floxal"[tiab] OR "floxedol"[tiab] OR "floxigen"[tiab] OR "floxil"[tiab] OR "floxin"[tiab] OR "floxstat"[tiab] OR "fugacin"[tiab] OR "grenis-oflo"[tiab] OR "gyroflox"[tiab] OR "inoflox"[tiab] OR "kinflocin"[tiab] OR "kinoxacin"[tiab] OR "liflox"[tiab] OR "loxinter"[tiab] OR "marfloxacin"[tiab] OR "medofloxin"[tiab] OR "medofloxine"[tiab] OR "mergexin"[tiab] OR "monoflocet"[tiab] OR "monoox"[tiab] OR "novecin"[tiab] OR "nufafloqo"[tiab] OR "o-flox"[tiab] OR "obide"[tiab] OR "occidal"[tiab] OR "ocuflox"[tiab] OR "ofcin"[tiab] OR "oflin"[tiab] OR "oflocee"[tiab] OR "oflocet"[tiab] OR "oflocin"[tiab] OR "ofloda"[tiab] OR "oflodex"[tiab] OR "oflodinex"[tiab] OR "oflodura"[tiab] OR "oflogen"[tiab] OR "oflohexal"[tiab] OR "oflovir"[tiab] OR "oflox"[tiab] OR "ofloxa-vision"[tiab] OR "ofloxacino"[tiab] OR "ofloxamed"[tiab] OR "ofloxavis"[tiab] OR "ofloxin"[tiab] OR "ofus"[tiab] OR "onexacin"[tiab] OR "operan"[tiab] OR "orocin"[tiab] OR "otiflox"[tiab] OR "otonil"[tiab] OR

"ottoflox"[tiab] OR "oxacid"[tiab] OR "oxatrex"[tiab] OR "pharflox"[tiab] OR "praxin"[tiab] OR "puiritol"[tiab] OR "qinolon"[tiab] OR "qipro"[tiab] OR "quinofree"[tiab] OR "quinolon"[tiab] OR "quotavil"[tiab] OR "rilox"[tiab] OR "romacin"[tiab] OR "sinflo"[tiab] OR "surnox"[tiab] OR "tabrin"[tiab] OR "taravid"[tiab] OR "tariflox"[tiab] OR "taroflox"[tiab] OR "telbit"[tiab] OR "trafloxal"[tiab] OR "tructum"[tiab] OR "urotarivid"[tiab] OR "viotisone"[tiab] OR "visuab"[tiab] OR "zanocin"[tiab] OR

"Moxifloxacin"[Mesh] OR "Moxifloxacin*"[tiab] OR Octegra[tiab] OR Proflox[tiab] OR Avelox[tiab] OR Avalox[tiab] OR Izilox[tiab] OR Actira[tiab] OR "avelon"[tiab] OR "bacterol"[tiab] OR "floxamic"[tiab] OR "floxitrat"[tiab] OR "izilox"[tiab] OR "kanavig"[tiab] OR "lifodrox"[tiab] OR "megaxin"[tiab] OR "melocin"[tiab] OR "moksacin"[tiab] OR "monafox"[tiab] OR "moxeza"[tiab] OR "moxibay"[tiab] OR "moxif"[tiab] OR "moxivig"[tiab] OR "octegra"[tiab] OR "proflox"[tiab] OR "tamvelier"[tiab] OR "vamocin"[tiab] OR "vegamox"[tiab] OR "vigamox"[tiab] OR "vigamoxi"[tiab] OR "xiflodrop"[tiab] OR "zimoxin"[tiab] OR

"Penicillins"[Mesh] OR penicillin*[tiab] OR

"Amoxicillin"[Mesh] OR "Amoxicillin*"[tiab] OR "Amoxycillin*"[tiab] OR "Hydroxyampicillin"[tiab] OR "Actimoxi"[tiab] OR "Clamoxyl"[tiab] OR "Penamox"[tiab] OR "Polymox"[tiab] OR "Trimox"[tiab] OR "Wymox"[tiab] OR "Amoxil"[tiab] OR "a gram"[tiab] OR "abdimox"[tiab] OR "acilina"[tiab] OR "acimox"[tiab] OR "adbiotin"[tiab] OR "agerpen"[tiab] OR "agram"[tiab] OR "alfamox"[tiab] OR "alfoxil"[tiab] OR "almodan"[tiab] OR "almorsan"[tiab] OR "alphamox"[tiab] OR "amagesen solutab"[tiab] OR "ameclina"[tiab] OR "amitron"[tiab] OR "amo-flamisan"[tiab] OR "amo-flamsian"[tiab] OR "amocillin"[tiab] OR "amoclen"[tiab] OR "amodex"[tiab] OR "amoflux"[tiab] OR "amohexal"[tiab] OR "amolin"[tiab] OR "amonex"[tiab] OR "amopen"[tiab] OR "amophar ge"[tiab] OR "amosine"[tiab] OR "amoval"[tiab] OR "amoxa"[tiab] OR "amoxal"[tiab] OR "amoxapen"[tiab] OR "amoxaren"[tiab] OR "amoxcil"[tiab] OR "amoxcillin"[tiab] OR "amoxcin"[tiab] OR "amoxi-basan"[tiab] OR "amoxicilina"[tiab] OR "amoxiclin"[tiab] OR "amoxicot"[tiab] OR "amoxidal"[tiab] OR "amoxidin"[tiab] OR "amoxidrops"[tiab] OR "amoxihexal"[tiab] OR "amoxillin"[tiab] OR "amoxina"[tiab] OR "amoxipen"[tiab] OR "amoxipenil"[tiab] OR "amoxisol"[tiab] OR "amoxivan"[tiab] OR "amoxivet"[tiab] OR "amoxy"[tiab] OR "amoxy-diolan"[tiab] OR "amoxypen"[tiab] OR "ampliron"[tiab] OR "apo-amoxi"[tiab] OR "ardine"[tiab] OR "aroxin"[tiab] OR "azillin"[tiab] OR "bacihexal"[tiab] OR "bactamox"[tiab] OR "bactox ge"[tiab] OR "beamoxy"[tiab] OR "betamox"[tiab] OR "bimox"[tiab] OR "bintamox"[tiab] OR "biomox"[tiab] OR "biotamoxal"[tiab] OR "bioxidona"[tiab] OR "bioxyllin"[tiab] OR "bristamox"[tiab] OR "broadmetz"[tiab] OR "cabermox"[tiab] OR "cilamox"[tiab] OR "clamox"[tiab] OR "clearamox"[tiab] OR "clonamox"[tiab] OR "coamoxin"[tiab] OR "damoxicil"[tiab] OR "dispermox"[tiab] OR "doxamil"[tiab] OR "draximox"[tiab] OR "edamox"[tiab] OR "efpinex"[tiab] OR "erphamoxy"[tiab] OR "eupen"[tiab] OR "farconcil"[tiab] OR "fisamox"[tiab] OR "flemoxin"[tiab] OR "flemoxine ge"[tiab] OR "fluamoxina"[tiab] OR "foxolin"[tiab] OR "fullcilina"[tiab] OR "gexcil"[tiab] OR "gimalxina"[tiab] OR "glamox"[tiab] OR "glassatan"[tiab] OR "gomcillin"[tiab] OR "grinsul"[tiab] OR "grunamox"[tiab] OR "hamoxillin"[tiab] OR "hiconcil"[tiab] OR "hidramox"[tiab] OR "hipen"[tiab] OR "hosboral"[tiab] OR "ibamox"[tiab] OR "ibiamox"[tiab] OR "ikamoxil"[tiab] OR "imacillin"[tiab] OR "imaxilin"[tiab] OR "inamox"[tiab] OR "infectomycin"[tiab] OR "intermox"[tiab] OR "isimoxin"[tiab] OR "izoltil"[tiab] OR "julphamox"[tiab] OR "jutamox"[tiab] OR "kamoxin"[tiab] OR "ladoxillin"[tiab] OR "lamoxy"[tiab] OR "larocilin"[tiab] OR "larocin"[tiab] OR "larotid"[tiab] OR "macromox"[tiab] OR "magnimox"[tiab] OR "maxamox"[tiab] OR "maxcil"[tiab] OR "medimox"[tiab] OR "meixil"[tiab] OR "metifarma"[tiab] OR "mopen"[tiab] OR "morgenxil"[tiab] OR "moxacin"[tiab] OR "moxaline"[tiab] OR "moxarin"[tiab] OR

"moxatag"[tiab] OR "moxilen"[tiab] OR "moxilin"[tiab] OR "moximar"[tiab] OR "moxitab"[tiab] OR "moxtid"[tiab] OR "moxylin"[tiab] OR "moxypen"[tiab] OR "moxyvit"[tiab] OR "neogram"[tiab] OR "novabritine"[tiab] OR "novamox"[tiab] OR "novamoxin"[tiab] OR "novenzymin"[tiab] OR "novoxil"[tiab] OR "nuvosyl"[tiab] OR "optium"[tiab] OR "oramox"[tiab] OR "ospamox"[tiab] OR "pamocil"[tiab] OR "pamoxicillin"[tiab] OR "pamoxin"[tiab] OR "panvilon"[tiab] OR "pasetocin"[tiab] OR "penbiosyn"[tiab] OR "pentyloxycillin"[tiab] OR "pharmoxyl"[tiab] OR "piramox"[tiab] OR "pondnoxcill"[tiab] OR "rancil"[tiab] OR "ranmoxy"[tiab] OR "ranoxil"[tiab] OR "ranoxyl"[tiab] OR "robamox"[tiab] OR "romoxil"[tiab] OR "ronemox"[tiab] OR "saltermox"[tiab] OR "sawacillin"[tiab] OR "sawamezin"[tiab] OR "servamox"[tiab] OR "shamoxil"[tiab] OR "sia-mox"[tiab] OR "sigamopen"[tiab] OR "sil-a-mox"[tiab] OR "silamox"[tiab] OR "simoxil"[tiab] OR "sintopen"[tiab] OR "solamocta"[tiab] OR "solpenox"[tiab] OR "sumox"[tiab] OR "superpeni"[tiab] OR "teramoxyl"[tiab] OR "tolodina"[tiab] OR "tormoxin"[tiab] OR "triafamox"[tiab] OR "triamoxil"[tiab] OR "trifamox"[tiab] OR "uro clamoxyl"[tiab] OR "uroclamoxyl"[tiab] OR "utimox"[tiab] OR "vastamox"[tiab] OR "velamox"[tiab] OR "vistrep"[tiab] OR "widecillin"[tiab] OR "winpen"[tiab] OR "xiltrop"[tiab] OR "zamocillin"[tiab] OR "zamox"[tiab] OR "zamoxil"[tiab] OR "zerrsox"[tiab] OR "zimox"[tiab] OR

"Co-amoxiclav"[tiab] OR Coamoxiclav[tiab] OR "Amoxi-Clavulanate"[tiab] OR "Amox-clav"[tiab] OR Synulox[tiab] OR Spektramox[tiab] OR Augmentin[tiab] OR Clavulin[tiab] OR "aclam"[tiab] OR "aktil"[tiab] OR "ambilan"[tiab] OR "amocla"[tiab] OR "amoclan"[tiab] OR "amoclane"[tiab] OR "amoclav"[tiab] OR "amoksiklav"[tiab] OR "amolanic"[tiab] OR "amometin"[tiab] OR "amoxi plus"[tiab] OR "amoxiclav"[tiab] OR "amoxiclav-bid"[tiab] OR "amoxiclav-teva"[tiab] OR "amoxsiklav"[tiab] OR "amoxxlin"[tiab] OR "ancla"[tiab] OR "auclatin duo dry syrup"[tiab] OR "augamox"[tiab] OR "augmaxcil"[tiab] OR "augmentan"[tiab] OR "augmentine"[tiab] OR "augmex"[tiab] OR "augpen"[tiab] OR "augucillin duo"[tiab] OR "augurcin"[tiab] OR "ausclav"[tiab] OR "auspilic"[tiab] OR "bactiv"[tiab] OR "bactoclav"[tiab] OR "bioclavid"[tiab] OR "cavumox"[tiab] OR "ciblor"[tiab] OR "clacillin duo dry syrup"[tiab] OR "clamax"[tiab] OR "clamentin"[tiab] OR "clamobit"[tiab] OR "clamonex"[tiab] OR "clamovid"[tiab] OR "clamoxin"[tiab] OR "clamoxyl duo 400"[tiab] OR "clamoxyl duoforte"[tiab] OR "clarin-duo"[tiab] OR "clavam"[tiab] OR "clavamox"[tiab] OR "clavar"[tiab] OR "clavinex"[tiab] OR "clavodar"[tiab] OR "clavoxil"[tiab] OR "clavoxilin plus"[tiab] OR "clavubactin"[tiab] OR "clavucid"[tiab] OR "clavudale"[tiab] OR "clavulox duo"[tiab] OR "clavumox"[tiab] OR "co amoxyclav"[tiab] OR "coamoxyclav"[tiab] OR "cramon duo"[tiab] OR "croanan duo dry syrup"[tiab] OR "curam"[tiab] OR "danoclav"[tiab] OR "darzitil plus"[tiab] OR "duamentin"[tiab] OR "duomox"[tiab] OR "e-moxclav"[tiab] OR "enhancin"[tiab] OR "eumetinex"[tiab] OR "fleming"[tiab] OR "forcid"[tiab] OR "forcid solutab"[tiab] OR "fugentin"[tiab] OR "fullicilina plus"[tiab] OR "gumentin"[tiab] OR "hibiotic"[tiab] OR "inciclav"[tiab] OR "klamonex"[tiab] OR "kmoxilin"[tiab] OR "lactamox"[tiab] OR "lansiclav"[tiab] OR "moxiclav"[tiab] OR "moxicle"[tiab] OR "moxyclav"[tiab] OR "natravox"[tiab] OR "neoduplamox"[tiab] OR "noprilam"[tiab] OR "nufaclav"[tiab] OR "omep plus"[tiab] OR "palentin"[tiab] OR "quali-mentin"[tiab] OR "ranclav"[tiab] OR "spectramox"[tiab] OR "stacillin"[tiab] OR "strenzen"[tiab] OR "suplentin"[tiab] OR "synermox"[tiab] OR "taromentin"[tiab] OR "taromentin es"[tiab] OR "velamox cl"[tiab] OR "vestaclav"[tiab] OR "viaclav"[tiab] OR "vulamox"[tiab] OR "xiclav"[tiab] OR "zami 8503"[tiab] OR

"Floxacillin"[Mesh] OR floxacillin*[tiab] OR Fluorochloroxacillin[tiab] OR Flucloxacillin[tiab] OR "flopen"[tiab] OR "floxapen"[tiab] OR "flucil"[tiab] OR "heracillin"[tiab] OR "stafoxil"[tiab] OR "staphylex"[tiab] OR

"Tetracyclines"[Mesh] OR "Tetracyclin*"[tiab] OR

"Doxycycline"[Mesh] OR "Doxycyclin*"[tiab] OR Vibramycin*[tiab] OR Atridox[tiab] OR Doryx[tiab] OR Hydramycin[tiab] OR Oracea[tiab] OR Periostat[tiab] OR Vibra-Tabs[tiab] OR Vibravenos[tiab] OR "adoxa"[tiab] OR "amermycin"[tiab] OR "apprilon"[tiab] OR "atrax"[tiab] OR "azudoxat"[tiab] OR "bactidox"[tiab] OR "banndoclin"[tiab] OR "basedillin"[tiab] OR "bassado"[tiab] OR "biocolyn"[tiab] OR "biodoxi"[tiab] OR "bronmycin"[tiab] OR "cloran"[tiab] OR "cyclidox"[tiab] OR "dentistar"[tiab] OR "deoxycycline"[tiab] OR "deoxymycin dispersal"[tiab] OR "deoxymykoin"[tiab] OR "deoxyoxytetracycline"[tiab] OR "desoxy oxytetracycline"[tiab] OR "desoxycycline"[tiab] OR "doinmycin"[tiab] OR "dosil"[tiab] OR "dotur"[tiab] OR "doxaciclin"[tiab] OR "doxacycline"[tiab] OR "doxat"[tiab] OR "doxatet"[tiab] OR "doxi-sergo"[tiab] OR "doxibiotic"[tiab] OR "doxicycline"[tiab] OR "doxilin"[tiab] OR "doximed"[tiab] OR "doximycin"[tiab] OR "doxin"[tiab] OR "doxine"[tiab] OR "doxirobe"[tiab] OR "doxocycline"[tiab] OR "doxsig"[tiab] OR "doxy"[tiab] OR "doxybiocin"[tiab] OR "doxycen"[tiab] OR "doxychel"[tiab] OR "doxycin"[tiab] OR "doxylag"[tiab] OR "doxylin"[tiab] OR "doxymycin"[tiab] OR "doxypuren"[tiab] OR "doxytec"[tiab] OR "doxytrim"[tiab] OR "dumoxin"[tiab] OR "duracycline"[tiab] OR "efracea"[tiab] OR "esdoxin"[tiab] OR "etidoxina"[tiab] OR "gewacyclin"[tiab] OR "ibralene"[tiab] OR "idocyclin"[tiab] OR "idocyklin"[tiab] OR "interdoxin"[tiab] OR "investin"[tiab] OR "longamycin"[tiab] OR "lydox"[tiab] OR "magdrin"[tiab] OR "medomycin"[tiab] OR "mespafin"[tiab] OR "mildox"[tiab] OR "miraclin"[tiab] OR "monodox"[tiab] OR "nanodox"[tiab] OR "nordox"[tiab] OR "oraycea"[tiab] OR "paldomycin"[tiab] OR "pernox gel"[tiab] OR "radox"[tiab] OR "remycin"[tiab] OR "respidox"[tiab] OR "roximycin"[tiab] OR "serodoxy"[tiab] OR "servidoxine"[tiab] OR "servidoxyne"[tiab] OR "siadocin"[tiab] OR "siclidon"[tiab] OR "sigadoxin"[tiab] OR "spanor"[tiab] OR "supracyclin"[tiab] OR "supramycina"[tiab] OR "tenutan"[tiab] OR "tolexine"[tiab] OR "torymycin"[tiab] OR "tsurupioxin"[tiab] OR "unidox"[tiab] OR "veemycin"[tiab] OR "viadoxin"[tiab] OR "vibra s"[tiab] OR "vibra-s"[tiab] OR "vibrabiotic"[tiab] OR "vibracina"[tiab] OR "vibradox"[tiab] OR "vibramicina"[tiab] OR "vibraveineuse"[tiab] OR "vibravet"[tiab] OR "viradoxyl-n"[tiab] OR "wanmycin"[tiab] OR "xyrosa"[tiab] OR "zadorin"[tiab] OR "zenavod"[tiab] OR

"Minocycline"[Mesh] OR "Minocyclin*"[tiab] OR "Minox 50"[tiab] OR Aknemin[tiab] OR "Aknin-Mino"[tiab] OR Aknosan[tiab] OR Mynocine[tiab] OR Arestin[tiab] OR Blemix[tiab] OR Cyclomin[tiab] OR Cyclops[tiab] OR Dentomycin[tiab] OR Dynacin[tiab] OR "Icht-Oral"[tiab] OR Klinomycin[tiab] OR Lederderm[tiab] OR Mestacine[tiab] OR Minakne[tiab] OR "Mino-Wolff"[tiab] OR Minocin[tiab] OR Minoclir[tiab] OR Minolis[tiab] OR Minomycin[tiab] OR Minoplus[tiab] OR Minotab[tiab] OR Akamin[tiab] OR "Akne-Puren"[tiab] OR "amzeeq"[tiab] OR "borymycin"[tiab] OR "cipancin"[tiab] OR "cyclimycin"[tiab] OR "cynomycin"[tiab] OR "klinotab"[tiab] OR "kyno"[tiab] OR "logryx"[tiab] OR "menocycline"[tiab] OR "micromycin"[tiab] OR "minaxen"[tiab] OR "mino-50"[tiab] OR "minoclin"[tiab] OR "minocyn"[tiab] OR "minogalen"[tiab] OR "minoline"[tiab] OR "minolira"[tiab] OR "minomax"[tiab] OR "minosil"[tiab] OR "minostad"[tiab] OR "minotrex"[tiab] OR "minozep"[tiab] OR "mirosin"[tiab] OR "parocline"[tiab] OR "periofeel"[tiab] OR "romin"[tiab] OR "sebomir"[tiab] OR "skinocyclin"[tiab] OR "solodyn"[tiab] OR "spicline"[tiab] OR "vectran"[tiab] OR "vectrin"[tiab] OR "ximino"[tiab] OR "zilxi"[tiab] OR

"Sulfanilamides"[Mesh] OR sulfanilamide*[tiab] OR sulfonamide*[tiab] OR sulphanilamide*[tiab] OR sulphonamide*[tiab] OR

Centrin[tiab] OR Cotrimoxazole[tiab] OR "Co-Trimoxazole"[tiab] OR Eslectin[tiab] OR Insozalin[tiab] OR Trimezol*[tiab] OR Centran[tiab] OR Trimedin[tiab] OR Septrin*[tiab] OR Bactifor[tiab] OR Sumetrolim[tiab] OR Abactrim[tiab] OR Bactrim[tiab] OR Bisepto[tiab] OR Biseptol480[tiab] OR Drylin[tiab] OR Eusaprim[tiab] OR Kepinol[tiab] OR Lescot[tiab] OR Metomide[tiab] OR Oriprim[tiab] OR Septra[tiab] OR Sulprim[tiab] OR Trimosulfa[tiab] OR

"abactrin"[tiab] OR "alfatrim"[tiab] OR "apo sulfatrim"[tiab] OR "bactar"[tiab] OR "bactipront"[tiab] OR "bactoreduct forte"[tiab] OR "bactramin"[tiab] OR "bactrimel"[tiab] OR "bethaprim"[tiab] OR "bispetol"[tiab] OR "chemotrim"[tiab] OR "comox"[tiab] OR "comoxol"[tiab] OR "cotrim"[tiab] OR "cotrimoxazol forte"[tiab] OR "cotrimstada forte"[tiab] OR "deprim"[tiab] OR "deprim forte"[tiab] OR "duobact"[tiab] OR "duobiocin"[tiab] OR "duobiocin forte"[tiab] OR "duratrimet"[tiab] OR "eltrianyl"[tiab] OR "escoprim"[tiab] OR "espectrin"[tiab] OR "fectrim"[tiab] OR "groprim"[tiab] OR "helveprim"[tiab] OR "imexim"[tiab] OR "infectrim"[tiab] OR "lagaprim"[tiab] OR "lagatrim"[tiab] OR "linaris"[tiab] OR "microtrim"[tiab] OR "neoprim"[tiab] OR "nopil"[tiab] OR "oecotrim"[tiab] OR "omsat"[tiab] OR "oribact"[tiab] OR "pharmaprim"[tiab] OR "potesept"[tiab] OR "resprim"[tiab] OR "resprin"[tiab] OR "scanprin"[tiab] OR "septran"[tiab] OR "septrim"[tiab] OR "sigaprim"[tiab] OR "sinersol"[tiab] OR "soltrim"[tiab] OR "sulfamethoprim"[tiab] OR "sulfaprim"[tiab] OR "sulfatrim"[tiab] OR "sulfotrim"[tiab] OR "sulmeprim"[tiab] OR "sumetrolin"[tiab] OR "supracombin"[tiab] OR "thiocuran"[tiab] OR "tms forte"[tiab] OR "trib"[tiab] OR "trigonyl"[tiab] OR "trimeth/sulfa"[tiab] OR "trimetoprim-sulfa"[tiab] OR "trimetoprimsulfamethoxazole"[tiab] OR "trimforte"[tiab] OR "trimoxazole"[tiab] OR "trimoxol"[tiab] OR "uro ts d"[tiab] OR "uroplus ds"[tiab] OR "uroplus ss"[tiab] OR

"Pyrimidines"[Mesh] OR pyrimidin*[tiab] OR

"Trimethoprim"[Mesh] OR trimethoprim*[tiab] OR trimpex[tiab] OR proloprim[tiab] OR "abaprim"[tiab] OR "alprim"[tiab] OR "catin"[tiab] OR "delprim"[tiab] OR "giprim"[tiab] OR "idotrim"[tiab] OR "infectotrimet"[tiab] OR "methoprim"[tiab] OR "monoprim"[tiab] OR "monotrim"[tiab] OR "motrim"[tiab] OR "primosept"[tiab] OR "primsol"[tiab] OR "solotrim"[tiab] OR "syraprim"[tiab] OR "tiempe"[tiab] OR "tmp-ratiopharm"[tiab] OR "tobyprim"[tiab] OR "trimesan"[tiab] OR "trimethoprin"[tiab] OR "trimetoprim"[tiab] OR "trimfect"[tiab] OR "trimono"[tiab] OR "trimopan"[tiab] OR "trinopan"[tiab] OR "triprim"[tiab] OR "trisul"[tiab] OR "uretrim"[tiab] OR "utisept"[tiab] OR "welcoprim"[tiab] OR "wellcoprim"[tiab] OR

"Cephalosporins"[Mesh] OR "Cephalosporin*"[tiab] OR cefalosporin*[tiab] OR

"Cefuroxime"[Mesh] OR "Cefuroxim*"[tiab] OR Cephuroxim*[tiab] OR Zinacef[tiab] OR Ketocef[tiab] OR "aksef"[tiab] OR "alporin"[tiab] OR "altacef"[tiab] OR "anaptivan"[tiab] OR "aprok"[tiab] OR "aprokam"[tiab] OR "biocefal"[tiab] OR "cefoxurime"[tiab] OR "cefumax"[tiab] OR "ceplus"[tiab] OR "ceroxime"[tiab] OR "curocef"[tiab] OR "curoxim"[tiab] OR "curoxima"[tiab] OR "curoxime"[tiab] OR "eroxmit"[tiab] OR "froxal"[tiab] OR "fucerox"[tiab] OR "furoxime"[tiab] OR "iceca"[tiab] OR "intracef"[tiab] OR "kefazol"[tiab] OR "kefurim"[tiab] OR "kefurox"[tiab] OR "kesint"[tiab] OR "laxinat"[tiab] OR "maxil"[tiab] OR "normafenac"[tiab] OR "polixima"[tiab] OR "prokam"[tiab] OR "supacef"[tiab] OR "tarsime"[tiab] OR "ucefaxim"[tiab] OR "ultroxim"[tiab] OR "uroxime"[tiab] OR "vekfazolin"[tiab] OR "ximaract"[tiab] OR "zinocef"[tiab]

Embase 11122023 => 1 + 2 = 4285 results

4. Bronchiectasis

'bronchiectasis'/exp/dm_di,dm_dr,dm_dt,dm_th OR 'bronchiectas*':ti,ab,kw OR 'bronchoectasia':ti,ab,kw OR 'bronchiectasis'/mj

5. Long term oral antibiotic treatment (excluding long-term macrolides)

'antibiotic agent'/de OR 'anti-bacterial':ti,ab,kw OR 'antibacterial':ti,ab,kw OR 'Bacteriocid*':ti,ab,kw OR 'anti-mycobacterial':ti,ab,kw OR 'antimycobacterial':ti,ab,kw OR 'antibiotic*':ti,ab,kw OR

'quinolone derivative'/exp OR 'quinoline derivative'/exp OR 'quinoline derived antiinfective agent'/exp OR fluoroquinolon*:ti,ab,kw OR quinolon*:ti,ab,kw OR chinolon*:ti,ab,kw OR quinolin*:ti,ab,kw OR chinolin*:ti,ab,kw OR

'ciprofloxacin'/exp OR 'cipro*':ti,ab,kw OR 'ciprinol':ti,ab,kw OR 'aceoto':ti,ab,kw OR 'acire':ti,ab,kw OR 'alcon cilox':ti,ab,kw OR 'apulmiq':ti,ab,kw OR 'araxacina':ti,ab,kw OR 'aristin-c':ti,ab,kw OR 'auripro':ti,ab,kw OR 'bacquinor':ti,ab,kw OR 'bactiflox':ti,ab,kw OR 'baflox':ti,ab,kw OR 'basemar':ti,ab,kw OR 'battizer':ti,ab,kw OR 'baycip':ti,ab,kw OR 'bernoflox':ti,ab,kw OR 'bivorilan':ti,ab,kw OR 'bosix':ti,ab,kw OR 'c-flox':ti,ab,kw OR 'c-floxacin':ti,ab,kw OR 'catex':ti,ab,kw OR 'cetraflux':ti,ab,kw OR 'cetraxal':ti,ab,kw OR 'chinocid':ti,ab,kw OR 'cidroxal':ti,ab,kw OR 'cifin':ti,ab,kw OR 'ciflan':ti,ab,kw OR 'ciflo':ti,ab,kw OR 'ciflosin':ti,ab,kw OR 'ciflot':ti,ab,kw OR 'ciflox':ti,ab,kw OR 'cifloxin':ti,ab,kw OR 'cifox':ti,ab,kw OR 'cifran':ti,ab,kw OR 'cilab':ti,ab,kw OR 'ciloquin':ti,ab,kw OR 'ciloxan':ti,ab,kw OR 'ciloxin':ti,ab,kw OR 'cimogal':ti,ab,kw OR 'cinaflox':ti,ab,kw OR 'cipad':ti,ab,kw OR 'ciperus':ti,ab,kw OR 'cipflox':ti,ab,kw OR 'ciphin':ti,ab,kw OR 'cipide':ti,ab,kw OR 'cipio':ti,ab,kw OR 'ciplox':ti,ab,kw OR 'ciplus':ti,ab,kw OR 'cipocin':ti,ab,kw OR 'ciprecu':ti,ab,kw OR 'ciriax':ti,ab,kw OR 'cirok':ti,ab,kw OR 'cirokan':ti,ab,kw OR 'cirox':ti,ab,kw OR 'ciroxin':ti,ab,kw OR 'citopcin':ti,ab,kw OR 'citrovenot':ti,ab,kw OR 'cobay':ti,ab,kw OR 'corsacin':ti,ab,kw OR 'cosflox':ti,ab,kw OR 'cuminol':ti,ab,kw OR 'cuspis':ti,ab,kw OR 'cycin':ti,ab,kw OR 'cyfloxin':ti,ab,kw OR 'cypral':ti,ab,kw OR 'cyprobay':ti,ab,kw OR 'cysfec':ti,ab,kw OR 'doriman':ti,ab,kw OR 'droll':ti,ab,kw OR 'eoxin':ti,ab,kw OR 'eprocin':ti,ab,kw OR 'estecina':ti,ab,kw OR 'felixene':ti,ab,kw OR 'fimoflox':ti,ab,kw OR 'flociprin':ti,ab,kw OR 'flontalexin':ti,ab,kw OR 'floroxin':ti,ab,kw OR 'floxager':ti,ab,kw OR 'floxantina':ti,ab,kw OR 'floxbio':ti,ab,kw OR 'fonterra':ti,ab,kw OR 'generflon':ti,ab,kw OR 'gerbat':ti,ab,kw OR 'ginorectol':ti,ab,kw OR 'giroflox':ti,ab,kw OR 'gonning':ti,ab,kw OR 'grifociprox':ti,ab,kw OR 'h-next':ti,ab,kw OR 'holdestin':ti,ab,kw OR 'ibixacin':ti,ab,kw OR 'inciflox':ti,ab,kw OR 'infectocipro':ti,ab,kw OR 'inkamil':ti,ab,kw OR 'iprolan':ti,ab,kw OR 'isotic':ti,ab,kw OR 'jayacin':ti,ab,kw OR 'k-sacin':ti,ab,kw OR 'kenzoflex':ti,ab,kw OR 'kinoves':ti,ab,kw OR 'kinox':ti,ab,kw OR 'kipocin':ti,ab,kw OR 'labentrol':ti,ab,kw OR 'ladinin':ti,ab,kw OR 'limox':ti,ab,kw OR 'linhaliq':ti,ab,kw OR 'lipoquin':ti,ab,kw OR 'lofucin':ti,ab,kw OR 'loxan':ti,ab,kw OR 'macar':ti,ab,kw OR 'medociprin':ti,ab,kw OR 'mitroken':ti,ab,kw OR 'nafloxin':ti,ab,kw OR 'neofloxin':ti,ab,kw OR 'nivoflox':ti,ab,kw OR 'novidat':ti,ab,kw OR 'novoquin':ti,ab,kw OR 'oftacilox':ti,ab,kw OR 'opthaflox':ti,ab,kw OR 'otanol':ti,ab,kw OR 'otiprio':ti,ab,kw OR 'otociprin':ti,ab,kw OR 'otosec':ti,ab,kw OR 'phaproxin':ti,ab,kw OR 'pharcina':ti,ab,kw OR 'poncoflox':ti,ab,kw OR 'probiox':ti,ab,kw OR 'prociflor':ti,ab,kw OR 'procin':ti,ab,kw OR 'proflaxin':ti,ab,kw OR 'profloxin':ti,ab,kw OR 'proksi 250':ti,ab,kw OR 'proksi 500':ti,ab,kw OR 'proquin':ti,ab,kw OR 'proxacin':ti,ab,kw OR 'pulmaquin':ti,ab,kw OR 'qilaflox':ti,ab,kw OR 'qinosyn':ti,ab,kw OR 'quilox':ti,ab,kw OR 'quinobiotic':ti,ab,kw OR 'quinoflox':ti,ab,kw OR 'quinolide':ti,ab,kw OR 'quinox':ti,ab,kw OR 'quintor':ti,ab,kw OR 'qupron':ti,ab,kw OR 'rancif':ti,ab,kw OR 'ravalton':ti,ab,kw OR 'revionorm':ti,ab,kw OR 'rigoran':ti,ab,kw OR 'rofcin':ti,ab,kw OR 'roflazin':ti,ab,kw OR 'rosacin eye drop':ti,ab,kw OR 'samper':ti,ab,kw OR

'sarf':ti,ab,kw OR 'sepcen':ti,ab,kw OR 'septicide':ti,ab,kw OR 'septocipro':ti,ab,kw OR 'sifloks':ti,ab,kw OR 'siprogut':ti,ab,kw OR 'siprox':ti,ab,kw OR 'sophixin ofteno':ti,ab,kw OR 'spitacin':ti,ab,kw OR 'strox':ti,ab,kw OR 'suiflox':ti,ab,kw OR 'superocin':ti,ab,kw OR 'syntoflox':ti,ab,kw OR 'topistin':ti,ab,kw OR 'truoxin':ti,ab,kw OR 'ufexil':ti,ab,kw OR 'ullax':ti,ab,kw OR 'unex':ti,ab,kw OR 'unicexal':ti,ab,kw OR 'uniflox':ti,ab,kw OR 'urodixin':ti,ab,kw OR 'uroxin':ti,ab,kw OR 'viprolox':ti,ab,kw OR 'zindolin':ti,ab,kw OR 'zipra':ti,ab,kw OR 'zumaflox':ti,ab,kw OR

'levofloxacin'/exp OR ('(S)-isomer' NEXT/3 'Ofloxacin'):ti,ab,kw OR Quixin:ti,ab,kw OR Levaquin:ti,ab,kw OR 'aeroquin':ti,ab,kw OR 'cravit':ti,ab,kw OR 'elequine':ti,ab,kw OR 'eyflox':ti,ab,kw OR 'floxacin':ti,ab,kw OR 'floxel':ti,ab,kw OR 'iquix':ti,ab,kw OR 'leroxacin':ti,ab,kw OR 'lesacin':ti,ab,kw OR 'levokacin':ti,ab,kw OR 'levox':ti,ab,kw OR 'levoxacin':ti,ab,kw OR 'mosardal':ti,ab,kw OR 'nofaxin':ti,ab,kw OR 'oftaquix':ti,ab,kw OR 'oxalux':ti,ab,kw OR 'prixar':ti,ab,kw OR 'quinsair':ti,ab,kw OR 'reskuin':ti,ab,kw OR 'supraflox':ti,ab,kw OR 'tavanic':ti,ab,kw OR 'unibiotic':ti,ab,kw OR 'venaxan':ti,ab,kw OR 'volequin':ti,ab,kw OR

'ofloxacin'/exp OR 'ofloxacin*':ti,ab,kw OR 'tarivid':ti,ab,kw OR 'akilen':ti,ab,kw OR 'audret':ti,ab,kw OR 'bactocin':ti,ab,kw OR 'bioquil':ti,ab,kw OR 'danoflox':ti,ab,kw OR 'effexin':ti,ab,kw OR 'eukinoft':ti,ab,kw OR 'exocin':ti,ab,kw OR 'exocine':ti,ab,kw OR 'flobacin':ti,ab,kw OR 'flodemex':ti,ab,kw OR 'flotavid':ti,ab,kw OR 'flovid':ti,ab,kw OR 'floxal':ti,ab,kw OR 'floxedol':ti,ab,kw OR 'floxigen':ti,ab,kw OR 'floxil':ti,ab,kw OR 'floxin':ti,ab,kw OR 'floxstat':ti,ab,kw OR 'fugacin':ti,ab,kw OR 'grenis-oflo':ti,ab,kw OR 'gyroflox':ti,ab,kw OR 'inoflox':ti,ab,kw OR 'kinflocin':ti,ab,kw OR 'kinoxacin':ti,ab,kw OR 'liflox':ti,ab,kw OR 'loxinter':ti,ab,kw OR 'marfloxacin':ti,ab,kw OR 'medofloxin':ti,ab,kw OR 'medofloxine':ti,ab,kw OR 'mergexin':ti,ab,kw OR 'monoflocet':ti,ab,kw OR 'monoox':ti,ab,kw OR 'novecin':ti,ab,kw OR 'nufafloqo':ti,ab,kw OR 'o-flox':ti,ab,kw OR 'obide':ti,ab,kw OR 'occidal':ti,ab,kw OR 'ocuflox':ti,ab,kw OR 'ofcin':ti,ab,kw OR 'oflin':ti,ab,kw OR 'oflocee':ti,ab,kw OR 'oflocet':ti,ab,kw OR 'oflocin':ti,ab,kw OR 'oflodal':ti,ab,kw OR 'oflodex':ti,ab,kw OR 'oflodinex':ti,ab,kw OR 'oflodura':ti,ab,kw OR 'oflogen':ti,ab,kw OR 'oflohexal':ti,ab,kw OR 'oflovir':ti,ab,kw OR 'oflox':ti,ab,kw OR 'ofloxa-vision':ti,ab,kw OR 'ofloxacino':ti,ab,kw OR 'ofloxamed':ti,ab,kw OR 'ofloxavis':ti,ab,kw OR 'ofloxin':ti,ab,kw OR 'ofus':ti,ab,kw OR 'onexacin':ti,ab,kw OR 'operan':ti,ab,kw OR 'orocin':ti,ab,kw OR 'otiflox':ti,ab,kw OR 'otonil':ti,ab,kw OR 'ottoflox':ti,ab,kw OR 'oxacid':ti,ab,kw OR 'oxatrex':ti,ab,kw OR 'pharflox':ti,ab,kw OR 'praxin':ti,ab,kw OR 'puiritol':ti,ab,kw OR 'qinolon':ti,ab,kw OR 'qipro':ti,ab,kw OR 'quinofree':ti,ab,kw OR 'quinolon':ti,ab,kw OR 'quotavil':ti,ab,kw OR 'rilox':ti,ab,kw OR 'romacin':ti,ab,kw OR 'sinflo':ti,ab,kw OR 'surnox':ti,ab,kw OR 'tabrin':ti,ab,kw OR 'taravid':ti,ab,kw OR 'tariflox':ti,ab,kw OR 'taroflox':ti,ab,kw OR 'telbit':ti,ab,kw OR 'trafloxal':ti,ab,kw OR 'tructum':ti,ab,kw OR 'urotarivid':ti,ab,kw OR 'viotisone':ti,ab,kw OR 'visuab':ti,ab,kw OR 'zanocin':ti,ab,kw OR

'moxifloxacin'/exp OR 'Moxifloxacin*':ti,ab,kw OR Octegra:ti,ab,kw OR Proflox:ti,ab,kw OR Avelox:ti,ab,kw OR Avalox:ti,ab,kw OR Izilox:ti,ab,kw OR Actira:ti,ab,kw OR 'avelon':ti,ab,kw OR 'bacterol':ti,ab,kw OR 'floxamic':ti,ab,kw OR 'floxitrat':ti,ab,kw OR 'izilox':ti,ab,kw OR 'kanavig':ti,ab,kw OR 'lifodrox':ti,ab,kw OR 'megaxin':ti,ab,kw OR 'melocin':ti,ab,kw OR 'moksacin':ti,ab,kw OR 'monafox':ti,ab,kw OR 'moxeza':ti,ab,kw OR 'moxibay':ti,ab,kw OR 'moxif':ti,ab,kw OR 'moxivig':ti,ab,kw OR 'octegra':ti,ab,kw OR 'proflox':ti,ab,kw OR 'tamvelier':ti,ab,kw OR 'vamocin':ti,ab,kw OR 'vegamox':ti,ab,kw OR 'vigamox':ti,ab,kw OR 'vigamoxi':ti,ab,kw OR 'xiflodrop':ti,ab,kw OR 'zimoxin':ti,ab,kw OR

'penicillin derivative'/exp OR penicillin*:ti,ab,kw OR

'amoxicillin'/exp OR 'Amoxicillin*':ti,ab,kw OR 'Amoxycillin*':ti,ab,kw OR 'Hydroxyampicillin':ti,ab,kw OR 'Actimoxi':ti,ab,kw OR 'Clamoxyl':ti,ab,kw OR 'Penamox':ti,ab,kw OR 'Polymox':ti,ab,kw OR 'Trimox':ti,ab,kw OR 'Wymox':ti,ab,kw OR 'Amoxil':ti,ab,kw OR 'a gram':ti,ab,kw OR 'abdimox':ti,ab,kw OR 'acilina':ti,ab,kw OR 'acimox':ti,ab,kw OR 'adbiotin':ti,ab,kw OR 'agerpen':ti,ab,kw OR 'agram':ti,ab,kw OR 'alfamox':ti,ab,kw OR 'alfoxil':ti,ab,kw OR 'almodan':ti,ab,kw OR 'almorsan':ti,ab,kw OR 'alphamox':ti,ab,kw OR 'amagesen solutab':ti,ab,kw OR 'ameclina':ti,ab,kw OR 'amitron':ti,ab,kw OR 'amo-flamisan':ti,ab,kw OR 'amo-flamsian':ti,ab,kw OR 'amocillin':ti,ab,kw OR 'amoclen':ti,ab,kw OR 'amodex':ti,ab,kw OR 'amoflux':ti,ab,kw OR 'amohexal':ti,ab,kw OR 'amolin':ti,ab,kw OR 'amonex':ti,ab,kw OR 'amopen':ti,ab,kw OR 'amophar ge':ti,ab,kw OR 'amosine':ti,ab,kw OR 'amoval':ti,ab,kw OR 'amoxa':ti,ab,kw OR 'amoxal':ti,ab,kw OR 'amoxapen':ti,ab,kw OR 'amoxaren':ti,ab,kw OR 'amoxcil':ti,ab,kw OR 'amoxcillin':ti,ab,kw OR 'amoxcin':ti,ab,kw OR 'amoxi-basan':ti,ab,kw OR 'amoxicilina':ti,ab,kw OR 'amoxiclin':ti,ab,kw OR 'amoxicot':ti,ab,kw OR 'amoxidal':ti,ab,kw OR 'amoxidin':ti,ab,kw OR 'amoxidrops':ti,ab,kw OR 'amoxihexal':ti,ab,kw OR 'amoxillin':ti,ab,kw OR 'amoxina':ti,ab,kw OR 'amoxipen':ti,ab,kw OR 'amoxipenil':ti,ab,kw OR 'amoxisol':ti,ab,kw OR 'amoxivan':ti,ab,kw OR 'amoxivet':ti,ab,kw OR 'amoxy':ti,ab,kw OR 'amoxy-diolan':ti,ab,kw OR 'amoxypen':ti,ab,kw OR 'ampliron':ti,ab,kw OR 'apo-amoxi':ti,ab,kw OR 'ardine':ti,ab,kw OR 'aroxin':ti,ab,kw OR 'azillin':ti,ab,kw OR 'bacihexal':ti,ab,kw OR 'bactamox':ti,ab,kw OR 'bactox ge':ti,ab,kw OR 'beamoxy':ti,ab,kw OR 'betamox':ti,ab,kw OR 'bimox':ti,ab,kw OR 'bintamox':ti,ab,kw OR 'biomox':ti,ab,kw OR 'biotamoxal':ti,ab,kw OR 'bioxidona':ti,ab,kw OR 'bioxyllin':ti,ab,kw OR 'bristamox':ti,ab,kw OR 'broadmetz':ti,ab,kw OR 'cabermox':ti,ab,kw OR 'cilamox':ti,ab,kw OR 'clamox':ti,ab,kw OR 'clearamox':ti,ab,kw OR 'clonamox':ti,ab,kw OR 'coamoxin':ti,ab,kw OR 'damoxicil':ti,ab,kw OR 'dispermox':ti,ab,kw OR 'doxamil':ti,ab,kw OR 'draximox':ti,ab,kw OR 'edamox':ti,ab,kw OR 'efpinex':ti,ab,kw OR 'erphamoxy':ti,ab,kw OR 'eupen':ti,ab,kw OR 'farconcil':ti,ab,kw OR 'fisamox':ti,ab,kw OR 'flemoxin':ti,ab,kw OR 'flemoxine ge':ti,ab,kw OR 'fluamoxina':ti,ab,kw OR 'foxolin':ti,ab,kw OR 'fullcilina':ti,ab,kw OR 'gexcil':ti,ab,kw OR 'gimalxina':ti,ab,kw OR 'glamox':ti,ab,kw OR 'glassatan':ti,ab,kw OR 'gomcillin':ti,ab,kw OR 'grinsul':ti,ab,kw OR 'grunamox':ti,ab,kw OR 'hamoxillin':ti,ab,kw OR 'hiconcil':ti,ab,kw OR 'hidramox':ti,ab,kw OR 'hipen':ti,ab,kw OR 'hosboral':ti,ab,kw OR 'ibamox':ti,ab,kw OR 'ibiamox':ti,ab,kw OR 'ikamoxil':ti,ab,kw OR 'imacillin':ti,ab,kw OR 'imaxilin':ti,ab,kw OR 'inamox':ti,ab,kw OR 'infectomycin':ti,ab,kw OR 'intermox':ti,ab,kw OR 'isimoxin':ti,ab,kw OR 'izoltil':ti,ab,kw OR 'julphamox':ti,ab,kw OR 'jutamox':ti,ab,kw OR 'kamoxin':ti,ab,kw OR 'ladoxillin':ti,ab,kw OR 'lamoxy':ti,ab,kw OR 'larocilin':ti,ab,kw OR 'larocin':ti,ab,kw OR 'larotid':ti,ab,kw OR 'macromox':ti,ab,kw OR 'magnimox':ti,ab,kw OR 'maxamox':ti,ab,kw OR 'maxcil':ti,ab,kw OR 'medimox':ti,ab,kw OR 'meixil':ti,ab,kw OR 'metifarma':ti,ab,kw OR 'mopen':ti,ab,kw OR 'morgenxil':ti,ab,kw OR 'moxacin':ti,ab,kw OR 'moxaline':ti,ab,kw OR 'moxarin':ti,ab,kw OR 'moxatag':ti,ab,kw OR 'moxilen':ti,ab,kw OR 'moxilin':ti,ab,kw OR 'moximar':ti,ab,kw OR 'moxitab':ti,ab,kw OR 'moxtid':ti,ab,kw OR 'moxylin':ti,ab,kw OR 'moxypen':ti,ab,kw OR 'moxyvit':ti,ab,kw OR 'neogram':ti,ab,kw OR 'novabritine':ti,ab,kw OR 'novamox':ti,ab,kw OR 'novamoxin':ti,ab,kw OR 'novenzymin':ti,ab,kw OR 'novoxil':ti,ab,kw OR 'nuvosyl':ti,ab,kw OR 'optium':ti,ab,kw OR 'oramox':ti,ab,kw OR 'ospamox':ti,ab,kw OR 'pamocil':ti,ab,kw OR 'pamoxicillin':ti,ab,kw OR 'pamoxin':ti,ab,kw OR 'panvilon':ti,ab,kw OR 'pasetocin':ti,ab,kw OR 'penbiosyn':ti,ab,kw OR 'pentyloxycillin':ti,ab,kw OR 'pharmoxyl':ti,ab,kw OR 'piramox':ti,ab,kw OR 'pondnoxcill':ti,ab,kw OR 'rancil':ti,ab,kw OR 'ranmoxy':ti,ab,kw OR 'ranoxil':ti,ab,kw OR 'ranoxyl':ti,ab,kw OR 'robamox':ti,ab,kw OR 'romoxil':ti,ab,kw OR 'ronemox':ti,ab,kw OR 'saltermox':ti,ab,kw OR 'sawacillin':ti,ab,kw OR 'sawamezin':ti,ab,kw OR 'servamox':ti,ab,kw OR 'shamoxil':ti,ab,kw OR 'sia-mox':ti,ab,kw OR 'sigamopen':ti,ab,kw OR 'sil-a-mox':ti,ab,kw OR 'silamox':ti,ab,kw OR 'simoxil':ti,ab,kw OR 'sintopen':ti,ab,kw OR 'solamocta':ti,ab,kw OR 'solpenox':ti,ab,kw OR 'sumox':ti,ab,kw OR

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'amoxicillin plus clavulanic acid'/exp OR 'Co-amoxiclav':ti,ab,kw OR Coamoxiclav:ti,ab,kw OR 'Amoxi-Clavulanate':ti,ab,kw OR 'Amox-clav':ti,ab,kw OR Synulox:ti,ab,kw OR Spektramox:ti,ab,kw OR Augmentin:ti,ab,kw OR Clavulin:ti,ab,kw OR 'aclam':ti,ab,kw OR 'aktil':ti,ab,kw OR 'ambilan':ti,ab,kw OR 'amocla':ti,ab,kw OR 'amoclan':ti,ab,kw OR 'amoclane':ti,ab,kw OR 'amoclav':ti,ab,kw OR 'amoksiklav':ti,ab,kw OR 'amolanic':ti,ab,kw OR 'amometin':ti,ab,kw OR 'amoxi plus':ti,ab,kw OR 'amoxiclav':ti,ab,kw OR 'amoxiclav-bid':ti,ab,kw OR 'amoxiclav-teva':ti,ab,kw OR 'amoxsiklav':ti,ab,kw OR 'amoxxlin':ti,ab,kw OR 'ancla':ti,ab,kw OR 'auclatin duo dry syrup':ti,ab,kw OR 'augamox':ti,ab,kw OR 'augmaxcil':ti,ab,kw OR 'augmentan':ti,ab,kw OR 'augmentine':ti,ab,kw OR 'augmex':ti,ab,kw OR 'augpen':ti,ab,kw OR 'augucillin duo':ti,ab,kw OR 'augurcin':ti,ab,kw OR 'ausclav':ti,ab,kw OR 'auspilic':ti,ab,kw OR 'bactiv':ti,ab,kw OR 'bactoclav':ti,ab,kw OR 'bioclavid':ti,ab,kw OR 'cavumox':ti,ab,kw OR 'ciblor':ti,ab,kw OR 'clacillin duo dry syrup':ti,ab,kw OR 'clamax':ti,ab,kw OR 'clamentin':ti,ab,kw OR 'clamobit':ti,ab,kw OR 'clamonex':ti,ab,kw OR 'clamovid':ti,ab,kw OR 'clamoxin':ti,ab,kw OR 'clamoxyl duo 400':ti,ab,kw OR 'clamoxyl duoforte':ti,ab,kw OR 'clarin-duo':ti,ab,kw OR 'clavam':ti,ab,kw OR 'clavamox':ti,ab,kw OR 'clavar':ti,ab,kw OR 'clavinex':ti,ab,kw OR 'clavodar':ti,ab,kw OR 'clavoxil':ti,ab,kw OR 'clavoxilin plus':ti,ab,kw OR 'clavubactin':ti,ab,kw OR 'clavucid':ti,ab,kw OR 'clavudale':ti,ab,kw OR 'clavulox duo':ti,ab,kw OR 'clavumox':ti,ab,kw OR 'co amoxyclav':ti,ab,kw OR 'coamoxyclav':ti,ab,kw OR 'cramon duo':ti,ab,kw OR 'croanan duo dry syrup':ti,ab,kw OR 'curam':ti,ab,kw OR 'danoclav':ti,ab,kw OR 'darzitil plus':ti,ab,kw OR 'duamentin':ti,ab,kw OR 'duomox':ti,ab,kw OR 'e-moxclav':ti,ab,kw OR 'enhancin':ti,ab,kw OR 'eumetinex':ti,ab,kw OR 'fleming':ti,ab,kw OR 'forcid':ti,ab,kw OR 'forcid solutab':ti,ab,kw OR 'fugentin':ti,ab,kw OR 'fullicilina plus':ti,ab,kw OR 'gumentin':ti,ab,kw OR 'hibiotic':ti,ab,kw OR 'inciclav':ti,ab,kw OR 'klamonex':ti,ab,kw OR 'kmoxilin':ti,ab,kw OR 'lactamox':ti,ab,kw OR 'lansiclav':ti,ab,kw OR 'moxiclav':ti,ab,kw OR 'moxicle':ti,ab,kw OR 'moxyclav':ti,ab,kw OR 'natravox':ti,ab,kw OR 'neoduplamox':ti,ab,kw OR 'noprilam':ti,ab,kw OR 'nufaclav':ti,ab,kw OR 'omep plus':ti,ab,kw OR 'palentin':ti,ab,kw OR 'quali-mentin':ti,ab,kw OR 'ranclav':ti,ab,kw OR 'spectramox':ti,ab,kw OR 'stacillin':ti,ab,kw OR 'strenzen':ti,ab,kw OR 'suplentin':ti,ab,kw OR 'synermox':ti,ab,kw OR 'taromentin':ti,ab,kw OR 'taromentin es':ti,ab,kw OR 'velamox cl':ti,ab,kw OR 'vestaclav':ti,ab,kw OR 'viaclav':ti,ab,kw OR 'vulamox':ti,ab,kw OR 'xiclav':ti,ab,kw OR 'zami 8503':ti,ab,kw OR

'flucloxacillin'/exp OR floxacillin*:ti,ab,kw OR Fluorochloroxacillin:ti,ab,kw OR Flucloxacillin:ti,ab,kw OR 'flopen':ti,ab,kw OR 'floxapen':ti,ab,kw OR 'flucil':ti,ab,kw OR 'heracillin':ti,ab,kw OR 'stafoxil':ti,ab,kw OR 'staphylex':ti,ab,kw OR

'tetracycline derivative'/exp OR 'Tetracyclin*':ti,ab,kw OR

'doxycycline'/exp OR 'Doxycyclin*':ti,ab,kw OR Vibramycin*:ti,ab,kw OR Atridox:ti,ab,kw OR Doryx:ti,ab,kw OR Hydramycin:ti,ab,kw OR Oracea:ti,ab,kw OR Periostat:ti,ab,kw OR Vibra-Tabs:ti,ab,kw OR Vibravenos:ti,ab,kw OR 'adoxa':ti,ab,kw OR 'amermycin':ti,ab,kw OR 'apprilon':ti,ab,kw OR 'atrax':ti,ab,kw OR 'azudoxat':ti,ab,kw OR 'bactidox':ti,ab,kw OR 'banndoclin':ti,ab,kw OR 'basedillin':ti,ab,kw OR 'bassado':ti,ab,kw OR 'biocolyn':ti,ab,kw OR 'biodoxi':ti,ab,kw OR 'bronmycin':ti,ab,kw OR 'cloran':ti,ab,kw OR 'cyclidox':ti,ab,kw OR 'dentistar':ti,ab,kw OR 'deoxycycline':ti,ab,kw OR 'deoxymycin dispersal':ti,ab,kw OR

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'cephalosporin derivative'/exp OR 'Cephalosporin*':ti,ab,kw OR cefalosporin*:ti,ab,kw OR

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NOT 'conference abstract':it

Scopus 11122023 => 1 + 2 = 2132 results

1. Bronchiectasis

TITLE-ABS("bronchiectas*"OR "bronchoectasia") OR AUTHKEY("bronchiectas*"OR "bronchoectasia")

2. Antibiotics

TITLE-ABS("anti-bacterial" OR "antibacterial" OR "Bacteriocid*" OR "anti-mycobacterial" OR "antimycobacterial" OR "antibiotic*" OR

"fluoroquinolon*" OR "quinolon*" OR "chinolon*" OR "quinolin*" OR "chinolin*" OR

"cipro*" OR "ciprinol" OR "aceoto" OR "acire" OR "alcon cilox" OR "apulmiq" OR "araxacina" OR "aristin-c" OR "auripro" OR "bacquinor" OR "bactiflox" OR "baflox" OR "basemar" OR "battizer" OR "baycip" OR "bernoflox" OR "bivorilan" OR "bosix" OR "c-flox" OR "c-floxacin" OR "catex" OR "cetraflux" OR "cetraxal" OR "chinocid" OR "cidroxal" OR "cifin" OR "ciflan" OR "ciflo" OR "ciflosin" OR "ciflot" OR "ciflox" OR "cifloxin" OR "cifox" OR "cifran" OR "cilab" OR "ciloquin" OR "ciloxan" OR "ciloxin" OR "cimogal" OR "cinaflox" OR "cipad" OR "ciperus" OR "cipflox" OR "ciphin" OR "cipide" OR "cipio" OR "ciplox" OR "ciplus" OR "cipocin" OR "ciprecu" OR "ciriax" OR "cirok" OR "cirokan" OR "cirox" OR "ciroxin" OR "citopcin" OR "citrovenot" OR "cobay" OR "corsacin" OR "cosflox" OR "cuminol" OR "cuspis" OR "cycin" OR "cyfloxin" OR "cypral" OR "cyprobay" OR "cysfec" OR "doriman" OR "droll" OR "eoxin" OR "eprocin" OR "estecina" OR "felixene" OR "fimoflox" OR "flociprin" OR "flontalexin" OR "floroxin" OR "floxager" OR "floxantina" OR "floxbio" OR "fonterra" OR "generflon" OR "gerbat" OR "ginorectol" OR "giroflox" OR "gonning" OR "grifociprox" OR "h-next" OR "holdestin" OR "ibixacin" OR "inciflox" OR "infectocipro" OR "inkamil" OR "iprolan" OR "isotic" OR "jayacin" OR "k-sacin" OR "kenzoflex" OR "kinoves" OR "kinox" OR "kipocin" OR "labentrol" OR "ladinin" OR "limox" OR "linhaliq" OR "lipoquin" OR "lofucin" OR "loxan" OR "macar" OR "medociprin" OR "mitroken" OR "nafloxin" OR "neofloxin" OR "nivoflox" OR "novidat" OR "novoquin" OR "oftacilox" OR "opthaflox" OR "otanol" OR "otiprio" OR "otociprin" OR "otosec" OR "phaproxin" OR "pharcina" OR "poncoflox" OR "probiox" OR "prociflor" OR "procin" OR "proflaxin" OR "profloxin" OR "proksi 250" OR "proksi 500" OR "proquin" OR "proxacin" OR "pulmaquin" OR "qilaflox" OR "qinosyn" OR "quilox" OR "quinobiotic" OR "quinoflox" OR "quinolide" OR "quinox" OR "quintor" OR "qupron" OR "rancif" OR "ravalton" OR "revionorm" OR "rigoran" OR "rofcin" OR "roflazin" OR "rosacin eye drop" OR "samper" OR "sarf" OR "sepcen" OR "septicide" OR "septocipro" OR "sifloks" OR "siprogut" OR "siprox" OR "sophixin ofteno" OR "spitacin" OR "strox" OR "suiflox" OR "superocin" OR "syntoflox" OR "topistin" OR "truoxin" OR "ufexil" OR "ullax" OR "unex" OR "unicexal" OR "uniflox" OR "urodixin" OR "uroxin" OR "viprolox" OR "zindolin" OR "zipra" OR "zumaflox" OR

"Levofloxacin*" OR ("(S)-isomer" W/3 "Ofloxacin") OR "Quixin" OR "Levaquin" OR "aeroquin" OR "cravit" OR "elequine" OR "eyflox" OR "floxacin" OR "floxel" OR "iquix" OR "leroxacin" OR "lesacin" OR "levokacin" OR "levox" OR "levoxacin" OR "mosardal" OR "nofaxin" OR "oftaquix" OR "oxalux" OR "prixar" OR "quinsair" OR "reskuin" OR "supraflox" OR "tavanic" OR "unibiotic" OR "venaxan" OR "volequin" OR

"ofloxacin*" OR "tarivid" OR "akilen" OR "audret" OR "bactocin" OR "bioquil" OR "danoflox" OR "effexin" OR "eukinoft" OR "exocin" OR "exocine" OR "flobacin" OR "flodemex" OR "flotavid" OR "flovid" OR "floxal" OR "floxedol" OR "floxigen" OR "floxil" OR "floxin" OR "floxstat" OR "fugacin" OR "grenis-oflo" OR "gyroflox" OR "inoflox" OR "kinflocin" OR "kinoxacin" OR "liflox" OR "loxinter" OR "marfloxacin" OR "medofloxin" OR "medofloxine"

OR "mergexin" OR "monoflocet" OR "monoox" OR "novecin" OR "nufafloqo" OR "o-flox" OR "obide" OR "occidal" OR "ocuflox" OR "ofcin" OR "oflin" OR "oflocee" OR "oflocet" OR "oflocin" OR "oflodal" OR "oflodex" OR "oflodinex" OR "oflodura" OR "oflogen" OR "oflohexal" OR "oflovir" OR "oflox" OR "ofloxa-vision" OR "ofloxacino" OR "ofloxamed" OR "ofloxavis" OR "ofloxin" OR "ofus" OR "onexacin" OR "operan" OR "orocin" OR "otiflox" OR "otonil" OR "ottoflox" OR "oxacid" OR "oxatrex" OR "pharflox" OR "praxin" OR "puiritol" OR "qinolon" OR "qipro" OR "quinofree" OR "quinolon" OR "quotavil" OR "rilox" OR "romacin" OR "sinflo" OR "surnox" OR "tabrin" OR "taravid" OR "tariflox" OR "taroflox" OR "telbit" OR "trafloxal" OR "tructum" OR "urotarivid" OR "viotisone" OR "visuab" OR "zanocin" OR

"Moxifloxacin*" OR "Octegra" OR "Proflox" OR "Avelox" OR "Avalox" OR "Izilox" OR "Actira" OR "avelon" OR "bacterol" OR "floxamic" OR "floxitrat" OR "izilox" OR "kanavig" OR "lifodrox" OR "megaxin" OR "melocin" OR "moksacin" OR "monafox" OR "moxeza" OR "moxibay" OR "moxif" OR "moxivig" OR "octegra" OR "proflox" OR "tamvelier" OR "vamocin" OR "vegamox" OR "vigamox" OR "vigamoxi" OR "xiflodrop" OR "zimoxin" OR

"penicillin*" OR

"Amoxicillin*" OR "Amoxycillin*" OR "Hydroxyampicillin" OR "Actimoxi" OR "Clamoxyl" OR "Penamox" OR "Polymox" OR "Trimox" OR "Wymox" OR "Amoxil" OR "a gram" OR "abdimox" OR "acilina" OR "acimox" OR "adbiotin" OR "agerpen" OR "agram" OR "alfamox" OR "alfoxil" OR "almodan" OR "almorsan" OR "alphamox" OR "amagesen solutab" OR "ameclina" OR "amitron" OR "amo-flamisan" OR "amo-flamsian" OR "amocillin" OR "amoclen" OR "amodex" OR "amoflux" OR "amohexal" OR "amolin" OR "amonex" OR "amopen" OR "amophar ge" OR "amosine" OR "amoval" OR "amoxa" OR "amoxal" OR "amoxapen" OR "amoxaren" OR "amoxcil" OR "amoxcillin" OR "amoxcin" OR "amoxi-basan" OR "amoxicilina" OR "amoxiclin" OR "amoxicot" OR "amoxidal" OR "amoxidin" OR "amoxidrops" OR "amoxihexal" OR "amoxillin" OR "amoxina" OR "amoxipen" OR "amoxipenil" OR "amoxisol" OR "amoxivan" OR "amoxivet" OR "amoxy" OR "amoxy-diolan" OR "amoxypen" OR "ampliron" OR "apo-amoxi" OR "ardine" OR "aroxin" OR "azillin" OR "bacihexal" OR "bactamox" OR "bactox ge" OR "beamoxy" OR "betamox" OR "bimox" OR "bintamox" OR "biomox" OR "biotamoxal" OR "bioxidona" OR "bioxyllin" OR "bristamox" OR "broadmetz" OR "cabermox" OR "cilamox" OR "clamox" OR "clearamox" OR "clonamox" OR "coamoxin" OR "damoxicil" OR "dispermox" OR "doxamil" OR "draximox" OR "edamox" OR "efpinex" OR "erphamoxy" OR "eupen" OR "farconcil" OR "fisamox" OR "flemoxin" OR "flemoxine ge" OR "fluamoxina" OR "foxolin" OR "fullcilina" OR "gexcil" OR "gimalxina" OR "glamox" OR "glassatan" OR "gomcillin" OR "grinsul" OR "grunamox" OR "hamoxillin" OR "hiconcil" OR "hidramox" OR "hipen" OR "hosboral" OR "ibamox" OR "ibiamox" OR "ikamoxil" OR "imacillin" OR "imaxilin" OR "inamox" OR "infectomycin" OR "intermox" OR "isimoxin" OR "izoltil" OR "julphamox" OR "jutamox" OR "kamoxin" OR "ladoxillin" OR "lamoxy" OR "larocilin" OR "larocin" OR "larotid" OR "macromox" OR "magnimox" OR "maxamox" OR "maxcil" OR "medimox" OR "meixil" OR "metifarma" OR "mopen" OR "morgenxil" OR "moxacin" OR "moxaline" OR "moxarin" OR "moxatag" OR "moxilen" OR "moxilin" OR "moximar" OR "moxitab" OR "moxtid" OR "moxylin" OR "moxypen" OR "moxyvit" OR "neogram" OR "novabritine" OR "novamox" OR "novamoxin" OR "novenzymin" OR "novoxil" OR "nuvosyl" OR "optium" OR "oramox" OR "ospamox" OR "pamocil" OR "pamoxicillin" OR "pamoxin" OR "panvilon" OR "pasetocin" OR "penbiosyn" OR "pentyloxycillin" OR "pharmoxyl" OR "piramox" OR "pondnoxcill" OR "rancil" OR "ranmoxy" OR "ranoxil" OR "ranoxyl" OR "robamox" OR "romoxil" OR "ronemox" OR "saltermox" OR "sawacillin" OR "sawamezin" OR "servamox" OR "shamoxil" OR "sia-mox" OR "sigamopen" OR "sil-a-mox" OR "silamox" OR "simoxil" OR "sintopen" OR "solamocta" OR "solpenox" OR "sumox" OR "superpeni" OR "teramoxyl" OR "tolodina" OR "tormoxin" OR "triafamox" OR

"triamoxil" OR "trifamox" OR "uro clamoxyl" OR "uroclamoxyl" OR "utimox" OR "vastamox" OR "velamox" OR "vistrep" OR "widecillin" OR "winpen" OR "xiltrop" OR "zamocillin" OR "zamox" OR "zamoxil" OR "zerrsox" OR "zimox" OR

"Co-amoxiclav" OR "Coamoxiclav" OR "Amoxi-Clavulanate" OR "Amox-clav" OR "Synulox" OR "Spektramox" OR "Augmentin" OR "Clavulin" OR "aclam" OR "aktil" OR "ambilan" OR "amocla" OR "amoclan" OR "amoclane" OR "amoclav" OR "amoksiklav" OR "amolanic" OR "amometin" OR "amoxi plus" OR "amoxiclav" OR "amoxiclav-bid" OR "amoxiclav-teva" OR "amoxsiklav" OR "amoxxlin" OR "ancla" OR "auclatin duo dry syrup" OR "augamox" OR "augmaxcil" OR "augmentan" OR "augmentine" OR "augmex" OR "augpen" OR "augucillin duo" OR "augurcin" OR "ausclav" OR "auspilic" OR "bactiv" OR "bactoclav" OR "bioclavid" OR "cavumox" OR "ciblor" OR "clacillin duo dry syrup" OR "clamax" OR "clamentin" OR "clamobit" OR "clamonex" OR "clamovid" OR "clamoxin" OR "clamoxyl duo 400" OR "clamoxyl duoforte" OR "clarin-duo" OR "clavam" OR "clavamox" OR "clavar" OR "clavinex" OR "clavodar" OR "clavoxil" OR "clavoxilin plus" OR "clavubactin" OR "clavucid" OR "clavudale" OR "clavulox duo" OR "clavumox" OR "co amoxyclav" OR "coamoxyclav" OR "cramon duo" OR "croanan duo dry syrup" OR "curam" OR "danoclav" OR "darzitil plus" OR "duamentin" OR "duomox" OR "e-moxclav" OR "enhancin" OR "eumetinex" OR "fleming" OR "forcid" OR "forcid solutab" OR "fugentin" OR "fullicilina plus" OR "gumentin" OR "hibiotic" OR "inciclav" OR "klamonex" OR "kmoxilin" OR "lactamox" OR "lansiclav" OR "moxiclav" OR "moxicle" OR "moxyclav" OR "natravox" OR "neoduplamox" OR "noprilam" OR "nufaclav" OR "omep plus" OR "palentin" OR "quali-mentin" OR "ranclav" OR "spectramox" OR "stacillin" OR "strenzen" OR "suplentin" OR "synermox" OR "taromentin" OR "taromentin es" OR "velamox cl" OR "vestaclav" OR "viaclav" OR "vulamox" OR "xiclav" OR "zami 8503" OR

"floxacillin*" OR "Fluorochloroxacillin" OR "Flucloxacillin" OR "flopen" OR "floxapen" OR "flucil" OR "heracillin" OR "stafoxil" OR "staphylex" OR

"Tetracyclin*" OR

"Doxycyclin*" OR "Vibramycin*" OR "Atridox" OR "Doryx" OR "Hydramycin" OR "Oracea" OR "Periostat" OR "Vibra-Tabs" OR "Vibravenos" OR "adoxa" OR "amermycin" OR "apprilon" OR "atrax" OR "azudoxat" OR "bactidox" OR "banndoclin" OR "basedillin" OR "bassado" OR "biocolyn" OR "biodoxi" OR "bronmycin" OR "cloran" OR "cyclidox" OR "dentistar" OR "deoxycycline" OR "deoxymycin dispersal" OR "deoxymykoin" OR "deoxyoxytetracycline" OR "desoxy oxytetracycline" OR "desoxycycline" OR "doinmycin" OR "dosil" OR "dotur" OR "doxaciclin" OR "doxacycline" OR "doxat" OR "doxatet" OR "doxi-sergo" OR "doxibiotic" OR "doxicycline" OR "doxilin" OR "doximed" OR "doximycin" OR "doxin" OR "doxine" OR "doxirobe" OR "doxocycline" OR "doxsig" OR "doxy" OR "doxybiocin" OR "doxycen" OR "doxychel" OR "doxycin" OR "doxylag" OR "doxylin" OR "doxymycin" OR "doxypuren" OR "doxytec" OR "doxytrim" OR "dumoxin" OR "duracycline" OR "efracea" OR "esdoxin" OR "etidoxina" OR "gewacyclin" OR "ibralene" OR "idocyclin" OR "idocyklin" OR "interdoxin" OR "investin" OR "longamycin" OR "lydox" OR "magdrin" OR "medomycin" OR "mespafin" OR "mildox" OR "miraclin" OR "monodox" OR "nanodox" OR "nordox" OR "oraycea" OR "paldomycin" OR "pernox gel" OR "radox" OR "remycin" OR "respidox" OR "roximycin" OR "serodoxy" OR "servidoxine" OR "servidoxyne" OR "siadocin" OR "siclidon" OR "sigadoxin" OR "spanor" OR "supracyclin" OR "supramycina" OR "tenutan" OR "tolexine" OR "torymycin" OR "tsurupioxin" OR "unidox" OR "veemycin" OR "viadoxin" OR "vibra s" OR "vibra-s" OR "vibrabiotic" OR "vibracina" OR "vibradox" OR "vibramicina" OR "vibraveineuse" OR "vibravet" OR "viradoxyl-n" OR "wanmycin" OR "xyrosa" OR "zadorin" OR "zenavod" OR

"Minocyclin*" OR "Minox 50" OR "Aknemin" OR "Aknin-Mino" OR "Aknosan" OR "Mynocine" OR "Arestin" OR "Blemix" OR "Cyclomin" OR "Cyclops" OR "Dentomycin" OR "Dynacin" OR "Icht-Oral" OR "Klinomycin" OR "Lederderm" OR "Mestacine" OR "Minakne" OR "Mino-Wolff" OR "Minocin" OR "Minoclir" OR "Minolis" OR "Minomycin" OR "Minoplus" OR "Minotab" OR "Akamin" OR "Akne-Puren" OR "amzeeq" OR "borymycin" OR "cipancin" OR "cyclimycin" OR "cynomycin" OR "klinotab" OR "kyno" OR "logryx" OR "menocycline" OR "micromycin" OR "minaxen" OR "mino-50" OR "minoclin" OR "minocyn" OR "minogalen" OR "minoline" OR "minolira" OR "minomax" OR "minosil" OR "minostad" OR "minotrex" OR "minoz ep" OR "mirosin" OR "parocline" OR "periofeel" OR "romin" OR "sebomir" OR "skinocyclin" OR "solodyn" OR "spicline" OR "vectran" OR "vectrin" OR "ximino" OR "zilxi" OR

"sulfanilamide*" OR "sulfonamide*" OR "sulphanilamide*" OR "sulphonamide*" OR

"Centrin" OR "Cotrimoxazole" OR "Co-Trimoxazole" OR "Eslectin" OR "Insozalin" OR "Trimezol*" OR "Centran" OR "Trimedin" OR "Septrin*" OR "Bactifor" OR "Sumetrolim" OR "Abactrim" OR "Bactrim" OR "Biseptol" OR "Biseptol480" OR "Drylin" OR "Eusaprim" OR "Kepinol" OR "Lescot" OR "Metomide" OR "Oriprim" OR "Septra" OR "Sulprim" OR "Trimosulfa" OR "abactrin" OR "alfatrim" OR "apo sulfatrim" OR "bactar" OR "bactipront" OR "bactoreduct forte" OR "bactramin" OR "bactrimel" OR "bethaprim" OR "bispetol" OR "chemotrim" OR "comox" OR "comoxol" OR "cotrim" OR "cotrimoxazol forte" OR "cotrimstada forte" OR "deprim" OR "deprim forte" OR "duobact" OR "duobiocin" OR "duobiocin forte" OR "duratrimet" OR "eltrianyl" OR "escoprim" OR "espectrin" OR "fectrim" OR "groprim" OR "helveprim" OR "imexim" OR "infectrim" OR "lagaprim" OR "lagatrim" OR "linaris" OR "microtrim" OR "neoprim" OR "nopil" OR "oecotrim" OR "omsat" OR "oribact" OR "pharmaprim" OR "potesept" OR "resprim" OR "resprin" OR "scanprin" OR "septran" OR "septrim" OR "sigaprim" OR "sinersol" OR "soltrim" OR "sulfamethoprim" OR "sulfaprim" OR "sulfatrim" OR "sulfotrim" OR "sulmeprim" OR "sumetrolin" OR "supracombin" OR "thiocuran" OR "tms forte" OR "trib" OR "trigonyl" OR "trimeth/sulfa" OR "trimetoprim-sulfa" OR "trimetoprimsulfamethoxazole" OR "trimforte" OR "trimoxazole" OR "trimoxol" OR "uro ts d" OR "uroplus ds" OR "uroplus ss" OR

"pyrimidin*" OR

"trimethoprim*" OR "trimpex" OR "proloprim" OR "abaprim" OR "alprim" OR "catin" OR "delprim" OR "giprim" OR "idotrim" OR "infectotrimet" OR "methoprim" OR "monoprim" OR "monotrim" OR "motrim" OR "primosept" OR "primsol" OR "solotrim" OR "syraprim" OR "tiempe" OR "tmp-ratiopharm" OR "tobyprim" OR "trimesan" OR "trimethoprin" OR "trimetoprim" OR "trimfect" OR "trimono" OR "trimopan" OR "trinopan" OR "triprim" OR "trisul" OR "uretrim" OR "utisept" OR "welcoprim" OR "wellcoprim" OR

"Cephalosporin*" OR "cefalosporin*" OR

"Cefuroxim*" OR "Cephuroxim*" OR "Zinacef" OR "Ketocef" OR "aksef" OR "alporin" OR "altacef" OR "anaptivan" OR "aprok" OR "aprokam" OR "biocefal" OR "cefoxurime" OR "cefumax" OR "ceplus" OR "ceroxime" OR "curocef" OR "curoxim" OR "curoxima" OR "curoxime" OR "eroxmit" OR "froxal" OR "fucerox" OR "furoxime" OR "iceca" OR "intracef" OR "kefazol" OR "kefurim" OR "kefurox" OR "kesint" OR "laxinat" OR "maxil" OR "normafenac" OR "polixima" OR "prokam" OR "supacef" OR "tarsime" OR "ucefaxim" OR "ultroxim" OR "uroxime" OR "vekfazolin" OR "ximaract" OR "zinocef") OR

AUTHKEY("anti-bacterial" OR "antibacterial" OR "Bacteriocid*" OR "anti-mycobacterial" OR "antimycobacterial" OR "antibiotic*" OR

"fluoroquinolon*" OR "quinolon*" OR "chinolon*" OR "quinolin*" OR "chinolin*" OR

"cipro*" OR "ciprinol" OR "aceoto" OR "acire" OR "alcon cilox" OR "apulmiq" OR "araxacina" OR "aristin-c" OR "auripro" OR "bacquinor" OR "bactiflox" OR "baflox" OR "basemar" OR "battizer" OR "baycip" OR "bernoflox" OR "bivorilan" OR "bosix" OR "c-flox" OR "c-floxacin" OR "catex" OR "cetraflux" OR "cetraxal" OR "chinocid" OR "cidroxal" OR "cifin" OR "ciflan" OR "ciflo" OR "ciflosin" OR "ciflot" OR "ciflox" OR "cifloxin" OR "cifox" OR "cifran" OR "cilab" OR "ciloquin" OR "ciloxan" OR "ciloxin" OR "cimogal" OR "cinaflox" OR "cipad" OR "ciperus" OR "cipflox" OR "ciphin" OR "cipide" OR "cipio" OR "ciplox" OR "ciplus" OR "cipocin" OR "ciprecu" OR "ciriax" OR "cirok" OR "cirokan" OR "cirox" OR "ciroxin" OR "citopcin" OR "citrovenot" OR "cobay" OR "corsacin" OR "cosflox" OR "cuminol" OR "cuspis" OR "cycin" OR "cyfloxin" OR "cypral" OR "cyprobay" OR "cysfec" OR "doriman" OR "droll" OR "eoxin" OR "eprocin" OR "estecina" OR "felixene" OR "fimoflox" OR "flociprin" OR "flontalexin" OR "floroxin" OR "floxager" OR "floxantina" OR "floxbio" OR "fonterra" OR "generflon" OR "gerbat" OR "ginorectol" OR "giroflox" OR "gonning" OR "grifociprox" OR "h-next" OR "holdestin" OR "ibixacin" OR "inciflox" OR "infectocipro" OR "inkamil" OR "iprolan" OR "isotic" OR "jayacin" OR "k-sacin" OR "kenzoflex" OR "kinoves" OR "kinox" OR "kipocin" OR "labentrol" OR "ladinin" OR "limox" OR "linhaliq" OR "lipoquin" OR "lofucin" OR "loxan" OR "macar" OR "medociprin" OR "mitroken" OR "nafloxin" OR "neofloxin" OR "nivoflox" OR "novidat" OR "novoquin" OR "oftacilox" OR "opthaflox" OR "otanol" OR "otiprio" OR "otociprin" OR "otosec" OR "phaproxin" OR "pharcina" OR "poncoflox" OR "probiox" OR "prociflor" OR "procin" OR "proflaxin" OR "profloxin" OR "proksi 250" OR "proksi 500" OR "proquin" OR "proxacin" OR "pulmaquin" OR "qilaflox" OR "qinosyn" OR "quilox" OR "quinobiotic" OR "quinoflox" OR "quinolide" OR "quinox" OR "quintor" OR "qupron" OR "rancif" OR "ravalton" OR "revionorm" OR "rigoran" OR "rofcin" OR "roflazin" OR "rosacin eye drop" OR "samper" OR "sarf" OR "sepcen" OR "septicide" OR "septocipro" OR "sifloks" OR "siprogut" OR "siprox" OR "sophixin ofteno" OR "spitacin" OR "strox" OR "suiflox" OR "superocin" OR "syntoflox" OR "topistin" OR "truoxin" OR "ufexil" OR "ullax" OR "unex" OR "unicexal" OR "uniflox" OR "urodixin" OR "uroxin" OR "viprolox" OR "zindolin" OR "zipra" OR "zumaflox" OR

"Levofloxacin*" OR ("(S)-isomer" W/3 "Ofloxacin") OR "Quixin" OR "Levaquin" OR "aeroquin" OR "cravit" OR "elequine" OR "eyflox" OR "floxacin" OR "floxel" OR "iquix" OR "leroxacin" OR "lesacin" OR "levokacin" OR "levox" OR "levoxacin" OR "mosardal" OR "nofaxin" OR "oftaquix" OR "oxalux" OR "prixar" OR "quinsair" OR "reskuin" OR "supraflox" OR "tavanic" OR "unibiotic" OR "venaxan" OR "volequin" OR

"ofloxacin*" OR "tarivid" OR "akilen" OR "audret" OR "bactocin" OR "bioquil" OR "danoflox" OR "effexin" OR "eukinoft" OR "exocin" OR "exocine" OR "flobacin" OR "flodemex" OR "flotavid" OR "flovid" OR "floxal" OR "floxedol" OR "floxigen" OR "floxil" OR "floxin" OR "floxstat" OR "fugacin" OR "grenis-oflo" OR "gyroflox" OR "inoflox" OR "kinflocin" OR "kinoxacin" OR "liflox" OR "loxinter" OR "marfloxacin" OR "medofloxin" OR "medofloxine" OR "mergexin" OR "monoflocet" OR "monoox" OR "novecin" OR "nufafloqo" OR "o-flox" OR "obide" OR "occidal" OR "ocuflox" OR "ofcin" OR "oflin" OR "oflocee" OR "oflocet" OR "oflocin" OR "oflodal" OR "oflodex" OR "oflodinex" OR "oflodura" OR "oflogen" OR "oflohexal" OR "oflovir" OR "oflox" OR "ofloxa-vision" OR "ofloxacino" OR "ofloxamed" OR "ofloxavis" OR "ofloxin" OR "ofus" OR "onexacin" OR "operan" OR "orocin" OR "otiflox" OR "otonil" OR "ottoflox" OR "oxacid" OR "oxatrex" OR "pharflox" OR "praxin" OR "puiritol" OR

"qinolon" OR "qipro" OR "quinofree" OR "quinolon" OR "quotavil" OR "rilox" OR "romacin" OR "sinflo" OR "surnox" OR "tabrin" OR "taravid" OR "tariflox" OR "taroflox" OR "telbit" OR "trafloxal" OR "tructum" OR "urotarivid" OR "viotisone" OR "visuab" OR "zanocin" OR

"Moxifloxacin*" OR "Octegra" OR "Proflox" OR "Avelox" OR "Avalox" OR "Izilox" OR "Actira" OR "avelon" OR "bacterol" OR "floxamic" OR "floxitrat" OR "izilox" OR "kanavig" OR "lifodrox" OR "megaxin" OR "melocin" OR "moksacin" OR "monafox" OR "moxeza" OR "moxibay" OR "moxif" OR "moxivig" OR "octegra" OR "proflox" OR "tamvelier" OR "vamocin" OR "vegamox" OR "vigamox" OR "vigamoxi" OR "xiflodrop" OR "zimoxin" OR

"penicillin*" OR

"Amoxicillin*" OR "Amoxycillin*" OR "Hydroxyampicillin" OR "Actimoxi" OR "Clamoxyl" OR "Penamox" OR "Polymox" OR "Trimox" OR "Wymox" OR "Amoxil" OR "a gram" OR "abdimox" OR "acilina" OR "acimox" OR "adbiotin" OR "agerpen" OR "agram" OR "alfamox" OR "alfoxil" OR "almodan" OR "almorsan" OR "alphamox" OR "amagesen solutab" OR "ameclina" OR "amitron" OR "amo-flamisan" OR "amo-flamsian" OR "amocillin" OR "amoclen" OR "amodex" OR "amoflux" OR "amohexal" OR "amolin" OR "amonex" OR "amopen" OR "amophar ge" OR "amosine" OR "amoval" OR "amoxa" OR "amoxal" OR "amoxapen" OR "amoxaren" OR "amoxcil" OR "amoxcillin" OR "amoxcin" OR "amoxi-basan" OR "amoxicilina" OR "amoxiclin" OR "amoxicot" OR "amoxidal" OR "amoxidin" OR "amoxidrops" OR "amoxihexal" OR "amoxillin" OR "amoxina" OR "amoxipen" OR "amoxipenil" OR "amoxisol" OR "amoxivan" OR "amoxivet" OR "amoxy" OR "amoxy-diolan" OR "amoxypen" OR "ampliron" OR "apo-amoxi" OR "ardine" OR "aroxin" OR "azillin" OR "bacihexal" OR "bactamox" OR "bactox ge" OR "beamoxy" OR "betamox" OR "bimox" OR "bintamox" OR "biomox" OR "biotamoxal" OR "bioxidona" OR "bioxyllin" OR "bristamox" OR "broadmetz" OR "cabermox" OR "cilamox" OR "clamox" OR "clearamox" OR "clonamox" OR "coamoxin" OR "damoxicil" OR "dispermox" OR "doxamil" OR "draximox" OR "edamox" OR "efpinex" OR "erphamoxy" OR "eupen" OR "farconcil" OR "fisamox" OR "flemoxin" OR "flemoxine ge" OR "fluamoxina" OR "foxolin" OR "fullcilina" OR "gexcil" OR "gimalxina" OR "glamox" OR "glassatan" OR "gomcillin" OR "grinsul" OR "grunamox" OR "hamoxillin" OR "hiconcil" OR "hidramox" OR "hipen" OR "hosboral" OR "ibamox" OR "ibiamox" OR "ikamoxil" OR "imacillin" OR "imaxilin" OR "inamox" OR "infectomycin" OR "intermox" OR "isimoxin" OR "izoltil" OR "julphamox" OR "jutamox" OR "kamoxin" OR "ladoxillin" OR "lamoxy" OR "larocilin" OR "larocin" OR "larotid" OR "macromox" OR "magnimox" OR "maxamox" OR "maxcil" OR "medimox" OR "meixil" OR "metifarma" OR "mopen" OR "morgenxil" OR "moxacin" OR "moxaline" OR "moxarin" OR "moxatag" OR "moxilen" OR "moxilin" OR "moximar" OR "moxitab" OR "moxtid" OR "moxylin" OR "moxypen" OR "moxyvit" OR "neogram" OR "novabritine" OR "novamox" OR "novamoxin" OR "novenzymin" OR "novoxil" OR "nuvosyl" OR "optium" OR "oramox" OR "ospamox" OR "pamocil" OR "pamoxicillin" OR "pamoxin" OR "panvilon" OR "pasetocin" OR "penbiosyn" OR "pentyloxycillin" OR "pharmoxyl" OR "piramox" OR "pondnoxcill" OR "rancil" OR "ranmoxy" OR "ranoxil" OR "ranoxyl" OR "robamox" OR "romoxil" OR "ronemox" OR "saltermox" OR "sawacillin" OR "sawamezin" OR "servamox" OR "shamoxil" OR "sia-mox" OR "sigamopen" OR "sil-a-mox" OR "silamox" OR "simoxil" OR "sintopen" OR "solamocta" OR "solpenox" OR "sumox" OR "superpeni" OR "teramoxyl" OR "tolodina" OR "tormoxin" OR "triafamox" OR "triamoxil" OR "trifamox" OR "uro clamoxyl" OR "uroclamoxyl" OR "utimox" OR "vastamox" OR "velamox" OR "vistrep" OR "widecillin" OR "winpen" OR "xiltrop" OR "zamocillin" OR "zamox" OR "zamoxil" OR "zerrsox" OR "zimox" OR

"Co-amoxiclav" OR "Coamoxiclav" OR "Amoxi-Clavulanate" OR "Amox-clav" OR "Synulox" OR "Spektramox" OR "Augmentin" OR "Clavulin" OR "aclam" OR "aktil" OR "ambilan" OR

"amocla" OR "amoclan" OR "amoclane" OR "amoclav" OR "amoksiklav" OR "amolanic" OR "amometin" OR "amoxi plus" OR "amoxiclav" OR "amoxiclav-bid" OR "amoxiclav-teva" OR "amoxsiklav" OR "amoxxlin" OR "ancla" OR "auclatin duo dry syrup" OR "augamox" OR "augmaxcil" OR "augmentan" OR "augmentine" OR "augmex" OR "augpen" OR "augucillin duo" OR "augurcin" OR "ausclav" OR "auspilic" OR "bactiv" OR "bactoclav" OR "bioclavid" OR "cavumox" OR "ciblor" OR "clacillin duo dry syrup" OR "clamax" OR "clamentin" OR "clamobit" OR "clamonex" OR "clamovid" OR "clamoxin" OR "clamoxyl duo 400" OR "clamoxyl duoforte" OR "clarin-duo" OR "clavam" OR "clavamox" OR "clavar" OR "clavinex" OR "clavodar" OR "clavoxil" OR "clavoxilin plus" OR "clavubactin" OR "clavucid" OR "clavudale" OR "clavulox duo" OR "clavumox" OR "co amoxyclav" OR "coamoxyclav" OR "cramon duo" OR "croanan duo dry syrup" OR "curam" OR "danoclav" OR "darzitil plus" OR "duamentin" OR "duomox" OR "e-moxclav" OR "enhancin" OR "eumetinex" OR "fleming" OR "forcid" OR "forcid solutab" OR "fugentin" OR "fullicilina plus" OR "gumentin" OR "hibiotic" OR "inciclav" OR "klamonex" OR "kmoxilin" OR "lactamox" OR "lansiclav" OR "moxiclav" OR "moxicle" OR "moxyclav" OR "natravox" OR "neoduplamox" OR "noprilam" OR "nufaclav" OR "omep plus" OR "palentin" OR "quali-mentin" OR "ranclav" OR "spectramox" OR "stacillin" OR "strenzen" OR "suplentin" OR "synermox" OR "taromentin" OR "taromentin es" OR "velamox cl" OR "vestaclav" OR "viaclav" OR "vulamox" OR "xiclav" OR "zami 8503" OR

"floxacillin*" OR "Fluorochloroxacillin" OR "Flucloxacillin" OR "flopen" OR "floxapen" OR "flucil" OR "heracillin" OR "stafoxil" OR "staphylex" OR

"Tetracyclin*" OR

"Doxycyclin*" OR "Vibramycin*" OR "Atridox" OR "Doryx" OR "Hydramycin" OR "Oracea" OR "Periostat" OR "Vibra-Tabs" OR "Vibravenos" OR "adoxa" OR "amermycin" OR "apprilon" OR "atrax" OR "azudoxat" OR "bactidox" OR "banndoclin" OR "basedillin" OR "bassado" OR "biocolyn" OR "biodoxi" OR "bronmycin" OR "cloran" OR "cyclidox" OR "dentistar" OR "deoxycycline" OR "deoxymycin dispersal" OR "deoxymykoin" OR "deoxyoxytetracycline" OR "desoxy oxytetracycline" OR "desoxycycline" OR "doinmycin" OR "dosil" OR "dotur" OR "doxaciclin" OR "doxacycline" OR "doxat" OR "doxatet" OR "doxi-sergo" OR "doxibiotic" OR "doxicycline" OR "doxilin" OR "doximed" OR "doximycin" OR "doxin" OR "doxine" OR "doxirobe" OR "doxocycline" OR "doxsig" OR "doxy" OR "doxybiocin" OR "doxycen" OR "doxychel" OR "doxycin" OR "doxylag" OR "doxylin" OR "doxymycin" OR "doxypuren" OR "doxytec" OR "doxytrim" OR "dumoxin" OR "duracycline" OR "efracea" OR "esdoxin" OR "etidoxina" OR "gewacyclin" OR "ibralene" OR "idocyclin" OR "idocyklin" OR "interdoxin" OR "investin" OR "longamycin" OR "lydox" OR "magdrin" OR "medomycin" OR "mespafin" OR "mildox" OR "miraclin" OR "monodox" OR "nanodox" OR "nordox" OR "oraycea" OR "paldomycin" OR "pernox gel" OR "radox" OR "remycin" OR "respidox" OR "roximycin" OR "serodoxy" OR "servidoxine" OR "servidoxyne" OR "siadocin" OR "siclidon" OR "sigadoxin" OR "spanor" OR "supracyclin" OR "supramycina" OR "tenutan" OR "tolexine" OR "torymycin" OR "tsurupioxin" OR "unidox" OR "veemycin" OR "viadoxin" OR "vibra s" OR "vibra-s" OR "vibrabiotic" OR "vibracina" OR "vibradox" OR "vibramicina" OR "vibraveineuse" OR "vibravet" OR "viradoxyl-n" OR "wanmycin" OR "xyrosa" OR "zadorin" OR "zenavod" OR

"Minocyclin*" OR "Minox 50" OR "Aknemin" OR "Aknin-Mino" OR "Aknosan" OR "Mynocine" OR "Arestin" OR "Blemix" OR "Cyclomin" OR "Cyclops" OR "Dentomycin" OR "Dynacin" OR "Icht-Oral" OR "Klinomycin" OR "Lederderm" OR "Mestacine" OR "Minakne" OR "Mino-Wolff" OR "Minocin" OR "Minoclir" OR "Minolis" OR "Minomycin" OR "Minoplus" OR "Minotab" OR "Akamin" OR "Akne-Puren" OR "amzeeq" OR "borymycin" OR "cipancin" OR

"cyclimycin" OR "cynomycin" OR "klinotab" OR "kyno" OR "logryx" OR "menocycline" OR "micromycin" OR "minaxen" OR "mino-50" OR "minoclin" OR "minocyn" OR "minogalen" OR "minoline" OR "minolira" OR "minomax" OR "minosil" OR "minostad" OR "minotrex" OR "minoz ep" OR "mirosin" OR "parocline" OR "periofeel" OR "romin" OR "sebomir" OR "skinocyclin" OR "solodyn" OR "spicline" OR "vectran" OR "vectrin" OR "ximino" OR "zilxi" OR

"sulfanilamide*" OR "sulfonamide*" OR "sulphanilamide*" OR "sulphonamide*" OR

"Centrin" OR "Cotrimoxazole" OR "Co-Trimoxazole" OR "Eslectin" OR "Insozalin" OR "Trimezol*" OR "Centran" OR "Trimedin" OR "Septrin*" OR "Bactifor" OR "Sumetrolim" OR "Abactrim" OR "Bactrim" OR "Biseptol" OR "Biseptol480" OR "Drylin" OR "Eusaprim" OR "Kepinol" OR "Lescot" OR "Metomide" OR "Oriprim" OR "Septra" OR "Sulprim" OR "Trimosulfa" OR "abactrin" OR "alfatrim" OR "apo sulfatrim" OR "bactar" OR "bactipront" OR "bactoreduct forte" OR "bactramin" OR "bactrimel" OR "bethaprim" OR "bispetol" OR "chemotrim" OR "comox" OR "comoxol" OR "cotrim" OR "cotrimoxazol forte" OR "cotrimstada forte" OR "deprim" OR "deprim forte" OR "duobact" OR "duobiocin" OR "duobiocin forte" OR "duratrimet" OR "eltrianyl" OR "escoprim" OR "espectrin" OR "fectrim" OR "groprim" OR "helveprim" OR "imexim" OR "infectrim" OR "lagaprim" OR "lagatrim" OR "linaris" OR "microtrim" OR "neoprim" OR "nopil" OR "oecotrim" OR "omsat" OR "oribact" OR "pharmaprim" OR "potesept" OR "resprim" OR "resprin" OR "scanprin" OR "septran" OR "septrim" OR "sigaprim" OR "sinersol" OR "soltrim" OR "sulfamethoprim" OR "sulfaprim" OR "sulfatrim" OR "sulfotrim" OR "sulmeprim" OR "sumetrolin" OR "supracombin" OR "thiocuran" OR "tms forte" OR "trib" OR "trigonyl" OR "trimeth/sulfa" OR "trimetoprim-sulfa" OR "trimetoprimsulfamethoxazole" OR "trimforte" OR "trimoxazole" OR "trimoxol" OR "uro ts d" OR "uroplus ds" OR "uroplus ss" OR

"pyrimidin*" OR

"trimethoprim*" OR "trimpex" OR "proloprim" OR "abaprim" OR "alprim" OR "catin" OR "delprim" OR "giprim" OR "idotrim" OR "infectotrimet" OR "methoprim" OR "monoprim" OR "monotrim" OR "motrim" OR "primosept" OR "primsol" OR "solotrim" OR "syraprim" OR "tiempe" OR "tmp-ratiopharm" OR "tobyprim" OR "trimesan" OR "trimethoprin" OR "trimetoprim" OR "trimfect" OR "trimono" OR "trimopan" OR "trinopan" OR "triprim" OR "trisul" OR "uretrim" OR "utisept" OR "welcoprim" OR "wellcoprim" OR

"Cephalosporin*" OR "cefalosporin*" OR

"Cefuroxim*" OR "Cephuroxim*" OR "Zinacef" OR "Ketocef" OR "aksef" OR "alporin" OR "altacef" OR "anaptivan" OR "aprok" OR "aprokam" OR "biocefal" OR "cefoxurime" OR "cefumax" OR "ceplus" OR "ceroxime" OR "curocef" OR "curoxim" OR "curoxima" OR "curoxime" OR "eroxmit" OR "froxal" OR "fucerox" OR "furoxime" OR "iceca" OR "intracef" OR "kefazol" OR "kefurim" OR "kefurox" OR "kesint" OR "laxinat" OR "maxil" OR "normafenac" OR "polixima" OR "prokam" OR "supacef" OR "tarsime" OR "ucefaxim" OR "ultroxim" OR "uroxime" OR "vekfazolin" OR "ximaract" OR "zinocef")

WoS Core Collection 11122023 => 1 + 2 = 1237 results

1. Bronchiectasis

TS=("bronchiectas*"OR "bronchoectasia")

2. Long term oral antibiotic treatment (excluding long-term macrolides)

TS=("anti-bacterial" OR "antibacterial" OR "Bacteriocid*" OR "anti-mycobacterial" OR "antimycobacterial" OR "antibiotic*" OR

"fluoroquinolon*" OR "quinolon*" OR "chinolon*" OR "quinolin*" OR "chinolin*" OR

"cipro*" OR "ciprinol" OR "aceoto" OR "acire" OR "alcon cilox" OR "apulmiq" OR "araxacina" OR "aristin-c" OR "auripro" OR "bacquinor" OR "bactiflox" OR "baflox" OR "basemar" OR "battizer" OR "baycip" OR "bernoflox" OR "bivorilan" OR "bosix" OR "c-flox" OR "c-floxacin" OR "catex" OR "cetraflux" OR "cetraxal" OR "chinocid" OR "cidroxal" OR "cifin" OR "ciflan" OR "ciflo" OR "ciflosin" OR "ciflot" OR "ciflox" OR "cifloxin" OR "cifox" OR "cifran" OR "cilab" OR "ciloquin" OR "ciloxan" OR "ciloxin" OR "cimogal" OR "cinaflox" OR "cipad" OR "ciperus" OR "cipflox" OR "ciphin" OR "cipide" OR "cipio" OR "ciplox" OR "ciplus" OR "cipocin" OR "ciprecu" OR "ciriax" OR "cirok" OR "cirokan" OR "cirox" OR "ciroxin" OR "citopcin" OR "citrovenot" OR "cobay" OR "corsacin" OR "cosflox" OR "cuminol" OR "cuspis" OR "cycin" OR "cyfloxin" OR "cypral" OR "cyprobay" OR "cysfec" OR "doriman" OR "droll" OR "eoxin" OR "eprocin" OR "estecina" OR "felixene" OR "fimoflox" OR "flociprin" OR "flontalexin" OR "floroxin" OR "floxager" OR "floxantina" OR "floxbio" OR "fonterra" OR "generflon" OR "gerbat" OR "ginorectol" OR "giroflox" OR "gonning" OR "grifociprox" OR "h-next" OR "holdestin" OR "ibixacin" OR "inciflox" OR "infectocipro" OR "inkamil" OR "iprolan" OR "isotic" OR "jayacin" OR "k-sacin" OR "kenzoflex" OR "kinoves" OR "kinox" OR "kipocin" OR "labentrol" OR "ladinin" OR "limox" OR "linhaliq" OR "lipoquin" OR "lofucin" OR "loxan" OR "macar" OR "medociprin" OR "mitroken" OR "nafloxin" OR "neofloxin" OR "nivoflox" OR "novidat" OR "novoquin" OR "oftacilox" OR "opthaflox" OR "otanol" OR "otiprio" OR "otociprin" OR "otosec" OR "phaproxin" OR "pharcina" OR "poncoflox" OR "probiox" OR "prociflor" OR "procin" OR "proflaxin" OR "profloxin" OR "proksi 250" OR "proksi 500" OR "proquin" OR "proxacin" OR "pulmaquin" OR "qilaflox" OR "qinosyn" OR "quilox" OR "quinobiotic" OR "quinoflox" OR "quinolide" OR "quinox" OR "quintor" OR "qupron" OR "rancif" OR "ravalton" OR "revionorm" OR "rigoran" OR "rofcin" OR "roflazin" OR "rosacin eye drop" OR "samper" OR "sarf" OR "sepcen" OR "septicide" OR "septocipro" OR "sifloks" OR "siprogut" OR "siprox" OR "sophixin ofteno" OR "spitacin" OR "strox" OR "suiflox" OR "superocin" OR "syntoflox" OR "topistin" OR "truoxin" OR "ufexil" OR "ullax" OR "unex" OR "unicexal" OR "uniflox" OR "urodixin" OR "uroxin" OR "viprolox" OR "zindolin" OR "zipra" OR "zumaflox" OR

"Levofloxacin*" OR ("(S)-isomer" NEAR/3 "Ofloxacin") OR "Quixin" OR "Levaquin" OR "aeroquin" OR "cravit" OR "elequine" OR "eyflox" OR "floxacin" OR "floxel" OR "iquix" OR "leroxacin" OR "lesacin" OR "levokacin" OR "levox" OR "levoxacin" OR "mosardal" OR "nofaxin" OR "oftaquix" OR "oxalux" OR "prixar" OR "quinsair" OR "reskuin" OR "supraflox" OR "tavanic" OR "unibiotic" OR "venaxan" OR "volequin" OR

"ofloxacin*" OR "tarivid" OR "akilen" OR "audret" OR "bactocin" OR "bioquil" OR "danoflox" OR "effexin" OR "eukinoft" OR "exocin" OR "exocine" OR "flobacin" OR "flodemex" OR "flotavid" OR "flovid" OR "floxal" OR "floxedol" OR "floxigen" OR "floxil" OR "floxin" OR "floxstat" OR "fugacin" OR "grenis-oflo" OR "gyroflox" OR "inoflox" OR "kinflocin" OR "kinoxacin" OR "liflox" OR "loxinter" OR "marfloxacin" OR "medofloxin" OR "medofloxine" OR "mergexin" OR "monoflocet" OR "monoox" OR "novecin" OR "nufafloqo" OR "o-flox" OR "obide" OR "occidal" OR "ocuflox" OR "ofcin" OR "oflin" OR "oflocee" OR "oflocet" OR "oflocin" OR "oflodal" OR "oflodex" OR "oflodinex" OR "oflodura" OR "oflogen" OR

"oflohexal" OR "oflovir" OR "oflox" OR "ofloxa-vision" OR "ofloxacino" OR "ofloxamed" OR "ofloxavis" OR "ofloxin" OR "ofus" OR "onexacin" OR "operan" OR "orocin" OR "otiflox" OR "otonil" OR "ottoflox" OR "oxacid" OR "oxatrex" OR "pharflox" OR "praxin" OR "puiritol" OR "qinolon" OR "qipro" OR "quinofree" OR "quinolon" OR "quotavil" OR "rilox" OR "romacin" OR "sinflo" OR "surnox" OR "tabrin" OR "taravid" OR "tariflox" OR "taroflox" OR "telbit" OR "trafloxal" OR "tructum" OR "urotarivid" OR "viotisone" OR "visuab" OR "zanocin" OR

"Moxifloxacin*" OR "Octegra" OR "Proflox" OR "Avelox" OR "Avalox" OR "Izilox" OR "Actira" OR "avelon" OR "bacterol" OR "floxamic" OR "floxitrat" OR "izilox" OR "kanavig" OR "lifodrox" OR "megaxin" OR "melocin" OR "moksacin" OR "monafox" OR "moxeza" OR "moxibay" OR "moxif" OR "moxivig" OR "octegra" OR "proflox" OR "tamvelier" OR "vamocin" OR "vegamox" OR "vigamox" OR "vigamoxi" OR "xiflodrop" OR "zimoxin" OR

"penicillin*" OR

"Amoxicillin*" OR "Amoxycillin*" OR "Hydroxyampicillin" OR "Actimoxi" OR "Clamoxyl" OR "Penamox" OR "Polymox" OR "Trimox" OR "Wymox" OR "Amoxil" OR "a gram" OR "abdimox" OR "acilina" OR "acimox" OR "adbiotin" OR "agerpen" OR "agram" OR "alfamox" OR "alfoxil" OR "almodan" OR "almorsan" OR "alphamox" OR "amagesen solutab" OR "ameclina" OR "amitron" OR "amo-flamisan" OR "amo-flamsian" OR "amocillin" OR "amoclen" OR "amodex" OR "amoflux" OR "amohexal" OR "amolin" OR "amonex" OR "amopen" OR "amophar ge" OR "amosine" OR "amoval" OR "amoxa" OR "amoxal" OR "amoxapen" OR "amoxaren" OR "amoxcil" OR "amoxcillin" OR "amoxcin" OR "amoxi-basan" OR "amoxicilina" OR "amoxiclin" OR "amoxicot" OR "amoxidal" OR "amoxidin" OR "amoxidrops" OR "amoxihexal" OR "amoxillin" OR "amoxina" OR "amoxipen" OR "amoxipenil" OR "amoxisol" OR "amoxivan" OR "amoxivet" OR "amoxy" OR "amoxy-diolan" OR "amoxypen" OR "ampliron" OR "apo-amoxi" OR "ardine" OR "aroxin" OR "azillin" OR "bacihexal" OR "bactamox" OR "bactox ge" OR "beamoxy" OR "betamox" OR "bimox" OR "bintamox" OR "biomox" OR "biotamoxal" OR "bioxidona" OR "bioxyllin" OR "bristamox" OR "broadmetz" OR "cabermox" OR "cilamox" OR "clamox" OR "clearamox" OR "clonamox" OR "coamoxin" OR "damoxicil" OR "dispermox" OR "doxamil" OR "draximox" OR "edamox" OR "efpinex" OR "erphamoxy" OR "eupen" OR "farconcil" OR "fisamox" OR "flemoxin" OR "flemoxine ge" OR "fluamoxina" OR "foxolin" OR "fullcilina" OR "gexcil" OR "gimalxina" OR "glamox" OR "glassatan" OR "gomcillin" OR "grinsul" OR "grunamox" OR "hamoxillin" OR "hiconcil" OR "hidramox" OR "hipen" OR "hosboral" OR "ibamox" OR "ibiamox" OR "ikamoxil" OR "imacillin" OR "imaxilin" OR "inamox" OR "infectomycin" OR "intermox" OR "isimoxin" OR "izoltil" OR "julphamox" OR "jutamox" OR "kamoxin" OR "ladoxillin" OR "lamoxy" OR "larocilin" OR "larocin" OR "larotid" OR "macromox" OR "magnimox" OR "maxamox" OR "maxcil" OR "medimox" OR "meixil" OR "metifarma" OR "mopen" OR "morgenxil" OR "moxacin" OR "moxaline" OR "moxarin" OR "moxatag" OR "moxilen" OR "moxilin" OR "moximar" OR "moxitab" OR "moxtid" OR "moxylin" OR "moxypen" OR "moxyvit" OR "neogram" OR "novabritine" OR "novamox" OR "novamoxin" OR "novenzymin" OR "novoxil" OR "nuvosyl" OR "optium" OR "oramox" OR "ospamox" OR "pamocil" OR "pamoxicillin" OR "pamoxin" OR "panvilon" OR "pasetocin" OR "penbiosyn" OR "pentyloxycillin" OR "pharmoxyl" OR "piramox" OR "pondnoxcill" OR "rancil" OR "ranmoxy" OR "ranoxil" OR "ranoxyl" OR "robamox" OR "romoxil" OR "ronemox" OR "saltermox" OR "sawacillin" OR "sawamezin" OR "servamox" OR "shamoxil" OR "sia-mox" OR "sigamopen" OR "sil-a-mox" OR "silamox" OR "simoxil" OR "sintopen" OR "solamocta" OR "solpenox" OR "sumox" OR "superpeni" OR "teramoxyl" OR "tolodina" OR "tormoxin" OR "triafamox" OR "triamoxil" OR "trifamox" OR "uro clamoxyl" OR "uroclamoxyl" OR "utimox" OR "vastamox" OR "velamox" OR "vistrep" OR "widecillin" OR "winpen" OR "xiltrop" OR "zamocillin" OR "zamox" OR "zamoxil" OR "zerrsox" OR "zimox" OR

"Co-amoxiclav" OR "Coamoxiclav" OR "Amoxi-Clavulanate" OR "Amox-clav" OR "Synulox" OR "Spektramox" OR "Augmentin" OR "Clavulin" OR "aclam" OR "aktil" OR "ambilan" OR "amocla" OR "amoclan" OR "amoclane" OR "amoclav" OR "amoksiklav" OR "amolanic" OR "amometin" OR "amoxi plus" OR "amoxiclav" OR "amoxiclav-bid" OR "amoxiclav-teva" OR "amoxsiklav" OR "amoxxlin" OR "ancla" OR "auclatin duo dry syrup" OR "augamox" OR "augmaxcil" OR "augmentan" OR "augmentine" OR "augmex" OR "augpen" OR "augucillin duo" OR "augurcin" OR "ausclav" OR "auspilic" OR "bactiv" OR "bactoclav" OR "bioclavid" OR "cavumox" OR "ciblor" OR "clacillin duo dry syrup" OR "clamax" OR "clamentin" OR "clamobit" OR "clamonex" OR "clamovid" OR "clamoxin" OR "clamoxyl duo 400" OR "clamoxyl duoforte" OR "clarin-duo" OR "clavam" OR "clavamox" OR "clavar" OR "clavinex" OR "clavodar" OR "clavoxil" OR "clavoxilin plus" OR "clavubactin" OR "clavucid" OR "clavudale" OR "clavulox duo" OR "clavumox" OR "co amoxyclav" OR "coamoxyclav" OR "cramon duo" OR "croanan duo dry syrup" OR "curam" OR "danoclav" OR "darzitil plus" OR "duamentin" OR "duomox" OR "e-moxclav" OR "enhancin" OR "eumetinex" OR "fleming" OR "forcid" OR "forcid solutab" OR "fugentin" OR "fullicilina plus" OR "gumentin" OR "hibiotic" OR "inciclav" OR "klamonex" OR "kmoxilin" OR "lactamox" OR "lansiclav" OR "moxiclav" OR "moxicle" OR "moxyclav" OR "natravox" OR "neoduplamox" OR "noprilam" OR "nufaclav" OR "omep plus" OR "palentin" OR "quali-mentin" OR "ranclav" OR "spectramox" OR "stacillin" OR "strenzen" OR "suplentin" OR "synermox" OR "taromentin" OR "taromentin es" OR "velamox cl" OR "vestaclav" OR "viaclav" OR "vulamox" OR "xiclav" OR "zami 8503" OR

"floxacillin*" OR "Fluorochloroxacillin" OR "Flucloxacillin" OR "flopen" OR "floxapen" OR "flucil" OR "heracillin" OR "stafoxil" OR "staphylex" OR

"Tetracyclin*" OR

"Doxycyclin*" OR "Vibramycin*" OR "Atridox" OR "Doryx" OR "Hydramycin" OR "Oracea" OR "Periostat" OR "Vibra-Tabs" OR "Vibravenos" OR "adoxa" OR "amermycin" OR "apprilon" OR "atrax" OR "azudoxat" OR "bactidox" OR "banndoclin" OR "basedillin" OR "bassado" OR "biocolyn" OR "biodoxi" OR "bronmycin" OR "cloran" OR "cyclidox" OR "dentistar" OR "deoxycycline" OR "deoxymycin dispersal" OR "deoxymykoin" OR "deoxyoxytetracycline" OR "desoxy oxytetracycline" OR "desoxycycline" OR "doinmycin" OR "dosil" OR "dotur" OR "doxaciclin" OR "doxacycline" OR "doxat" OR "doxatet" OR "doxi-sergo" OR "doxibiotic" OR "doxicycline" OR "doxilin" OR "doximed" OR "doximycin" OR "doxin" OR "doxine" OR "doxirobe" OR "doxocycline" OR "doxsig" OR "doxy" OR "doxybiocin" OR "doxycen" OR "doxychel" OR "doxycin" OR "doxylag" OR "doxylin" OR "doxymycin" OR "doxypuren" OR "doxytec" OR "doxytrim" OR "dumoxin" OR "duracycline" OR "efracea" OR "esdoxin" OR "etidoxina" OR "gewacyclin" OR "ibralene" OR "idocyclin" OR "idocyklin" OR "interdoxin" OR "investin" OR "longamycin" OR "lydox" OR "magdrin" OR "medomycin" OR "mespafin" OR "mildox" OR "miraclin" OR "monodox" OR "nanodox" OR "nordox" OR "oraycea" OR "paldomycin" OR "pernox gel" OR "radox" OR "remycin" OR "respidox" OR "roximycin" OR "serodoxy" OR "servidoxine" OR "servidoxyne" OR "siadocin" OR "siclidon" OR "sigadoxin" OR "spanor" OR "supracyclin" OR "supramycina" OR "tenutan" OR "tolexine" OR "torymycin" OR "tsurupioxin" OR "unidox" OR "veemycin" OR "viadoxin" OR "vibra s" OR "vibra-s" OR "vibrabiotic" OR "vibracina" OR "vibradox" OR "vibramicina" OR "vibraveineuse" OR "vibravet" OR "viradoxyl-n" OR "wanmycin" OR "xyrosa" OR "zadorin" OR "zenavod" OR

"Minocyclin*" OR "Minox 50" OR "Aknemin" OR "Aknin-Mino" OR "Aknosan" OR "Mynocine" OR "Arestin" OR "Blemix" OR "Cyclomin" OR "Cyclops" OR "Dentomycin" OR "Dynacin" OR "Icht-Oral" OR "Klinomycin" OR "Lederderm" OR "Mestacine" OR "Minakne" OR "Mino-

Wolff" OR "Minocin" OR "Minoclir" OR "Minolis" OR "Minomycin" OR "Minoplus" OR "Minotab" OR "Akamin" OR "Akne-Puren" OR "amzeeq" OR "borymycin" OR "cipancin" OR "cyclimycin" OR "cynomycin" OR "klinotab" OR "kyno" OR "logryx" OR "menocycline" OR "micromycin" OR "minaxen" OR "mino-50" OR "minoclin" OR "minocyn" OR "minogalen" OR "minoline" OR "minolira" OR "minomax" OR "minosil" OR "minostad" OR "minotrex" OR "minoz ep" OR "mirosin" OR "parocline" OR "periofeel" OR "romin" OR "sebomir" OR "skinocyclin" OR "solodyn" OR "spicline" OR "vectran" OR "vectrin" OR "ximino" OR "zilxi" OR

"sulfanilamide*" OR "sulfonamide*" OR "sulphanilamide*" OR "sulphonamide*" OR

"Centrin" OR "Cotrimoxazole" OR "Co-Trimoxazole" OR "Eslectin" OR "Insozalin" OR "Trimezol*" OR "Centran" OR "Trimedin" OR "Septrin*" OR "Bactifor" OR "Sumetrolim" OR "Abactrim" OR "Bactrim" OR "Biseptol" OR "Biseptol480" OR "Drylin" OR "Eusaprim" OR "Kepinol" OR "Lescot" OR "Metomide" OR "Oriprim" OR "Septra" OR "Sulprim" OR "Trimosulfa" OR "abactrin" OR "alfatrim" OR "apo sulfatrim" OR "bactar" OR "bactipront" OR "bactoreduct forte" OR "bactramin" OR "bactrimel" OR "bethaprim" OR "bispetol" OR "chemotrim" OR "comox" OR "comoxol" OR "cotrim" OR "cotrimoxazol forte" OR "cotrimstada forte" OR "deprim" OR "deprim forte" OR "duobact" OR "duobiocin" OR "duobiocin forte" OR "duratrimet" OR "eltrianyl" OR "escoprim" OR "espectrin" OR "fectrim" OR "groprim" OR "helveprim" OR "imexim" OR "infectrim" OR "lagaprim" OR "lagatrim" OR "linaris" OR "microtrim" OR "neoprim" OR "nopil" OR "oecotrim" OR "omsat" OR "oribact" OR "pharmaprim" OR "potesept" OR "resprim" OR "resprin" OR "scanprin" OR "septran" OR "septrim" OR "sigaprim" OR "sinersol" OR "soltrim" OR "sulfamethoprim" OR "sulfaprim" OR "sulfatrim" OR "sulfotrim" OR "sulmeprim" OR "sumetrolin" OR "supracombin" OR "thiocuran" OR "tms forte" OR "trib" OR "trigonyl" OR "trimeth/sulfa" OR "trimetoprim-sulfa" OR "trimetoprimsulfamethoxazole" OR "trimforte" OR "trimoxazole" OR "trimoxol" OR "uro ts d" OR "uroplus ds" OR "uroplus ss" OR

"pyrimidin*" OR

"trimethoprim*" OR "trimpex" OR "proloprim" OR "abaprim" OR "alprim" OR "catin" OR "delprim" OR "giprim" OR "idotrim" OR "infectotrimet" OR "methoprim" OR "monoprim" OR "monotrim" OR "motrim" OR "primosept" OR "primsol" OR "solotrim" OR "syraprim" OR "tiempe" OR "tmp-ratiopharm" OR "tobyprim" OR "trimesan" OR "trimethoprin" OR "trimetoprim" OR "trimfect" OR "trimono" OR "trimopan" OR "trinopan" OR "triprim" OR "trisul" OR "uretrim" OR "utisept" OR "welcoprim" OR "wellcoprim" OR

"Cephalosporin*" OR "cefalosporin*" OR

"Cefuroxim*" OR "Cephuroxim*" OR "Zinacef" OR "Ketocef" OR "aksef" OR "alporin" OR "altacef" OR "anaptivan" OR "aprok" OR "aprokam" OR "biocefal" OR "cefoxurime" OR "cefumax" OR "ceplus" OR "ceroxime" OR "curocef" OR "curoxim" OR "curoxima" OR "curoxime" OR "eroxmit" OR "froxal" OR "fucerox" OR "furoxime" OR "iceca" OR "intracef" OR "kefazol" OR "kefurim" OR "kefurox" OR "kesint" OR "laxinat" OR "maxil" OR "normafenac" OR "polixima" OR "prokam" OR "supacef" OR "tarsime" OR "ucefaxim" OR "ultroxim" OR "uroxime" OR "vekfazolin" OR "ximaract" OR "zinocef")

NOT DT=("meeting abstract")

PICO 6

Pubmed (including Medline) 11122023 => 1 + 2 = 924 results

3. Bronchiectasis

"Bronchiectasis"[Mesh] OR "bronchiectas*"[tiab] OR "bronchoectasia"[tiab]

4. Eradication

Eradicat*[tiab] OR clearance[tiab] OR eliminat*[tiab]

Embase 11122023 => 1 + 2 = 1372 results

5. Bronchiectasis

'bronchiectasis'/exp OR 'bronchiectas*':ti,ab,kw OR 'bronchoectasia':ti,ab,kw

6. Eradication

'pathogen clearance'/exp OR 'eradication therapy'/exp OR Eradicat*:ti,ab,kw OR clearance:ti,ab,kw OR eliminat*:ti,ab,kw

NOT 'conference abstract'/it

Scopus 11122023 => 1 + 2 = 1243 results

1. Bronchiectasis

TITLE-ABS("bronchiectas*"OR "bronchoectasia") OR AUTHKEY("bronchiectas*"OR "bronchoectasia")

2. Eradication

TITLE-ABS(Eradicat* OR clearance OR eliminat*) OR AUTHKEY(Eradicat* OR clearance OR eliminat*)

WoS 11122023 => 1 + 2 = 837 results

1. Bronchiectasis

TS=("bronchiectas*" OR "bronchoectasia")

2. Eradication

TS=(Eradicat* OR "clearance" OR eliminat*)

NOT DT=("meeting abstract")

Narrative 1

Pubmed (including Medline) 24012024 => 2716 results

3. Bronchiectasis

"Bronchiectasis"[Mesh] OR "bronchiectas*"[tiab] OR "bronchoectasia"[tiab]

4. Etiology/Severity/comorbidity/…

"Bronchiectasis/etiology"[Mesh:NoExp] OR "Patient Acuity"[Mesh] OR "Comorbidity"[Mesh] OR "caus*"[tiab] OR "etiolog*"[tiab] OR "aetiolog*"[tiab] OR "severity"[tiab] OR "comorbid*"[tiab] OR "co-morbid*"[tiab] OR "multimorbid*"[tiab] OR multi-morbid*[tiab] OR "concurrent chronic"[tiab] OR "multipe chronic"[tiab:~0] OR "simultaneous chronic"[tiab] OR "long term condition*"[tiab] OR "longterm condition*"[tiab] OR "coexist*"[tiab] OR "co-exist*"[tiab] OR "Cumulative Illness Rating Scale"[tiab] OR "treatable trait*"[tiab]

((1) AND (2))

AND 2014/01/01:3000/12/31[crdt]

Narrative 1 (checked and approved)

PMID

11029331[uid] OR 26431397[uid] OR 27864036[uid]

Embase (Embase.com) 24012024 => 4075 results

5. Bronchiectasis

'bronchiectasis'/exp OR 'bronchiectas*':ti,ab,kw OR 'bronchoectasia':ti,ab,kw

6. Etiology/Severity/comorbidity/…

'bronchiectasis'/exp/dm_et OR 'disease severity assessment'/exp OR 'disease severity'/de OR 'comorbidity'/exp OR 'comorbidity assessment'/exp OR 'comorbidity index'/exp OR 'multiple chronic conditions'/exp OR 'etiolog*':ti,ab,kw OR 'aetiolog*':ti,ab,kw OR 'severity':ti,ab,kw OR 'comorbid*':ti,ab,kw OR 'co-morbid*':ti,ab,kw OR 'multimorbid*':ti,ab,kw OR 'multi-morbid*':ti,ab,kw OR 'concurrent chronic':ti,ab,kw OR 'multipe chronic':ti,ab,kw OR 'simultaneous chronic':ti,ab,kw OR 'long term condition*':ti,ab,kw OR 'longterm condition*':ti,ab,kw OR 'coexist*':ti,ab,kw OR 'co-exist*':ti,ab,kw OR 'Cumulative Illness Rating Scale':ti,ab,kw OR (('bronchiectas*' OR 'bronchoectasia') NEAR/9 ('caus*')):ti,ab,kw OR 'treatable trait'/exp OR 'treatable trait*':ti,ab,kw

(((1) AND (2))

NOT 'conference abstract':it)

AND [01-01-2014]/sd NOT [01-01-3001]/sd

Scopus 11122023 => 2585 results

1. Bronchiectasis

TITLE-ABS("bronchiectas*"OR "bronchoectasia") OR AUTHKEY("bronchiectas*"OR "bronchoectasia")

2. Exacerbation

TITLE-ABS("caus*" OR "etiolog*" OR "aetiolog*" OR "severity" OR "comorbid*" OR "co-morbid*" OR "multimorbid*" OR "multi-morbid*" OR "concurrent chronic" OR "multipe chronic" OR "simultaneous chronic" OR "Cumulative Illness Rating Scale" OR "long term condition*" OR "longterm condition*" OR "coexist*" OR "co-exist*" OR "treatable trait*") OR AUTHKEY("caus*" OR "etiolog*" OR "aetiolog*" OR "severity" OR "comorbid*" OR "co-morbid*" OR "multimorbid*" OR "multi-morbid*" OR "concurrent chronic" OR "multipe chronic" OR "simultaneous chronic" OR "Cumulative Illness Rating Scale" OR "long term condition*" OR "longterm condition*" OR "coexist*" OR "co-exist*" OR "treatable trait*")

((1) AND (2))

AND PUBYEAR > 2013

WoS Core Collection 24012024 => 2335 results

Science Citation Index Expanded

(SCI-EXPANDED)--1955-present

Social Sciences Citation Index

(SSCI)--1956-present

Arts & Humanities Citation Index

(AHCI)--1975-present

Conference Proceedings Citation Index – Science

(CPCI-S)--1990-present

Conference Proceedings Citation Index – Social Science & Humanities

(CPCI-SSH)--1990-present

Emerging Sources Citation Index

(ESCI)--2019-present

1. Bronchiectasis

TS=("bronchiectas*"OR "bronchoectasia")

2. Etiology/Severity/comorbidity/…

TS=("caus*" OR "etiolog*" OR "aetiolog*" OR "severity" OR "comorbid*" OR "co-morbid*" OR "multimorbid*" OR "multi-morbid*" OR "concurrent chronic" OR "multipe chronic" OR "simultaneous chronic" OR "long term condition*" OR "longterm condition*" OR "coexist*" OR "co-exist*" OR "Cumulative Illness Rating Scale" OR "treatable trait*")

(((1) AND (2))

NOT DT=("meeting abstract"))

AND LD=2014-01-01/2024-12-31

Narrative 2 and Narrative 3

Pubmed (including Medline) 24012024 => 1 + 2 + 3 = 294 results

3. Bronchiectasis

"Bronchiectasis"[Mesh] OR "bronchiectas*"[tiab] OR "bronchoectasia"[tiab]

4. Exacerbation

"Disease Progression"[Mesh:NoExp] OR "Clinical Deterioration"[Mesh] OR "progressi*"[tiab] OR "exacerbat*"[tiab] OR "deteriorat*"[tiab] OR aggravat*[tiab]

5. Guideline

"Guideline" [Publication Type] OR guideline*[tiab] OR "Guidelines as Topic"[Mesh] OR "Consensus"[Mesh] OR consensus*[tiab] OR "Consensus Development Conferences as Topic"[Mesh] OR "Consensus Development Conference" [Publication Type] OR statement*[tiab] OR "Delphi Technique"[Mesh] OR "delphi"[tiab] OR recommend*[tiab]

Narrative 3 (checked and approved)

PMID

35690367[uid] OR 34261186[uid] OR 32002044[uid] OR 28990652[uid]

Narrative 2 (checked and approved)

PMID

34112732[uid]

Embase (Embase.com) 24012024 => 1 + 2 + 3 = 605 results

6. Bronchiectasis

'bronchiectasis'/exp OR 'bronchiectas*':ti,ab,kw OR 'bronchoectasia':ti,ab,kw

7. Exacerbation

'disease exacerbation'/de OR 'deterioration'/exp OR 'progressi*':ti,ab,kw OR 'exacerbat*':ti,ab,kw OR 'deteriorat*':ti,ab,kw OR 'aggravat*':ti,ab,kw

8. Guideline

'practice guideline'/de OR guideline*:ti,ab,kw OR 'consensus'/de OR 'consensus development'/exp OR consensus*:ti,ab,kw OR statement*:ti,ab,kw OR 'Delphi study'/exp OR delphi:ti,ab,kw OR 'recommendations'/exp OR 'recommend*':ti,ab,kw

NOT 'conference abstract':it

Scopus 24012024 => 1 + 2 + 3 = 313 results

1. Bronchiectasis

TITLE-ABS("bronchiectas*"OR "bronchoectasia") OR AUTHKEY("bronchiectas*"OR "bronchoectasia")

2. Exacerbation

TITLE-ABS("progressi*" OR "exacerbat*" OR "deteriorat*" OR "aggravat*") OR AUTHKEY("progressi*" OR "exacerbat*" OR "deteriorat*" OR "aggravat*")

3. Guideline

TITLE-ABS("guideline*" OR "consensus*" OR "statement*" OR "delphi" OR "recommend*") OR AUTHKEY("guideline*" OR "consensus*" OR "statement*" OR "delphi" OR "recommend*")

WoS Core Collection 24012024 => 1 + 2 + 3 = 356 results

1. Bronchiectasis

TS=("bronchiectas*"OR "bronchoectasia")

2. Exacerbation

TS=("progressi*" OR "exacerbat*" OR "deteriorat*" OR "aggravat*")

3. Guideline

TS=("guideline*" OR "consensus*" OR "statement*" OR "delphi" OR "recommend*")

NOT DT=("meeting abstract")

Embase (Embase.com) 21022025 => ((1 AND 2 AND 3) NOT 'conference abstract':it) AND [24-12-2023]/sd NOT [21-02-2025]/sd = 92 results

1. Bronchiectasis

'bronchiectasis'/exp OR 'bronchiectas*':ti,ab,kw OR 'bronchoectasia':ti,ab,kw

2. Exacerbation

'disease exacerbation'/de OR 'deterioration'/exp OR 'progressi*':ti,ab,kw OR 'exacerbat*':ti,ab,kw OR 'deteriorat*':ti,ab,kw OR 'aggravat*':ti,ab,kw

3. Guideline

'practice guideline'/de OR guideline*:ti,ab,kw OR 'consensus'/de OR 'consensus development'/exp OR consensus*:ti,ab,kw OR statement*:ti,ab,kw OR 'Delphi study'/exp OR delphi:ti,ab,kw OR 'recommendations'/exp OR 'recommend*':ti,ab,kw

NOT 'conference abstract':it

Appendix 1- evidence summaries and evidence-to-decision frameworks for all questions

Author(s): Beatriz Herrero, James D Chalmers, Stefano Aliberti

Question: Should airway clearance techniques vs. no airway clearance be used for adult people with bronchiectasis?

Setting: Outpatients with bronchiectasis

Bibliography:

1.Munoz, G., de Gracia, J., Buxo, M., Alvarez, A., Vendrell, M.. Long-term benefits of airway clearance in bronchiectasis: a randomised placebo-controlled trial.Eur Respir J; Jan 2018.

2.Murray, M. P., Pentland, J. L., Hill, A. T.. A randomised crossover trial of chest physiotherapy in non-cystic fibrosis bronchiectasis.Eur Respir J; Nov 2009.

3.Nicolini, A., Cardini, F., Landucci, N., Lanata, S., Ferrari-Bravo, M., Barlascini, C.. Effectiveness of treatment with high-frequency chest wall oscillation in patients with bronchiectasis.BMC Pulm Med; Apr 4 2013.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Airway clearance techniques (ACTs)	Standard Care	Relative (95% CI)	Absolute (95% CI)		
Exacerbations (% participants with at least one exacerbation during follow-up)[1,2]												
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	18/39 (46.2%)	23/40 (57.5%)	**OR 0.58** (0.21 to 1.58)	**135 fewer per 1,000** (from 354 fewer to 106 more)	⨁⨁◯◯ Low[a,b]	CRITICAL
Exacerbations (exacerbation frequency)[1]												
1	randomised trials	not serious[a]	not serious	not serious	serious[c]	none	19	20	Not applicable	MD **1 lower** (2 lower to 0)	⨁⨁⨁◯ Moderate[a,b]	CRITICAL
HRQoL (LCQ, total score) after the intervention[1,2]												
2	randomised trials	serious[a]	serious[d]	not serious	serious[c]	none	39	40	Not applicable	MD **2.81 higher** (0.72 higher to 4.9 higher)	⨁◯◯◯ Very low[a,b]	CRITICAL
HRQoL (SGRQ) after the intervention[1,2]												
2	randomised trials	serious[a]	serious[d]	not serious	serious[c]	none	39	40	Not applicable	MD **12.51 lower** (22.39 lower to 2.62 lower)	⨁◯◯◯ Very low[a,b]	CRITICAL
Breathlessness (mMRC scale) after the intervention[1,3]												
2	randomised trials	serious[a]	not serious	not serious	not serious	none	19	20	Not applicable	MD **1.36 lower** (2.14 lower to 0.58 lower)	⨁⨁⨁◯ Moderate[a]	CRITICAL
Sputum quantity (mL) at the end of intervention[1,2]												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Airway clearance techniques (ACTs)	Standard Care	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	serious[a]	not serious	not serious	Serious[c]	none	39	40	Not applicable	MD **6.2 higher** (0.46 higher to 11.95 higher)	⨁⨁◯◯ Low[a]	CRITICAL
Hospitalizations												
0							No data was identified for this outcome				-	CRITICAL
Patient satisfaction and feedback												
0							No studies were identified for this outcome				-	CRITICAL

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Explanations

a. All included studies except Munoz et al are not blinded.

b. 95% confidence interval (CI) includes both potential benefit and harm

c. 95% confidence interval (CI) includes clinically relevant benefit but also includes no clinically relevant benefit

d. Inconsistent results between studies

Author(s): James D Chalmers, Beatriz Herrero, Stefano Aliberti

Question: Should Mucoactive drugs versus No mucoactive drugs be used for bronchiectasis

Setting: Outpatients with bronchiectasis

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mucoactive drugs	No mucoactive drugs	Relative (95% CI)	Absolute (95% CI)		
Exacerbations - Exacerbation frequency (mean number of exacerbations)[1,6,8]												
3	randomised trials	serious[a]	not serious	serious[b]	not serious	none	334	328	NA	MD **0.28 lower** (0.63 lower to 0.07 higher)	⨁⨁◯◯ Low[a,b]	CRITICAL
Exacerbation frequency – RR[1,4]												
2	randomised trials	not serious	not serious	not serious	serious[c]	none	NA/409	NA/401	**Rate ratio 0.99** (0.80 to 1.23)	**Not estimable**	⨁⨁⨁◯ Moderate[c]	CRITICAL
Exacerbations (% participants free of exacerbations during follow-up)[1,2,8]												
3	randomised trials	serious[a]	serious[d]	serious[b]	serious[c]	none	298/545 (54.7%)	161/420 (38.3%)	**OR 1.48** (0.88 to 2.51)	**96 more per 1,000** (from 30 fewer to 226 more)	⨁◯◯◯ Very low[a,b,c]	CRITICAL
Hospitalisations - (% participants free of hospital admission)[6]												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mucoactive drugs	No mucoactive drugs	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	serious[b]	serious[c]	none	19/20 (95.0%)	17/20 (85.0%)	**OR 3.35** (0.32 to 35.36)	**100 more per 1,000** (from 205 fewer to 145 more)	⨁⨁◯◯ Low[b,c]	CRITICAL
Time to first exacerbation hazard ratio[1]												
1	randomised trials	not serious	not serious	serious[b]	not serious	none	NA/233	NA/228	**HR 0.78** (0.63 to 0.96)	Not estimable	⨁⨁⨁◯ Moderate[b]	CRITICAL
Symptoms (Cough - VAS) - up to 3 months[3,7]												
2	randomised trials	not serious	not serious	serious[e]	not serious	none	37	37	NA	SMD **1.41 lower** (1.92 lower to 0.89 lower)	⨁⨁⨁◯ Moderate[d]	CRITICAL
HRQoL (SGRQ, total score) [1,2,7]												
3	randomised trials	not serious	not serious	serious[b]	not serious	none	481	353	NA	MD **2 lower** (3.6 lower to 0.4 lower)	⨁⨁⨁◯ Moderate[b]	CRITICAL
Adverse events related to study medication(% participants with at least one adverse event)[1,4,6,7]												
4	randomised trials	not serious	not serious	serious[b]	serious[c]	none	76/441 (17.2%)	57/446 (12.8%)	**OR 1.40** (0.96 to 2.04)	**42 more per 1,000** (from 4 fewer to 102 more)	⨁⨁◯◯ Low[b,c]	CRITICAL
HRQoL (QoL-B - Respiratory domain) - 3 months[7]												
1	randomised trials	not serious	not serious	serious[e]	serious[f]	none	22	22	NA	MD **11.42 lower** (20.38 lower to 2.46 lower)	⨁⨁◯◯ Low[d,e]	CRITICAL
24-h sputum quantity[8]												
1	randomised trials	serious[a]	not serious	not serious	not serious	none	81	80	NA	MD **11.82 lower** (19.31 lower to 4.33 lower)	⨁⨁⨁◯ Moderate[a]	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mucoactive drugs	No mucoactive drugs	Relative (95% CI)	Absolute (95% CI)		
Patients feedback / continue with treatment[6]												
1	randomised trials	not serious	not serious	serious[b]	not serious	none	23/29 (79.3%)	6/29 (20.7%)	**OR 14.69** (4.12 to 52.36)	**586 more per 1,000** (from 311 more to 725 more)	⨁⨁⨁◯ Moderate[b]	IMPORTANT
Activities of Daily Living : not reported												
0						No data reported for this outcome					-	

CI: confidence interval; **HR:** hazard ratio; **MD:** mean difference; **OR:** odds ratio; **SMD:** standardised mean difference

Explanations

a. Open label design for Qi et al

b. Control for Nicolson is isotonic saline, Control for mannitol is low dose mannitol.

c. Confidence interval includes relevant benefits and harms

d. Confidence intervals do not fully overlap demonstrating important inconsistency

e. Large amount of data from a subset which is exclusively primary ciliary dyskinesia

f. CIs include benefits without clinical significance (below with minimum clinically important difference)

Author(s): James Chalmers and Stefano Aliberti

Question: Should Inhaled antibiotics versus No inhaled antibiotics be used for Bronchiectasis

Setting: Outpatients with bronchiectasis

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Inhaled antibiotics	No inhaled antibiotics	Relative (95% CI)	Absolute (95% CI)		
Frequency of exacerbations[1,2,3,7,8,10,14,15]												
13	randomised trials	not serious	not serious	not serious	not serious	none	NA/1891	NA/1326	**Rate ratio 0.80** (0.70 to 0.92)	Not estimable	⨁⨁⨁⨁ High	CRITICAL
Number of patients with at least one exacerbation[1,2,3,4,5,7,8,9,10,12,13,14,15]												
18	randomised trials	not serious	not serious	not serious	not serious	none	830/2108 (39.4%)	667/1550 (43.0%)	**RR 0.85** (0.76 to 0.94)	**65 fewer per 1,000** (from 103 fewer to 26 fewer)	⨁⨁⨁⨁ High	CRITICAL
Frequency of severe exacerbations[3,6,7,11,12,15]												
8	randomised trials	not serious	not serious	not serious	not serious	none	NA/880	NA/628	**Rate ratio 0.57** (0.35 to 0.94)	Not estimable	⨁⨁⨁⨁ High	CRITICAL
Time to first exacerbation[1,2,3,7,8,9,10,14,15]												
14	randomised trials	not serious	not serious	not serious	not serious	none	NA/1800	NA/1319	**HR 0.81** (0.71 to 0.93)	Not estimable	⨁⨁⨁⨁ High	CRITICAL
QOL-B RSS[1,2,3,7,8,10,14]												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Inhaled antibiotics	No inhaled antibiotics	Relative (95% CI)	Absolute (95% CI)		
11	randomised trials	not serious	not serious	not serious	serious[a]	none	1399	916	NA-	MD **2.14 higher** (0.28 lower to 4.57 higher)	⨁⨁⨁◯ Moderate[a]	CRITICAL
SGRQ[1,2,4,6,9,12,15]												
8	randomised trials	not serious	not serious	not serious	serious[a]	none	1105	774	NA	MD **2.63 lower** (5.37 lower to 0.1 higher)	⨁⨁⨁◯ Moderate[a]	CRITICAL
Isolates with resistant MIC at the end of treatment[1-15]												
18	randomised trials	serious[b]	not serious	not serious	not serious	none	330/1591 (20.7%)	105/1236 (8.5%)	**RR 1.96** (1.55 to 2.48)	**82 more per 1,000** (from 47 more to 126 more)	⨁⨁⨁◯ Moderate[b]	IMPORTANT
Number of patients reporting TEAE[1,2,3,4,6,7,8,9,10,12,13,15]												
15	randomised trials	not serious	not serious	not serious	serious[a]	none	1607/2082 (77.2%)	1194/1519 (78.6%)	**OR 1.04** (0.81 to 1.35)	**7 more per 1,000** (from 38 fewer to 46 more)	⨁⨁⨁◯ Moderate[a]	CRITICAL
All cause mortality[1,2,3,5,6,8,9,10,11,12,,14,15]												
15	randomised trials	not serious	not serious	not serious	serious[c]	none	30/2007 (1.5%)	19/1513 (1.3%)	**OR 1.04** (0.57 to 1.89)	**0 fewer per 1,000** (from 5 fewer to 11 more)	⨁⨁⨁◯ Moderate[c]	CRITICAL

CI: confidence interval; **HR:** hazard ratio; **MD:** mean difference; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Confidence interval is wide and includes a possible benefit or harm

b. Selective outcome reporting: Inconsistent sampling and reporting across multiple studies. Threshold for resistance varies between organisms.

c. Small number of events and wide confidence interval, that includes large benefit or harm

Author(s): James Chalmers and Stefano Aliberti

Question: Should macrolides vs No Macrolides be used for Bronchiectasis

Setting: Outpatients with bronchiectasis

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Macrolides	No Macrolides	Relative (95% CI)	Absolute (95% CI)		
No of patients with exacerbations[1-5]												
5	randomised trials	not serious	not serious	not serious	not serious	none	92/206 (44.7%)	138/199 (69.3%)	**RR 0.64** (0.46 to 0.89)	**250 fewer per 1,000** (from 374 fewer to 76 fewer)	⊕⊕⊕⊕ High	CRITICAL
Time to first exacerbation[3,5]												
2	randomised trials	not serious	not serious	not serious	not serious	none	42/114 (36.8%)	78/110 (70.9%)	**HR 0.32** (0.21 to 0.47)	**383 fewer per 1,000** (from 481 fewer to 269 fewer)	⊕⊕⊕⊕ High	CRITICAL
Exacerbation frequency[3-6]												
4	randomised trials	not serious	not serious	not serious	not serious	none	NA/189	NA/182	**Rate ratio 0.48** (0.37 to 0.62)	**Not applicable**	⊕⊕⊕⊕ High	CRITICAL
SGRQ total score[2,3,4,5,6,7,9]												
7	randomised trials	serious[a]	not serious	not serious	not serious	none	256	252	NA	MD **7.26 lower** (10.94 lower to 3.59 lower)	⊕⊕⊕◯ Moderate[a]	CRITICAL
Antibiotic resistance organisms[3,5]												
2	randomised trials	serious[b]	not serious	not serious	serious[c]	none	NA/66	NA/67	**OR 1.08** (0.22 to 5.19)	**Not estimable**	⊕⊕◯◯ Low[b,c]	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Macrolides	No Macrolides	Relative (95% CI)	Absolute (95% CI)		
Isolation of new pathogens[3,4]												
2	randomised trials	serious[d]	not serious	not serious	serious[c]	none	19/105 (18.1%)	22/103 (21.4%)	**OR 0.82** (0.41 to 1.63)	**31 fewer per 1,000** (from 113 fewer to 93 more)	⨁⨁◯◯ Low[c,d]	IMPORTANT
Adverse events[1,3,4,5,7,9]												
6	randomised trials	not serious	not serious	not serious	serious[c]	none	98/229 (42.8%)	101/227 (44.5%)	**OR 0.86** (0.53 to 1.39)	**37 fewer per 1,000** (from 147 fewer to 82 more)	⨁⨁⨁◯ Moderate[c]	CRITICAL
Mortality[4,6,7]												
3	randomised trials	not serious	not serious	not serious	serious[e]	none	2/108 (1.9%)	0/107 (0.0%)	**OR 5.63** (0.26 to 121.88)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁⨁⨁◯ Moderate[e]	CRITICAL
Severe exacerbations[5]												
1	randomised trials	not serious	not serious	not serious	serious[e]	none	1/43 (2.3%)	2/40 (5.0%)	**OR 0.45** (0.04 to 5.19)	**27 fewer per 1,000** (from 48 fewer to 165 more)	⨁⨁⨁◯ Moderate[e]	CRITICAL

CI: confidence interval; **HR:** hazard ratio; **MD:** mean difference; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Lack of blinding (De Diego et al and Liu et al) . Incomplete accounting of patients and outcome events and selective outcome reporting (Juthong et al).

b. Incomplete outcome reporting and possible selective reporting of outcomes

c. The confidence interval include both relevant benefits and harms

d. This endpoint is highly dependent on systematic monitoring for pathogens which was not protocolised in the studies (Selective outcome reporting in risk of bias assessment)

e. Small number of events and wide confidence interval of the overall effect

Author(s): Pieter Goeminne

Question: Should Long-term non-macrolide oral antibiotics be used compared to no long term oral antibiotics for adult patients with bronchiectasis and a history of exacerbations

Setting: Outpatients

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Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Number of exacerbation[1]									
1	randomised trials	serious[a]	not serious	not serious	very serious[b,c,d]	none	- 17 patients in the amoxicillin group and 19 in the placebo group - In the intervention group exacerbations were (2 (0-7)) and in the placebo group (4 (0-9)) . - No information is provided if this is median or mean. The methodology mentions only that "The majority of the variables were not normally distributed and therefore group results are expressed as medians and non-parametric tests were used for analysis." - The study clearly states: "after adjusting for the number of exacerbations experienced in the year before the study this difference was not significant."	⨁◯◯◯ Very low[a,b,c,d]	CRITICAL
Mortality[2]									
1	randomised trials	serious[a]	not serious	serious[e]	very serious[c,d]	none	- 38 patients on penicillin, 44 patients on oxytetracyclin and 40 patients on placebo. - One patient died in each group.	⨁◯◯◯ Very low[a,c,d,e]	CRITICAL
AB resistance[1]									
1	randomised trials	serious[a]	not serious	not serious	very serious[c,d]	none	- 17 patients in the amoxicillin group and 19 in the placebo group - Five events of AB resistance were recorded in the amoxicillin group (3 H. infl. resistances and 2 Gram negative resistances) whereas 2 events were seen in the placebo group (1 H. infl resistance and 1 Gram negative resistance).	⨁◯◯◯ Very low[a,c,d]	IMPORTANT
New PPM[1]									

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
1	randomised trials	serious[a]	not serious	not serious	very serious[c,d]	none	- 17 patients in the amoxicillin group and 19 in the placebo group - 11 events of new PPM were recorded in the amoxicillin group (6 non-Pseudomonal Gram negatives, 4 Pseudomonas and 1 Moraxella) whereas 8 events of new PPM where recorded in the placebo group (3 non-Pseudomonas Gram negatives, 3 Moraxella, 1 Pseudomonas and 1 Staph aureus).	⨁◯◯◯ Very low[a,c,d]	IMPORTANT

Aes[1,2]

2	randomised trials	serious[a]	not serious	serious[e]	serious[f]	none	- Curie et al.: 17 patients in the amoxicillin group and 19 in the placebo group A total of 34 AEs in the amoxicillin group and 20 AEs in the control group. - Scadding et al.: 38 in the penicillin group; 44 in the oxytetracyclin group and 40 in the placebo group. A total of 42 AEs in the penicillin group, 49 AEs in the oxytetracyclin group and 40 in the placebo group.	⨁◯◯◯ Very low[a,e,f]	CRITICAL

Symptoms % sputum volume reduction[1,2]

2	randomised trials	serious[a,g]	not serious	serious[e]	serious[c,f]	none	- Curie et al.: 16 patients in the amoxicillin group and 19 in the placebo group - Scadding et al.: 36 in the penicillin group; 40 in the oxytetracyclin group and 36 in the placebo group. - Curie et al.: a 58% sputum volume reduction in the amoxicillin group and a 19% reduction in the placebo group at 32 weeks. - Scadding et al.: Sputum volume reduction reported at 4 timepoints between three interventions: Week 1-4: penicillin 11% reduction; oxytetracyclin 34% reduction; placebo 11% reduction Week 8-20: penicillin 26% reduction; oxytetracyclin 46% reduction; placebo 16% reduction Week 24-36: penicillin 30% reduction; oxytetracyclin 43% reduction; placebo 21% reduction Week 40-52: penicillin 26% reduction; oxytetracyclin 36% reduction; placebo 24% reduction	⨁◯◯◯ Very low[a,c,e,f,g]	CRITICAL

Symptoms % dyspnea reduction[2]

1	randomised trials	serious[g]	not serious	serious[e]	very serious[d]	none	- Scadding et al.: 36 in the penicillin group; 40 in the oxytetracyclin group and 36 in the placebo group. - Dyspnea reduction reported at 4 timepoints between three interventions:Week 1-4: penicillin 1% reduction; oxytetracyclin 5% reduction; placebo 3% reductionWeek 8-20: penicillin 15% reduction; oxytetracyclin 15% reduction; placebo 6% reduction Week 24-36: penicillin 18% reduction; oxytetracyclin 17% reduction; placebo 6% reduction Week 40-52: penicillin 11% reduction; oxytetracyclin 14% reduction; placebo 9% reduction	⨁◯◯◯ Very low[d,e,g]	CRITICAL

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
QoL - not reported									
0	-	-	-	-	-	-	No data were reported for this outcome	-	CRITICAL
Severe exacerbations - not reported									
0	-	-	-	-	-	-	No data were reported for this outcome	-	CRITICAL

CI: confidence interval

Explanations

a. There's no data on how randomization was performed.

b. Unclear reporting of the data

c. Relatively few patients and/or few events

d. One included study only but with no reported overall difference between groups

e. One patient 15 yo died of fibrocystic disease of the pancreas, suggesting cystic fibrosis as an underlying cause.

f. Pooling of data difficult or not possible, so we cannot judge the precision of the overall effect

g. No use of validated outcome measure

Author(s): James D Chalmers, Stefano Aliberti

Question:Should Eradication treatment compared to no eradication treatment be used for Bronchiectasis

Setting: patients with new or recurrent isolation of a pathogenic microorganism

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pseudomonas eradication treatment	no eradication treatment	Relative (95% CI)	Absolute (95% CI)		
Exacerbations (follow-up: mean 1 years; assessed with: Frequency of exacerbations)[2]												
1	non-randomised studies	very serious[a]	not serious	serious[b]	serious[c]		30	30	-	mean **1.84 lower** (0 to 0)	⨁◯◯◯ Very low[a,b]	CRITICAL
Severe exacerbations (follow-up: mean 1 years; assessed with: frequency)[2]												
1	non-randomised studies	very serious[a]	not serious	serious[b]	serious[c]		30	30	-	MD **0.1 lower** (0 to 0)	⨁◯◯◯ Very low[a,b]	CRITICAL
Eradication of Pseudomonas from sputum cultures (follow-up: range 6 months to 24 months; assessed with: negative cultures)[1-6]												
6	non-randomised studies	very serious[a,d]	not serious	serious[b]	not serious		119/287 (41.5%)	287/287 (100.0%)	not estimable	41.5% eradication rate over 1 year	⨁◯◯◯ Very low[a,b]	CRITICAL
Symptoms and quality of life[6]												
1	non-randomised studies	very serious[a,d]	not serious	serious[b]	serious[c]		Orriols reported improvements in the SGRQ for both the tobramycin and placebo groups from baseline above the MCID of 4 points				⨁◯◯◯ Very low[a,b]	CRITICAL
Adverse events[3,4]												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pseudomonas eradication treatment	no eradication treatment	Relative (95% CI)	Absolute (95% CI)		
2	non-randomised studies	very serious[a,d]	not serious	serious[b]	serious[c]		Vallieres et al reported respiratory symptoms associated with nebulised colistimethate sodium were infrequent as only two patients had to prematurely discontinue the inhaled treatment out of 54 patients. Blanco-Aparicio report mild adverse effects (cough and/or wheezing) were reported by five (7.5%) patients during the first month of treatment but did not result in discontinuation of therapy.				⨁◯◯◯ Very low[a,b]	CRITICAL

Antibiotic resistance[2,6]

2	non-randomised studies	very serious[a,e]	not serious	serious[b]	serious[c]		Reported in one study (White et al). In 6/11 patients, *Pseudomonas* remained fully sensitive (including to ciprofloxacin) following treatment. In four patients, new antibiotic resistance occurred: aztreonam (*n* = 1), ciprofloxacin (*n* = 1), ciprofloxacin and gentamicin (*n* = 1), amikacin and gentamicin (*n* = 1). Orriols et al reported tobramycin-resistant *P. aeruginosa* was not detected in sputum during the study. However, other opportunistic organisms were identified in sputum cultures of 2 patients in the tobramycin group and in 6 patients in the placebo group				⨁◯◯◯ Very low[a,b]	IMPORTANT

Mortality

0							No data was identified				-	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Method of data collection is unclear and it is unclear whether it is standardised between time periods.

b. this is a before and after study rather than a parallel group study

c. No measure of precision is included.

d. No standardisation of testing to ensure detection of PA in most studies.

e. high risk of reporting bias and selective reporting

Author(s): James D Chalmers and Stefano Aliberti

Question: Should long-term inhaled corticosteroids be used (compared to no long-term inhaled corticosteroids) in adults with bronchiectasis?

Setting: Outpatients with bronchiectasis

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Inhaled corticosteroids	no Inhaled corticosteroids	Relative (95% CI)	Absolute (95% CI)		
Average number of exacerbations[2,3,5]												
3	randomised trials	serious[a]	not serious	not serious	serious[b]	none	109	104	NA	MD **0.2 lower** (0.57 lower to 0.16 higher)	⨁⨁◯◯ Low[a,b]	CRITICAL
Number of patients with an exacerbation[2,4,6]												
3	randomised trials	serious[a]	not serious	not serious	serious[b]	none	23/66 (34.8%)	23/62 (37.1%)	**OR 0.89** (0.24 to 3.26)	**27 fewer per 1,000** (from 247 fewer to 287 more)	⨁⨁◯◯ Low[a,b]	CRITICAL
Mortality[2,3]												
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	0/100 (0.0%)	3/70 (4.3%)	**OR 0.14** (0.01 to 2.71)	**37 fewer per 1,000** (from 42 fewer to 65 more)	⨁⨁◯◯ Low[a,b]	IMPORTANT
24h sputum volume[1,3,4,5]												
3	randomised trials	very serious[c]	not serious	not serious	serious[b]	none	92	91	NA	MD **3.37 lower** (8.18 lower to 1.43 higher)	⨁◯◯◯ Very low[b,c]	IMPORTANT
FEV1[1-4]												
4	randomised trials	very serious[c]	not serious	not serious	serious[b]	none	98	93	NA	MD **0.03 higher** (0.19 lower to 0.12 higher)	⨁◯◯◯ Very low[b,c]	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Inhaled corticosteroids	no Inhaled corticosteroids	Relative (95% CI)	Absolute (95% CI)		
SGRQ total score[2,3]												
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	66	61	NA	MD **3.54 lower** (8 lower to 0.92 higher)	⨁⨁◯◯ Low[a,b]	CRITICAL
QOL-B score[6]												
1	randomised trials	serious[d]	not serious	not serious	serious[b]	none	11	16	NA	MD **3.7 higher** (9.59 lower to 16.99 higher)	⨁⨁◯◯ Low[b,d]	CRITICAL
Adverse events[2.3.5.6]												
4	randomised trials	not serious	not serious	not serious	serious[e]	none	24/117 (20.5%)	10/113 (8.8%)	**OR 3.19** (1.34 to 7.61)	**148 more per 1,000** (from 27 more to 336 more)	⨁⨁⨁◯ Moderate[e]	CRITICAL
Hospitalisation[2]												
1	randomised trials	serious[f]	not serious	not serious	serious[b]	none	1/37 (2.7%)	4/33 (12.1%)	**OR 0.20** (0.02 to 1.90)	**94 fewer per 1,000** (from 118 fewer to 86 more)	⨁⨁◯◯ Low[b,f]	CRITICAL
Pneumonia												
0									not estimable		-	
New NTM isolation												
0									not estimable		-	

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Explanations

a. Lack of blinding. Selective outcome reporting. Incomplete accounting for patients and outcome events.

b. Confidence intervals include relevant benefits and harms

c. Lack of blinding, use of unvalidated measurement methods, incomplete accounting for patients and outcomes and possible carry over effects in cross-over randomized trial

d. trial prematurely terminated

e. Confidence interval is wide and includes clinically relevant harm

f. Incomplete outcome reporting

Author(s): Beatriz Herrero, James D Chalmers, Stefano Aliberti

Question: Pulmonary rehabilitation (exercise training) compared to No PR (usual care) for Bronchiectasis

Setting: outpatients

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pulmonary rehabilitation (exercise training)	No PR (usual care)	Relative (95% CI)	Absolute (95% CI)		
Exercise capacity (6MWT,m) after the intervention[1,2,3]												
3	randomised trials	serious[a]	not serious	not serious	not serious	none	73	75	not applicable	MD **41.13 higher** (28.74 higher to 53.53 higher)	⨁⨁⨁◯ Moderate[a]	IMPORTANT
Exercise capacity (6MWT, m) at the end of follow-up[1]												
1	randomised trials	not serious	not serious	not serious	serious[b]	none	30	25	not applicable	MD **6.74 lower** (29.61 lower to 16.13 higher)	⨁⨁⨁◯ Moderate[b]	IMPORTANT
Exercise capacity (ISWT,m) after the intervention[1,4,5,6]												
4	randomised trials	serious[a,c]	not serious	not serious	not serious	none	86	91	not applicable	MD **72.83 higher** (51.44 higher to 94.23 higher)	⨁⨁⨁◯ Moderate[a,c]	IMPORTANT
Exercise capacity (ISWT, m) at the end of follow-up[1,5]												
2	randomised trials	serious[a]	not serious	not serious	Serious[b]	none	42	40	not applicable	MD **39.41 higher** (33.02 lower to 111.83 higher)	⨁⨁◯◯ Low[a]	IMPORTANT
Activities of daily living (steps per day) after the intervention[2,6]												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pulmonary rehabilitation (exercise training)	No PR (usual care)	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	serious[a,c]	not serious	not serious	Serious[b]	none	43	43	not applicable	MD **1443 higher** (176 higher to 2709 higher)	⨁⨁◯◯ Low[a]	CRITICAL

Activities of daily living (steps per day) at the end of follow-up[6]

1	randomised trials	serious[a,c]	not serious	not serious	Serious[b]	none	19	18	not applicable	MD **18.1 higher** (2284.05 lower to 2320.25 higher)	⨁⨁◯◯ Low[a,c]	CRITICAL

Breathlessness (mMRC scale) after the intervention[2,3]

2	randomised trials	serious[a]	not serious	not serious	Serious[b]	none	36	36	not applicable	MD **0.85 lower** (1.42 lower to 0.28 lower)	⨁⨁◯◯ Low[a,d]	CRITICAL

HRQoL (SGRQ total score) after the intervention[3,5]

2	randomised trials	serious[a]	not serious	not serious	not serious	none	32	36	not applicable	MD **9.21 lower** (13.2 lower to 5.22 lower)	⨁⨁⨁◯ Moderate[a]	CRITICAL

HRQoL (SGRQ total score) at the end of follow-up[5]

1	randomised trials	serious[a]	not serious	not serious	Serious[b]	none	12	15	not applicable	MD **8.6 lower** (14.34 lower to 2.86 lower)	⨁⨁◯◯ Low[a]	CRITICAL

HRQoL (LCQ) after the intervention - HRQoL (LCQ, total score) after the intervention[1,5]

2	randomised trials	serious[a]	not serious	not serious	serious[e]	none	49	54	not applicable	MD **1.2 higher** (0.95 lower to 3.35 higher)	⨁⨁◯◯ Low[a,e]	CRITICAL

HRQoL (LCQ) at the end of follow-up - HQoL (LCQ , total score) at the end of follow-up[1,5]

2	randomised trials	serious[a]	very serious[d]	not serious	Serious[b]	none	42	40	not applicable	MD **0.98 higher** (0.32 lower to 2.29 higher)	⨁◯◯◯ Very low[a,d,e]	CRITICAL

HRQoL (QoL-B) after the intervention - HRQoL (QoL-B ; respiratory domain) after the intervention[6]

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pulmonary rehabilitation (exercise training)	No PR (usual care)	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[a,c]	not serious	not serious	Serious[b]	none	27	28	not applicable	MD **3.6 higher** (3.18 lower to 10.38 higher)	⨁◯◯◯ Very low[a,c]	CRITICAL
Symptoms (fatigue -FSS) after the intervention[3]												
1	randomised trials	serious[a]	not serious	not serious	Serious[b]	none	20	21	not applicable	MD **1.3 lower** (1.55 lower to 1.05 lower)	⨁⨁◯◯ Low[a]	CRITICAL
Exacerbations (% participants with at least one exacerbation during follow-up)[1]												
1	randomised trials	serious[a]	not serious	not serious	Serious[b]	none	12/30 (40.0%)	18/25 (72.0%)	**OR 0.26** (0.08 to 0.81)	**319 fewer per 1,000** (from 549 fewer to 44 fewer)	⨁⨁◯◯ Low[a]	CRITICAL
Mortality (event) during the follow-up[1]												
1	randomised trials	not serious	not serious	not serious	very serious[e]	none	0/30 (0.0%)	1/25 (4.0%)	**OR 0.27** (0.01 to 6.87)	**29 fewer per 1,000** (from 40 fewer to 183 more)	⨁⨁◯◯ Low[a,e]	CRITICAL
Severe exacerbation												
0							No data identified for this outcome				-	

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Explanations

a. All of the available studies have a lack of blinding

b. The 95% confidence interval crosses the line of no clinically significant effect

c. High risk of attrition bias was detected, as one study only 37/66 participants allocated to the intervention provided 6 month data

d. The two included studies show opposite conclusions with no overlap of the CIs.

e. Downgraded twice for imprecision as based on a single event therefore no meaningful conclusions can be reached

Evidence to Decisions (EtD) framework

Narrative question: 1. How can underlying causes of bronchiectasis be identified and how can the severity, comorbidities and other treatable traits be evaluated

Domain	Judgement	Research evidence	Additional considerations
Priority **Is the Problem a priority**	○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No direct research evidence on the priority was identified but the large number of publications retrieved would indicate this area is considered important by the research community.	Causes • Identifying the cause of bronchiectasis is regarded as a priority as it can change management and identifying the cause is desirable for patients. Severity • Bronchiectasis is a heterogeneous disease with a wide spectrum of severities and therefore severity assessment and prognostication is a priority to guide management Co-morbidity • Evidence suggests co-morbidities are common and impact on mortality and quality of life making identification and treatment of co-morbidities potentially important. Treatable traits • Bronchiectasis is a heterogeneous disease and therefore identifying biomarkers or clinical factors which can guide treatment is considered important
Certainty of evidence	What is the overall certainty of the evidence of effects? ○ Very Low ○ Low ●Moderate ○ High ○ No included studies	There is a moderate degree of certainty because of the high level of consistency in the literature between studies on the frequency of underlying causes, the high level of validation of severity assessment tools and associated prognostic features and publications related to comorbidities.	Causes • The causes of bronchiectasis are well described and the number of studies is large and there is consistency between studies (with some geograophical variation. • There is uncertainty over the value of screening for certain causes in certain territories e.g ABPA screening In Southern Europe, and CF screening or PCD screening (which patients to investigate) Severity • The evidence for most prognostic markers is very strong and consistent and the severity assessment tools (particularly BSI) are well validated. Co-morbidity • The relationship between co-morbidities and poor outcomes is well established with a high quality and consistency of evidence even data are from observational studies. Treatable traits As above.
Current practice		Current practice according to the 2017 ERS guidelines as well as other guidelines is to test for underlying causes using standardized testing. This includes ABPA and immunodeficiency testing. Practice varies in terms of testing for other underlying conditions. For severity, there are no studies identified informing what is done in clinical practice but guidelines suggest to use severity tools such as the bronchiectasis severity index (mentioned by the ERS 2017 guidelines and explicitly recommended by the 2018 BTS guidelines). There is limited evidence on current practice regarding co-morbidity and treatable traits	

Values	Is there important uncertainty about or variability in how much people value the main outcomes? o Important uncertainty or variability o Possibly important uncertainty or variability XProbably no important uncertainty or variability o Not important uncertainty or variability o No known undesirable outcomes	Causes • There is debate in the medical community about the value of aetiological testing. The main question is what to test for and when • Patients value identifying the cause highly. Severity • There is no uncertainty or variability in the need to identify patients at risk of worse outcome. How best to do this and whether to use scoring or individual risk factors is debated. Co-morbidity • There is no uncertainty about the need to manage patient holistically and to treat underlying conditions. The extent to which patients should be screened as part of routine BE care may be debated. Treatable traits The utility of the treatable traits concept can be debated but the principle that patients with bronchiectasis should be treated in a personalized way is not debated.	Input from the patient members of the guideline panel indicates - They consider identifying the cause of bronchiectasis as a highly important part of management - Identifying patients at risk of future poor outcomes is considered highly important by patients - Holistic management taking into account health issues not related directly to bronchiectasis is considered highly important.
Summary of evidence/ Benefits and harms	How substantial are the benefits of the intervention compared to harms? o Trivial o Small o Moderate X Large o Varies o Don't know	Desirable (large) Causes • Several causes are potentially treatable where this would result in desirable effects : Immunodeficiency, NTM, ABPA, cystic fibrosis. • Some causes alter management in terms of prognosis and follow-up eg COPD, PCD, RA • Patients want to know what caused their bronchiectasis Severity • Better targeting of treatment towards patients at higher risk of complications should result in better cost-effectiveness of treatment Co-morbidity • Several co-morbidities are increased in people with bronchiectasis and are associated with mortality or quality of life. Examples include cardiovascular disease, osteoporosis, depression, anxiety and rhinosinusitis. These have treatments or preventative measures available the use of which may bring desirable benefits Treatable traits • Literature search identifies a number of aetiologies and co-morbidities as treatable traits and also identifies symptoms,	Causes - The fact that investigation of underlying causes can lead to highly effective treatments strongly favours underlying cause testing in a standardized way. Exactly how to do this and which tests to recommend can be debated but the basic principle is strongly favoured by the evidence. Severity - Evidence strongly favours classifying patients by their risk of poor outcome. Again, the best method to do this can be debated but the principle is not debated. Co-morbidity - Evidence strongly favours the need to identify and treat co-morbid conditions. Treatable traits As above, the evidence strongly favours identifying and treating appropriate traits.

	How substantial are the harms of the intervention compared to benefits? ○ Trivial ○ Small X Moderate ○Large ○ Varies ○ Don't know	exacerbations, pseudomonas and a number of other traits which are treatable and modifiable in disease Undesirable (moderate) Causes • Standardised testing for underlying causes carries an associated cost and burden for patients. Immunoglobulins and ABPA testing are relatively inexpensive, NTM testing is more expensive and involved, and testing for rarer causes like CF/PCD have significant resource implications which need to be considered. Severity • Severity assessment tools are not perfect and so potential undesirable effects of these tools include misclassifying patients resulting in under/over treatment. Co-morbidity • There are few if any undesirable effects to investigating co-morbidities. • Treatable traits Currently most treatable traits are not supported by prospective clinical trial evidence and so when specific traits are used to guide treatment they may lead to inappropriate treatment or an increased use of medication in some circumstances	
Equity	What would be the impact on health equity? ○ Reduced ○ Probably reduced ○ Probably no impact ●Probably increased ○ Increased ○ Varies ○ Don't know	Evidence suggests that testing for underlying causes, severity and co-morbidity are rarely performed and more likely to be performed in specialist centres. Testing is less common in LMICs	. Standardised testing is likely to increased health equity
Acceptability	Is the intervention acceptable to key stakeholders? ○ No ○ Probably no ○ Probably yes	We did not specifically look for studies on acceptability but patient and healthcare provider feedback as well as the adoption into other guidelines suggests it is acceptable.	Causes - Testing is current guideline practice and is accepted (wanted) by patients Severity - Unclear whether standard use of a severity assessment tool is acceptable to clinicians but prognostication in general is well estalbihsed as a core part of chronic disease management. Co-morbidity - Accepted (it is probably negligent not to consider diseases other than bronchiectasis)

	XYes o Varies o Don't know		Treatable traits Precision medicine is generally popular/accepted by patients and clinicians
Feasibility	Is the intervention Feasible to implement ? o No o Probably no o Probably yes oYes **X** Varies o Don't know	We did not specifically look for studies on feasibility but these proposed interventions are considered standard of care in many centres and are therefore considered feasible.	The answer to this question varies depending on the intervention recommended Causes - Routine testing for ABPA, immunoglobulins, NTM= highly feasible - Routine testing for CF/PCD- not feasible - Targeted testing for CF/PCD= feasible with some caveats Severity - Severity assessment is feasible to widely implement Co-morbidity - Feasible Treatable traits - Highly dependent on the algorithm used and biomarkers required
Resources required	How large are the resource requirements (costs)? o Large costs X Moderate costs o Negligible costs and savings o Moderate savings o Large savings oVaries o Don't know	We did not specifically collect data on costs but can infer probable costs based on clinical knowledge and experience.	Causes - There is a cost implication to standardized testing and particularly to testing for specific underlying causes (e.g PCD). Exact resource implications are not reported in any papers identified by the literature search. Severity - There are essential zero or minimal costs to severity assessment but more frequent follow-up for patients at higher risk may have resource implications. Co-morbidity - Investigation and treatment of potential morbidities (e.g Dexa for osteoporosis or echo of LVF would have resource implications) Treatable traits As abov Cost-effectiveness: Causes - Screening for underlying causes if probably cost effective - Immunodeficiency and ABPA are common and likely testing is costeffective - NTM testing may be cost effective - Alpha-1 antitrypsin deficiency testing is probably not cost effective - CF and PCD testing are likely only cost effective in highly enriched populations

			Severity - Likely to be high cost effective Co-morbidity - Likely to be highly cost effective Treatable traits
Certainty of the evidence of required resources	X Very low o Low o Moderate o High o No included studies	We did not specifically look for studies on required resources. The included studies in our review did not have any data for any of the aspects of this question that directly addressed the costs or cost-effectiveness of different screening pathways. We base our assessment on clinical experience.	

Narrative question:

TYPE OF RECOMMENDATION	Strong recommendation against the intervention o	Conditional recommendation against the intervention o	Conditional recommendation for either the intervention or the alternative o	Conditional recommendation for the intervention o	Strong recommendation for the intervention XXX

Recommendation	**Recommendations**
	Management of patients with bronchiectasis should include standardized testing to identify the underlying cause of bronchiectasis, to evaluate disease severity and activity as well as risk of poor outcome, and to identify co-morbidities and associated treatable traits (Strong recommendation for the intervention, moderate certainty of evidence stemming from narrative review of the evidence)
	
	Investigation and management considerations (the following is based on the evidence from systematic searches, panel discussions, the clinical experience and current practice of the panel and recommendations in other guidelines)
	• All patients newly diagnosed with bronchiectasis should be screened for immunodeficiency by measurement of serum immunoglobulins (IgG, IgM, IgA), ABPA by measurement of total IgE, Aspergillus specific IgG and IgE, as well as blood eosinophils, and NTM by mycobacterial microscopy and culture.
	• In patients at high risk of NTM infection based on clinical and radiological features a minimum of three sputum samples or a bronchoalveolar lavage should be obtained.
	• Alpha-1 antitrypsin testing should not be performed routinely but should be considered in patients with suggestive clinical and radiological features such as basal emphysema or severe airflow obstruction.
	• Patients with symptoms onset during childhood or with specific clinical or radiological features (independent of age of onset) should be screened for CF and PCD.
	• Newly diagnosed patients with bronchiectasis should have a bronchiectasis severity index calculated to assess the risk of future complications (table
	• Patients at higher risk of future complications should be identified. Such patients should be considered for more frequent follow-up and a lower threshold for treatment. High-risk groups include:
	  • Patients with COPD, PCD, or rheumatoid arthritis (RA)-associated bronchiectasis
	  • Patients with *Pseudomonas aeruginosa* or other enteric Gram-negative infections
	  • Patients with 2 or more exacerbations per year or 1 severe exacerbation (defined as requiring hospitalization or intravenous antibiotics) in the previous year
	  • Patients with severe symptoms including high volumes of daily sputum production and sputum purulence
	  • Patients with NTM infection
	  • Patients with ABPA
	• Assessment of co-morbid illnesses should be part of the evaluation of all patients with bronchiectasis:
	  • Patients at risk should be investigated for associated cardiovascular disease
	  • Patients at risk should be investigated for associated osteoporosis
	  • Patients should be screened for symptoms of anxiety and depression and appropriate management initiated
	  • Rhinosinusitis and gastroesophageal reflux disease (GRD) are common co-morbidities of bronchiectasis that should be identified and managed appropriately.
	• Treatable trait burden and the impact on associated conditions should be considered as part of treatment decisions when managing bronchiectasis

	• The assessments described here including considering the underlying cause, co-morbidities, disease activity and treatable traits, should be considered at all patient visits and not just at diagnosis.
Justification	The recommendation to test for underlying causes in bronchiectasis is justified by the potential benefits of identifying treatable conditions that can improve patient outcomes. Despite potential increases in healthcare costs and complexity, the prioritisation of diagnosing treatable underlying causes outweighs these concerns. The recommendation to limit testing for A1ATD, CF and PCD to patients with suggestive clinical features emphasises a targeted diagnostic approach that balances the need for comprehensive evaluation with the risk of excessive testing burden. Assessing disease severity is essential to ensure a standardised evaluation of bronchiectasis, facilitating appropriate management strategies. Additionally, recognising and treating comorbidities aligns with a holistic approach to patient care, ultimately improving clinical outcomes. The concept of treatable traits emphasizes the importance of a personalized approach to the treatment of bronchiectasis. Therapies targeting the underlying cause, associated co-morbidities, and key disease features (infection, impaired mucociliary clearance, inflammation etc) are dependent on a comprehensive assessment of the patient to identify treatable traits.
Subgroup considerations	Age : Co-morbidities increase with age, while CF and PCD are less likely as aetiology as patients get older therefore testing approaches will change with age Sex : largely unaffected Region : Some aetiologies are more common in specific regions. ABPA is believed to vary geographically (although no data were identified to support this). CF is more common in white European patients. PCD is more common in some populations, particular where there is consanguinity. Testing facilities and capabilities vary by region. Microbiology varies by region
Implementation consideration	Implementation of testing for underlying causes in bronchiectasis requires a structured approach to address several challenges, including regional disparities in diagnostic capabilities, variability in disease aetiology, and the absence of standardized follow-up and management protocols. Testing for certain underlying causes (particularly PCD) is difficult to implement in many regions due to limited access to specialized diagnostic facilities. The evidence for the treatment of certain treatable traits (e.g cardiovascular disease secondary prevention) is strong whereas in other cases it is not. It is important to note that the screening approaches described here are first line investigations and in patients with a strong clinical suspicion further testing may be appropriate. An example of this is immunodeficiency. Low immunoglobulins/functional antibodies may detect a large number of immunodeficiencies but patients should be referred to an immunologist if they have features that suggest immunodeficiency even if immunoglobulins are normal.
Monitoring and evaluation	The process of aetiological testing is typically undertaken at diagnosis. It is important to emphasise this is an ongoing process – if patients clinical features change such that they suggest a new diagnosis then testing should be reviewed. Furthermore patients who have been previously classified as having one aetiology (particularly idiopathic/postinfective) who have never had testing should still undergo aetiological evaluation if it has never been performed. Although formalized severity assessment is recommended at diagnosis it should be noted that this is an ongoing process and an assessment of future risk should be a key part of every review in a patient with bronchiectasis.
Research priorities	A large scale study performing genetic testing for PCD and cystic fibrosis is required to determine the true prevalence of these conditions in adult bronchiectasis and to develop optimal screening strategies Studies utilizing comprehensive aetiological testing approaches in different regions/countries are required to determine if the recommended screening strategy outlined here is appropriate globally

PICO QUESTION 1

Should airway clearance techniques be used (compared to no airway clearance techniques) in adults with bronchiectasis?	
POPULATION:	Adults with bronchiectasis
INTERVENTION:	Airway clearance techniques
COMPARISON:	No airway clearance techniques
MAIN OUTCOMES:	Exacerbations (critical) Quality of Life (critical) Symptoms measured using symptom questionnaires or other validated methods (critical) Hospitalisations (critical) Activities of daily living (critical) Patient satisfaction/ feedback (critical) Sputum quantity (critical) Breathlessness (critical)
SETTING:	**OUTPATIENTS**
PERSPECTIVE:	**CLINICAL RECOMMENDATIONS FOR INDIVIDUAL PATIENTS**
BACKGROUND:	Airway clearance is considered the standard of care for bronchiectasis in many regions.
CONFLICT OF INTERESTS:	None reported

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	The efficacy of airway clearance techniques has been identified as important for patients and for clinicians	A number of studies have investigated different airway clearance techniques and there is high variability in their selection and accessibility across Europe and worldwide in practice

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Trivial o Small X Moderate o Large	There is a clinically significant improvement in the SGRQ and LCQ scores as well as mMRC dyspnoea score indicating improved quality of life, symptoms and performance status in people receiving airway clearance techniques. Effects on exacerbations are less clear.	Most studies are short term, although one longer term study over 1 year shows improved

o Varies o Don't know		quality of life and reduced exacerbations.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large o Moderate o Small o Trivial o Varies X Don't know	There were no studies identified that examined undesirable effects, adverse effects or patient burden related to this intervention.	The major undesirable effect reported by patients is the burden of treatment. Some techniques e.g postural techniques may exacerbate conditions like gastroesophageal reflux.

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
X Very low o Low o Moderate o High o No included studies	Based on GRADE assessment the certainty of evidence is very low. This takes into account that outcomes have a high degree of imprecision and other reasons for downgrading.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or variability o Possibly important uncertainty or variability o Probably no important uncertainty or variability X No important uncertainty or variability	We did not specifically look for studies addressing patient values	Patients and the panel consistently rated the main outcomes (exacerbations, quality of life and symptoms) as critical. There was more uncertainty around the importance of sputum volume and dyspnea in the absence of other outcomes

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison o Probably favors the intervention X Favors the intervention o Varies o Don't know	The potential benefit associated with treatment in terms of quality of life and symptoms combined with the fact that this intervention has no known adverse effects favours the intervention	Patient members of the panel consider that the beneficial effects outweigh the treatment burden considerations.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings oVaries X Don't know	We did not look for studies that examined the resources required.	It is known that the intervention requires physiotherapist availability and resource. Resources will vary depending on whether manual techniques or devices are used

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High X No included studies	There were no included studies	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies X No included studies	We did not look for studies that examined the cost effectiveness of the intervention	no additional considerations

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact X Probably increased ○ Increased ○ Varies ○ Don't know	We did not look for studies assessing health equity	Airway clearance is performed by the patient themselves and is a low cost intervention if performed by the patient without equipment. Nevertheless a trained healthcare professional is usually required to teach the patient. Therefore it may be assumed that widespread use of airway clearance would promote health equity.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes X Yes ○ Varies ○ Don't know	The studies identified show a high uptake and persistence with airway clearance suggesting it is acceptable	Patient members of the panel indicate that airway clearance is acceptable and that the comparator may not be acceptable.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes X Yes ○ Varies ○ Don't know	No feasibility issues were identified	Airway clearance is widely used and is feasible to implement in real life practice.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	X

CONCLUSIONS

Recommendation

Recommendation

We recommend that patients with bronchiectasis should be taught airway clearance techniques (strong recommendation for the intervention, very low certainty of evidence)

Remarks

- Airway clearance techniques (ACTs) are best taught by a respiratory physiotherapy with appropriate experience.
- There is no evidence that one technique is superior to another and, therefore, treatment should be personalized.
- Airway clearance devices may be used to support manual ACTs.
- Previous ERS guidelines limited ACTs to patients with chronic productive cough. The current recommendation acknowledges that some patients with a dry cough, particularly those with mucus plugging on chest CT, may benefit from ACTs. Instruction in ACTs may also assist patients during periods of increased symptoms, such as exacerbations.

Justification

ACTs are associated with improved quality of life and symptoms, and may reduce exacerbations. Airway clearance is a key component of daily bronchiectasis management. Despite the low certainty of evidence, the panel issued a strong recommendation based on the following: i) ACTs are self-administered, low-cost, and accessible; ii) Patients widely recognise their benefits; iii) The recommendation was strongly supported by patient representatives. Although adverse effects and harms were not systematically reported or collected, ACTs are widely believed to be safe and low risk of adverse events. These factors outweigh the limitations of the evidence base and highlight a need for broader implementation. Airway clearance is underutilized in clinical practice, and this recommendation should encourage increased uptake among healthcare professionals and policy.

Subgroup considerations

There is no evidence of subgroup effects in the data identified. The studies to date include a wide spectrum of bronchiectasis patients suggesting broad efficacy

Implementation considerations

Airway clearance techniques require appropriate training and personalization of the techniques. Not all patients will have access to a specialist respiratory physiotherapist. No studies were identified on optimal delivery of the intervention.

Monitoring and evaluation

Patients who have received training in airway clearance techniques may require additional review to ensure the techniques are still performed correctly, are suitable to patient needs and/or to modify techniques if the disease changes.

Research priorities

Large randomized controlled trials of airway clearance techniques in bronchiectasis would be desirable, but present complex challenges due to airway clearance being standard of care. Key research priorities in this area include

- What the impact of airway clearance techniques on exacerbations over the long term (e.g 12 months or greater)
- What is the optimal method of delivery of airway clearance technique training

- Are virtual methods such as online training or video/remote training effective for delivery of airway clearance techniques
- What is the added benefit of airway clearance devices?
- Is exercise as effective as airway clearance techniques in improving respiratory symptoms and should patients performing regular exercise also use airway clearance techniques regularly?[58]
- What is the effectiveness and optimal application of ACTs during acute exacerbations, and how should these techniques be adapted based on exacerbation severity and individual patient characteristics?

PICO QUESTION 2

Should mucoactive drugs be used (compared with no mucoactive drugs) in adults with bronchiectasis?	
POPULATION:	Adults with bronchiectasis
INTERVENTION:	Mucoactive drugs
COMPARISON:	No mucoactive drugs
MAIN OUTCOMES:	Exacerbations (critical) Quality of Life (critical) Symptoms measured using symptom questionnaires or other validated methods (important) Adverse events (critical) Severe exacerbations/ Hospitalisations (critical) Activities of daily living (critical) Patient satisfaction/ feedback (important) Sputum volume (important)
SETTING:	**OUTPATIENTS**
PERSPECTIVE:	**CLINICAL RECOMMENDATIONS FOR INDIVIDUAL PATIENTS**
BACKGROUND:	Inhaled mucoactive treatments (e.g hypertonic saline) and oral mucoactive treatments (N-acetylcysteine and Carbocisteine) are used to manage symptoms in European practice.
CONFLICT OF INTERESTS:	None reported

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	Respiratory symptoms (such as cough and sputum production) are the most common in patients with bronchiectasis and impair quality of life and social interactions and are therefore of high importance	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Trivial o Small X Moderate o Large o Varies o Don't know	The pooled data shows statistically significant improvements in quality of life and symptoms which are clinically meaningful. However, the evidence regarding exacerbations shows variability across studies	Exacerbation data for two studies was not reported in a format which could be pooled.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large o Moderate X Small o Trivial o Varies o Don't know	There is evidence of adverse effects. There is an important trend to an increase in AEs overall, and the trial of DNAse shows worse exacerbation rate (incorporating non protocol defined events) and worse FEV1 at the end of treatment	Some trials exclude patients who have bronchospasm to the drug after a first test dose and so these data are not reflected in the reported AEs but would be important for application of these treatments in practice.

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
X Very low o Low o Moderate o High o No included studies	From GRADE assessment, , the certainty of evidence is very low.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or variability o Possibly important uncertainty or variability o Probably no important uncertainty or variability X No important uncertainty or variability	We did not specifically look for studies assessing patient values	Patients and clinicians in the TF fully agreed that exacerbations, quality of life and symptoms are key outcomes

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison X Probably favors the intervention o Favors the intervention o Varies o Don't know	There is clear evidence of benefit but there are also important safety signals. The balance would suggest a beneficial effect driven by trials of hypertonic saline, mannitol and N-acetylcysteine. DNAse showed no evidence of effectiveness and potential harm.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings oVaries X Don't know	We did not look for studies on resources required	It is known that nebulized mucoactive treatments require not only the drug but also provision of nebulizer devices.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High X No included studies	We did not look for studies on resources required	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison o Probably favors the intervention o Favors the intervention o Varies X No included studies	We did not look for studies studies examining cost effectiveness	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased o Varies X Don't know	We did not look for studies on health equity	We are not aware of any impact on health equity. The included studies did not assess this

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	Although we did not look for studies on acceptability, the uptake of the intervention suggests it is acceptable.	Registry data suggests mucoactive drugs are widely used. Patient members of the panel commented that mucoactive drugs are acceptable, with a preference for a lower treatment burden (e.g oral rather than inhaled where possible)

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no	We did not search for studies assessing feasibility	Oral mucoactive drugs may be easier to introduce than

○ Probably yes X Yes ○ Varies ○ Don't know		nebulized drugs due to the need to provide nebulizer devices and test doses.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION- MUCOACTIVE DRUGS

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	X	○

TYPE OF RECOMMENDATION- RECOMBINANT DNASE

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	X	○	○	○

CONCLUSIONS

Recommendation

Recommendation

We suggest to offer mucoactive treatments to patients with bronchiectasis where airway clearance has failed to control symptoms (conditional recommendation for the intervention, very low certainty of evidence)

We suggest not to offer recombinant DNAse to patients with bronchiectasis (conditional recommendation against the intervention, very low certainty of evidence)

Remarks

- The choice of mucoactive treatment should be guided by patient's co-morbidities and concerns around treatment burden and tolerability.
- Mucoactive treatments are best delivered as part of a comprehensive airway clearance regimen, which includes personalized airway clearance instruction with or without devices, and regular physical exercise.

Justification

Mucus in bronchiectasis is typically hyperconcentrated and viscous, impairing mucociliary clearance. Mucus plugging, a common radiological feature, is associated with exacerbation risk and disease severity. Oral mucoactive agents, such as carbocisteine or N-acetylcysteine, reduce mucus viscosity though evidence is limited. Nebulized hypertonic saline and inhaled mannitol hydrate mucus and stimulate cough to facilitate clearance. Mucoactive treatments may improve symptom burden and quality of life when used in addition to airway clearance and exercise. Despite limited evidence our recommendation prioritises improvements in quality of life and symptoms, and is supported by the lack of significantly increased adverse events. One study assessing inhaled mannitol suggests greater benefit in patients with more severe symptoms. Highly symptomatic patients with poor quality of life could therefore be considered for mucoactive treatment. Inhaled mucoactive treatments may cause wheezing or bronchospasm. The use of pre-treatment bronchodilators can mitigate this risk. Notably, recombinant human DNase was ineffective and reduced FEV_1 in a previous trial. Therefore, its use is not recommended. A conditional recommendation against recombinant DNAse was made due to a lack of evidence of benefit and possible harms. These data come from a single trial which had important limitations including a lack of standardized CT scanning at baseline and moderate sample size. This justifies a conditional, rather than strong recommendation against.

Subgroup considerations

DNAse as above

One study looking at inhaled mannitol showed that patients with worse baseline symptoms had a greater benefit from mucoactive drugs, therefore patients with poor quality of life and high symptoms should be considered for these treatments.

Implementation considerations

A test dose to identify bronchospasm was used in many studies. Patients starting mannitol or hypertonic saline should be considered for a test dose to look for bronchospasm. Pre-treatment with inhaled bronchodilators helps to prevent bronchospasm.

Monitoring and evaluation

Mucoactive treatments are given primarily to improve symptoms and quality of life. If no symptomatic improvement is evident after a reasonable trial mucoactive drugs e.g 3 months, then they should be discontinued.

Research priorities

Large randomized controlled trials utilizing precision medicine approaches, which tailor mucoactive treatments towards individual patients with high symptom burden and/or particular sputum characteristics (i.e abnormal mucins, mucus properties or DNA content), are needed as moderately sized trials show inconsistent results. Recombinant human DNase proved ineffective in a trial published in 1998. However, given the strong link between neutrophil extracellular traps and poor disease outcomes, and increasing recognition of bronchiectasis endotypes, further research is warranted in order to clarify whether specific subgroups of adults with bronchiectasis may benefit from recombinant human DNase.

PICO QUESTION 3

Should long term inhaled antibiotics be used (compared with no long term inhaled antibiotics) in adults with bronchiectasis?

POPULATION:	Adults with bronchiectasis
INTERVENTION:	Long term inhaled antibiotics
COMPARISON:	No Long term inhaled antibiotics
MAIN OUTCOMES:	Exacerbations (critical) Severe exacerbations (critical) Quality of life (critical) Adverse events (critical) New isolation of pathogens (critical) Mortality (critical) Antibiotic resistance (important)
SETTING:	**OUTPATIENT**
PERSPECTIVE:	**CLINICAL RECOMMENDATIONS FOR INDIVIDUAL PATIENTS**
BACKGROUND:	Inhaled antibiotics are used to prevent exacerbations in patients with chronic airway infection, predominantly *P. aeruginosa*
CONFLICT OF INTERESTS:	10 panel members declared relevant COIs and did not vote on this question.

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes X Yes ○ Varies ○ Don't know	Inhaled antibiotics are widely used, and reducing exacerbations is a major clinical priority for people with bronchiectasis.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small X Moderate ○ Large ○ Varies ○ Don't know	Clinically relevant reductions in exacerbations have been reported and demonstrated in our meta-analysis. All of the exacerbation endpoints are consistent with benefit. There is no consistent improvement in symptoms demonstrated. The benefit on exacerbations is primarily derived from studies of patients infected with *Pseudomonas aeruginosa*. Notably the PROMIS, ORBIT, IBEST and so single centre studies enrolled exclusively *P. aeruginosa* positive patients. Some benefit was demonstrated in the RESPIRE trials, but not in the AIR-BX studies. These latter two programmes included patients with *P. aeruginosa* and patients without *P. aeruginosa*.	The effect on severe exacerbations is larger than for moderate exacerbations. Severe exacerbations are clinically relevant.

Undesirable Effects

How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large ○ Moderate X Small ○ Trivial ○ Varies ○ Don't know	There is no significant increase in the risk of overall adverse events between the groups and no difference in the risk of all cause mortality. The 95% CI includes an upper limit of 46 more adverse events per 1000 patients treated. The data therefore suggests a profile very similar to placebo. There is a significant increase in resistance with inhaled antibiotics.	Some studies report an increase in adverse effects including bronchospasm, particularly in studies of aminoglycosides.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low X Moderate ○ High ○ No included studies	Based on GRADE assessment.	The majority of evidence comes from studies of patients infected with *P. aeruginosa* and so the certainty of evidence is lower in patients without *P. aeruginosa* infection.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability X No important uncertainty or variability	We did not search for studies assessing patient values	All outcomes were rated as critical or important with consistent rating among the clinical and patient reviewers for the majority of clinically relevant outcomes with the exception of resistance. There is no agreement within the community about the clinical relevance and interpretation of antibiotic resistance and so this was rated important by some members of the panel and not important by others.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison o Probably favors the intervention X Favors the intervention o Varies o Don't know	There is a clear clinically relevant reduction in the risk of exacerbations in people receiving long term inhaled antibiotics. This is especially the case for severe exacerbations which are clinically important. The balance of risk and benefits is favourable. There is no significant increase in the risk of adverse events. The majority of evidence comes from studies of patients with *P. aeruginosa* infection and a history of frequent exacerbations.	As there are several potentially effective treatments the position of inhaled antibiotics relative to other treatments in view of the treatment burden must be considered.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings oVaries X Don't know	We did not search for studies assessing resources	Inhaled antibiotics are not inexpensive and require services to deliver as well as nebulizer devices. Therefore there are resource implications for their use and administration. Sometimes caregivers need to be involved in preparing medication or administering which is not the case for oral medications in many cases. Challenge testing is performed in many countries/healthcare settings which requires organizational resources. Compared to other medications used for bronchiectasis the cost difference is substantial.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Very low o Low o Moderate o High X No included studies	There are no formal assessments of the costs involved	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison X Probably favors the intervention o Favors the intervention o Varies X No included studies	We did not search for cost-effectiveness stuides	The cost effectiveness likely depends on the patient population in which they are used. The large reduction in severe exacerbations means large cost savings may be possible if used in patients at high risk of severe exacerbations

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased o Varies X Don't know	We did not look for evidence with regard to health equity.	Inhaled antibiotics are not available in all countries and nebulizer device access also varies. Therefore access to these medications may be limited to high income countries or countries with health systems where the treatments are reimbursed Registry data shows use of inhaled antibiotics are currently limited to specific countries and particularly high income countries.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes o Yes o Varies X Don't know	We did not look for studies on acceptability.	Inhaled antibiotics are used by approx. 7% of patients with bronchiectasis in Europe according to the EMBARC registry. Adherence data suggests that many patients do not continue to use inhaled antibiotics (approx. 50% in some studies). Drop out rates in randomized trials are often around 30%. Treatment burden is an important consideration for patients

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes o Yes o Varies X Don't know	Studies identified no significant issues with feasibility but we did not specifically look for feasibility studies.	Inhaled antibiotic administration feasibility depends a lot on healthcare system, including the availability of nebulizers, reimbursement, availability of services to deliver the treatments including test doses. There are regulatory issues. Therefore feasibility varies and this is reflected in large differences between countries in the use of these medications.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the	Probably favors the intervention	Favors the intervention	Varies	Don't know

	JUDGEMENT						
			intervention or the comparison				
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION- PSEUDOMONAS AERUGINOSA CHRONIC INFECTION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	X

TYPE OF RECOMMENDATION- NON-PSEUDOMONAS AERUGINOSA INFECTION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	X	○

CONCLUSIONS

Recommendation

Recommendation

We recommend to offer long term inhaled antibiotics to patients at high risk of exacerbations and chronic infection with *Pseudomonas aeruginosa despite standard care* (Strong recommendation for the intervention, moderate certainty of evidence)

We suggest to offer long term inhaled antibiotics to patients at high risk of exacerbations and chronic infection with pathogens other than *Pseudomonas aeruginosa despite standard care* (Conditional recommendation for the intervention, moderate certainty of evidence)

Remarks

- Patient at high risk of exacerbations include patients with a history of 2 or more exacerbations in the prior year OR 1 severe exacerbation OR 1 exacerbation plus severe daily symptoms.
- Inhaled antibiotics should be prescribed for a defined period and treatment response should be formally evaluated. If ineffective or poorly tolerated it should be discontinued
- Inhaled antibiotics are drug and device combinations and, therefore, patients should be provided with an appropriate nebulizer along with the medication.
- Many clinicians would perform a supervised test dose of inhaled antibiotics because of the risk of bronchospasm.

Justification

A strong recommendation was made for patients chronically infected with *P. aeruginosa,* based on clinically relevant reduction in exacerbation frequency, including severe exacerbations. A conditional recommendation was made for patients with other chronic infections, given the predominance of *P. aeruginosa* in the available meta-analysis and the availability of effective treatments, including long term macrolides, in these patients. The recommendation prioritises the clinically relevant improvements in exacerbation outcomes, in the context of the poor outcomes experienced by patients with chronic *P. aeruginosa* infection, and is also informed by the lack of any significant increase in adverse events. The panel acknowledged the risk of antimicrobial resistance which is important at population level but is of uncertain significance for the individual patient in the context of inhaled antibiotics. Feedback from patients also supported a strong recommendation.

Previous guidelines recommended the use of long-term treatments such as inhaled antibiotics for patients with 3 or more exacerbations per year. The current wording of the recommendation reflects the understanding that the number of exacerbations in the previous year is an important risk factor for future exacerbations but is not the only risk factor. Patients with a high burden of daily symptoms are also at high risk of future exacerbations, and the threshold to commence long-term treatments may be lower in patients with other important prognostic features. Clinical features associated with a higher risk of future exacerbations include *P. aeruginosa* infection, PCD, COPD, RA and sputum purulence. The present recommendation, therefore, suggests that patients with 2 or more exacerbations are likely to be at high risk of future exacerbations, but that some patients with a lower number of exacerbations with a high symptom burden may also benefit from preventative treatment. The threshold to commence treatment should be individualised taking into account the key risk factors in each individual patient as well as considerations around the balance of risks and benefits, availability, cost and the burden of treatment.

Antimicrobial stewardship is a key consideration. Long-term antibiotic treatment should be used after other aspects of treatment have been optimised and, therefore, other options such as airway clearance, vaccination against respiratory pathogens, treatment of underlying causes and co-morbidities have been addressed.

Subgroup considerations

P. aeruginosa and non-*P. aeruginosa* infected patients as described above.

Implementation considerations

Inhalation of antibiotics requires not just an appropriate medication but also access to and supply of an appropriate nebulizer.

Monitoring and evaluation

Treatment should be prescribed for a defined period and reevaluated. If there is no evidence of efficacy then inhaled antibiotics should be discontinued and other therapies considered to reduce exacerbations.

Research priorities

Although inhaled antibiotics show efficacy in studies, predicting individual response remains a challenge as reflected by inconsistent results across RCTs. The panel, therefore, recommends studies that should focus on precision approaches to optimize treatment selection. Key research questions include: i) Can inflammatory or microbial biomarkers predict patients' response to inhaled antibiotics?; ii) What is the best way of identifying patients at risk of future exacerbations? Iii) What is the impact of inhaled antibiotics on antimicrobial resistance and what, if any, are the clinical consequences of resistance on treatment efficacy and future outcomes.

PICO QUESTION 4

Should long-term macrolides be used (compared with no long-term macrolides) in adults with bronchiectasis?	
POPULATION:	Adults with bronchiectasis
INTERVENTION:	Long term macrolide treatment
COMPARISON:	No Long term macrolide treatment
MAIN OUTCOMES:	Exacerbations (critical) Quality of life (critical) Adverse events (critical) New isolation of pathogens (important) Mortality (critical) Antibiotic resistance (important) Hospitalisation (critical)
SETTING:	**OUTPATIENT**
PERSPECTIVE:	**CLINICAL RECOMMENDATIONS FOR INDIVIDUAL PATIENTS**
BACKGROUND:	Macrolides are used as a prophylactic treatment to prevent exacerbations. Current usage is just under 20% of all patients with bronchiectasis in Europe according to the EMBARC registry
CONFLICT OF INTERESTS:	None declared.

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	Macrolides are widely used, and reducing exacerbations is a major clinical priority for people with bronchiectasis	Patients believe that long term treatments to prevent exacerbations and prevent deterioration are a priority.

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Trivial o Small o Moderate X Large o Varies o Don't know	Large highly clinically relevant reductions in exacerbations, estimated as a 52% reduction in exacerbations, have been reported and demonstrated in our meta-analysis. There is also a significant improvement in quality of life as measured by the st Georges respiratory questionnaire. Benefits are consistent across multiple subgroups including patients with frequent (>2) and less frequent exacerbations, and patients with P. aeruginosa infection who are not conventionally treated with macrolides for their antibiotic effect.	Lack of available data on severe exacerbations Sample size overall of studies is low (371 patients for exacerbation frequency for example) nevertheless the studies show very strong beneficial effects.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large o Moderate X Small o Trivial o Varies o Don't know	While some studies show an increase in adverse events (notably the BAT trial) the overall adverse event profile shows no significant increase in adverse events. The confidence intervals are wide and include the possibility of an increase in antimicrobial resistance, isolation of new pathogens and to a lesser extent adverse events. There was very little data on mortality.	Macrolides are known to have adverse effects related to Gastrointestinal side effects and antimicrobial resistance in some cases.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low X Moderate o High No included studies	Based on GRADE assessment.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or variability o Possibly important uncertainty or variability o Probably no important uncertainty or variability X No important uncertainty or variability	We did not search for studies assessing patient values	All outcomes were rated as critical or important with consistent rating among the clinical and patient reviewers Patient members of the panel confirmed that the outcomes used were of high clinical importance to them.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison o Probably favors the intervention X Favors the intervention o Varies o Don't know	There is a clear clinically relevant reduction in the risk of exacerbations in people receiving long term macrolides. No significant increased risk of adverse events was observed. The balance of risk and benefits is favourable.	There is a lack of evidence for some important outcomes including severe exacerbations. There is also limited data on mortality and poor quality evidence on resistance. The clinical relevance of resistance to macrolides at the individual patient level is not known.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs X Moderate costs o Negligible costs and savings o Moderate savings o Large savings oVaries o Don't know	We did not specifically look for studies assessing required resources.	Macrolides are inexpensive, but monitoring recommended by some guidelines (ECG, NTM culture, hearing examination etc) has a degree of cost and resource (staff time) associated with it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low X Low o Moderate o High o No included studies	We did not specifically look for studies on resources required. We base our judgment on required resources on clinical experience	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison X Probably favors the intervention o Favors the intervention o Varies o No included studies	We did not specifically seek cost effectiveness studies.	There are no cost effectiveness studies that were identified by our search but it is highly likely the intervention is cost effective in view of the magnitude of benefit.

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased X Increased o Varies o Don't know	We did not search for studies assessing health equity	Macrolides are widely available and cheap and therefore support health equity as they can be easily deployed in resource poor settings. Macrolides are more feasible to prescribe than some alternative treatments such as inhaled antibiotics which may favour health equity.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	We did not search for studies assessing acceptability. Completion rates for the trials suggest the intervention is acceptable to patients.	Macrolides are widely used by clinicians and patients and are well accepted.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	The clinical trials identified no issues with the feasibility of the intervention	Macrolides are widely used by clinicians and patients and are therefore feasible to use in practice.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	X

CONCLUSIONS

Recommendation

Recommendation

We recommend to offer long-term macrolides to patients at high risk of exacerbations despite standard care (Strong recommendation for the intervention, moderate certainty of evidence)

Remarks

- Macrolides are effective in a broad group of patients with bronchiectasis at high risk of exacerbations including patients with chronic *P. aeruginosa* infection, patients with airway infection caused by other pathogens, and those without evidence of airway infection.
- Macrolides should not be prescribed as monotherapy to patients with NTM infection. NTM infection should be excluded before initiating macrolide therapy.

- The most widely used long-term macrolide is azithromycin, typically at a dose of 250 mg daily or three times per week, or 500 mg three times per week.
- In view of the risk of adverse effects, patient education, baseline screening, and appropriate follow-up are important when prescribing macrolides.

Justification

A strong recommendation is supported by a highly clinically relevant reduction in exacerbations and a highly meaningful improvement in quality of life with long-term macrolide treatment. The trials show no major safety concerns, and in studies of 6 to 12 months duration, antimicrobial resistance was not identified as a significant issue. The largest studies included patients with at least 1 exacerbation per year, and benefit was demonstrated across multiple patient subgroups including those with low exacerbation frequency and the subgroup of patients with *P. aeruginosa* infection.

While previous guidelines recommended the use of long-term treatments such as macrolides for patients with 3 or more exacerbations per year, the current wording of the recommendation reflects the recognition that past exacerbation frequency is a key, but not exclusive, predictor of future risk. Patients with a high burden of daily symptoms are also at high risk of future exacerbations, and, in such cases, the threshold for initiating long-term treatments may be lower. Clinical features associated with a higher risk of future exacerbations include *P. aeruginosa* infection, PCD, COPD, RA and sputum purulence. The present recommendation therefore suggests that patients with >=2 exacerbations are likely to be at high risk of future exacerbations, but that some patients with a lower number of exacerbations with a high symptom burden or other risk factors may also benefit from preventative treatment. The threshold to commence treatment should be individualised, based on patient-specific risk factors, risk-benefit balance, and treatment burden.

Subgroup considerations

A meta-analysis of RCTs shows a highly significant reduction in exacerbations in the severe subgroup infected with P. aeruginosa infection. While based on a small sample size (61 patients), the results are convincing and support the use of macrolides in this patient population. Time to first exacerbation, SGRQ and lung function changes are also consistently as least as good in the P. aeruginosa subpopulation compared to the non-Pseudomonas subpopulation.

Implementation considerations

Appropriate monitoring before and after prescription of macrolide is important, including testing for LFTs, ECG (QT interval) and NTM culture prior to treatment.

Adverse effects appear larger in studies that use higher doses and so clinicians may wish to commence patients on the lowest effective dose (250mg or 500mg three times per week)

Monitoring and evaluation

Patients should be monitored, for example refer to BTS macrolide guidance. Patients receiving macrolide maintenance therapy should be monitored at least yearly for efficacy (no. of exacerbations, symptoms) and side effects). The optimal duration of treatment with macrolides is not known and the longest studies are up to 12 months. Consider the withdrawal of macrolide treatment after one year if there is no obvious efficacy or alternatively if remission of exacerbations and symptoms is reached. In the latter case, a careful discussion about the risks and benefits of withdrawal is needed due to the risk of relapse.

Research priorities

What is the long term safety of macrolides in terms of antimicrobial resistance, emergent pathogens and adverse effects beyond 12 months

Can macrolide treatment at an early stage of disease (e.g mild bronchiectasis with infrequent exacerbations but risk factors for progression) result in slowing progression of disease or achieve remission?

What the optimal monitoring strategy for adverse events of macrolides? Do all patients require ECG pre and post macrolide treatment? Is NTM screening required for all patients or only patients with high risk clinical features? What is the value of audiology screening before or after macrolide treatment?

In patients who are clinically stable with a low symptom/exacerbation burden can macrolides be safely discontinued?

PICO QUESTION 5

Should long-term non-macrolide oral antibiotics be used (compared to no long-term non-macrolide oral antibiotics) in adults with bronchiectasis?	
POPULATION:	Adult patients with bronchiectasis
INTERVENTION:	Long-term non-macrolide oral antibiotics
COMPARISON:	No long term non macrolide oral antibiotics
MAIN OUTCOMES:	Exacerbations (critical) Quality of life (critical) Mortality (critical) Adverse events (critical) Symptoms measured using symptom questionnaires or other validated methods (important) Severe exacerbations (critical) Antibiotic resistance (important) Occurrence of new potential pathogenic microorganisms (important)
SETTING:	**OUTPATIENTS**
PERSPECTIVE:	**CLINICAL RECOMMENDATIONS FOR INDIVIDUAL PATIENTS**
BACKGROUND:	Long term non-macrolide oral antibiotics are a potential prophylactic treatment to prevent exacerbations that have been widely used in some regions in the past and continue to be used in some patients.
CONFLICT OF INTERESTS:	None reported

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	Although macrolides provide an excellent evidence based treatment for adult patients with frequent exacerbations, there is a real concern of pathogen resistance, certainly in regions where non-tuberculous mycobacteria are frequently present in these patients. Also, cardiovascular and gastro-intestinal side-effects of macrolide necessitate the need for alternatives.	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
X Trivial o Small o Moderate o Large o Varies o Don't know	The analysis shows no clinically meaningful benefit in any of the outcomes. Some reduction can be seen for shortness of breath and sputum volume outcomes, however these reductions were limited.	

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate X Small ○ Trivial ○ Varies ○ Don't know	The analysis shows only a small increase in number of adverse events in the treatment arm. There was also a small increase in new potential pathogenic organisms in the treatment arm as well as a small increase in antibiotic resistance. However, no statistical analysis was possible.	Oral antibiotics are known to carry a risk of increasing antimicrobial resistance and common side effects are known to include gastrointestinal side effects. Long term risks in relation to antimicrobial resistance are unknown.

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
X Very low ○ Low ○ Moderate ○ High ○ No included studies	The certainty of evidence is very low, based on GRADE assessment.	

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability X No important uncertainty or variability	We did not search for studies assessing patient values	The endpoints such as exacerbations, symptoms and antibiotic resistance were all considered important by the patient representatives of the panel

Balance of effects
Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

X Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison o Probably favors the intervention o Favors the intervention o Varies o Don't know	The limited positive effects of the interventions and the small increase in undesirable effects does not support the use of the intervention.	The availability of better alternative treatments such as long term macrolides and inhaled antibiotics also impacts on this consideration.

Resources required
How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings oVaries X Don't know	We did not look for studies on resource requirements	Penicillin, oxytetracycline and amoxicillin are inexpensive and widely available and therefore resource requirements are low. None of these treatments are currently widely used as long-term non-macrolide treatment ,therefore no significant savings can be suspected either.

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High X No included studies	We did not look for studies on resource requirements	

Cost effectiveness
Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies X No included studies	We did not look for studies on cost-effectiveness	

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies X Don't know	We did not look for studies on health equity	A cheap and widely available therapy that can be implemented in low resource settings could have a positive effect on health equity.

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies X Don't know	We did not look for studies assessing acceptability	The treatment is widely used and is acceptable to patients and clinicians.

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies X Don't know	We did not look for studies assessing feasibility	There are no implementation concerns as this therapy is widely used.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	**Favors the comparison**	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
o	X	o	o	o

CONCLUSIONS

Recommendation

Recommendation

The panel suggests NOT to offer long-term non-macrolide oral antibiotics as a first line treatment to adult patients with bronchiectasis and a high risk of exacerbations (conditional recommendation against the intervention, very low certainty of evidence).

Remarks

Long-term non-macrolide oral antibiotics may have a role in specific situations where patients are at high risk of frequent exacerbations and other options such as long-term macrolides are contraindicated or have proven ineffective.

Justification

The overall risk-benefit balance of long-term non-macrolide oral antibiotics appears to be unfavorable, given the lack of a clear reduction in exacerbations and other clinically relevant outcomes. The available studies are, however, hampered by small populations, unclear reporting of data, questionable inclusion criteria and sometimes a low number of events, resulting in very low certainty of evidence. Therefore, routine use of non-macrolide oral antibiotics is not recommended, as there is limited evidence, a risk of adverse effects and more effective first-line alternatives exist.

There are exceptional circumstances where non-macrolide maintenance antibiotics may be an appropriate treatment for bronchiectasis patients. This includes in patients at high risk of NTM or regions with high NTM prevalence[16], or in patients unable to take macrolides due to adverse effects. Therefore, in cases where macrolides are contraindicated or ineffective, and there is clear evidence of infection in respiratory cultures, a trial of long-term, targeted non-macrolide antibiotic therapy may be justified.

Subgroup considerations

In patients where macrolides are contraindicated or have been ineffective and where other treatment options have been exhausted, a trial of long-term non-macrolide antibiotics might be considered.

Implementation considerations

Physicians and healthcare workers should be advised on the current lack of evidence supporting the use of non-macrolide long-term antibiotics in patients with bronchiectasis. Only in cases where macrolides are contra-indicated non-macrolides can be considered, but healthcare professionals should know that current data only show limited reduction in shortness of breath and sputum volume.

Monitoring and evaluation

As with all long term treatments a formal evaluation of efficacy is recommended if this treatment is used and the treatment should be stopped if ineffective.

Research priorities

Randomized controlled trial of long term non-macrolide oral antibiotics are needed to establish if they reduce exacerbations and improve symptoms, and which patient populations are most likely to benefit.

PICO QUESTION 7

Should long-term inhaled corticosteroids be used (compared to no long-term inhaled corticosteroids) in adults with bronchiectasis?	
POPULATION:	Adults with bronchiectasis
INTERVENTION:	Long term Inhaled corticosteroids
COMPARISON:	No long term inhaled corticosteroids
MAIN OUTCOMES:	Exacerbations (critical) Hospitalisation (critical) Quality of life (critical) Adverse events (critical) New isolation of non tuberculous mycobacteria (critical) FEV1 (important) Mortality (important) Sputum quantity (important) Pneumonia (important)
SETTING:	**OUTPATIENT**
PERSPECTIVE:	**CLINICAL RECOMMENDATIONS FOR INDIVIDUAL PATIENTS**
BACKGROUND:	Inhaled corticosteroids are widely used in Europe as anti-inflammatory treatments with >50% of patients currently receiving them according to European registry data.
CONFLICT OF INTERESTS:	None declared

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	Inhaled corticosteroids are widely used by approximately 50% of European patients with bronchiectasis according to EMBARC. Establishing their efficacy is important.	Co-morbid asthma and COPD is common in bronchiectasis and these diseases are often treated with ICS.

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

x Trivial o Small o Moderate o Large o Varies o Don't know	The evidence from the meta-analysis do not identify any clinically meaningful effects of treatment including no significant effect on exacerbations, quality of life, symptoms or quality of life	Indirect evidence from other diseases suggests benefits in people with asthma or some patients with COPD

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large X Moderate o Small o Trivial o Varies o Don't know	The trials demonstrate a significant increase in the frequency of adverse events in the treatment group compared to control/placebo group. These events are generally reported to be mild to moderate and include candidiasis, sore throat and cough. Infections were reported. Important adverse events like pneumonia, risk of NTM and others are not reported in any of the studies	There are well known adverse effects of inhaled corticosteroids in other diseases such as pneumonia, osteoporosis, diabetes, and local adverse effects such as candidiasis.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low X Low o Moderate o High o No included studies	According to GRADE rules the certainty of evidence is low.	The studies are small and so confidence in the reported effect estimates is low. There is a high risk of bias in the evidence presented. Studies include those which were open label, with selective reporting of outcomes and other important methodological limitations.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or variability o Possibly important uncertainty or variability X Probably no important uncertainty or variability o No important uncertainty or variability	We did not search for studies addressing patient values	All outcomes were rated as critical or important with consistent rating among the clinical and patient reviewers

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favors the comparison X Probably favors the comparison o Does not favor either the intervention or the comparison o Probably favors the intervention o Favors the intervention o Varies o Don't know	There is a significant increase in the frequency of adverse events with no clear evidence of clinical benefit, based on the absence of any statistically significant benefit on a critical or important efficacy outcome.	This data does not apply to patients with COPD or asthma who were predominantly excluded from the studies. Approximately 25-40% of patients with bronchiectasis will have coexisting COPD or asthma. The known side effect profile of corticosteroids suggests that a positive evidence base supporting their use is required in order to recommend them. In the absence of any clear evidence of exacerbation or symptom benefit, the balance of risks and benefits would favor avoiding corticosteroids

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings oVaries X Don't know	We did not specifically look for studies on resource use.	Inhaled corticosteroids are not highly expensive but are also not lacking in costs and in the absence of clear benefits, if they were used routinely they would incur a modest increase in healthcare costs

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate High X No included studies	We did not look for studies on resource requirements and so can only infer from what we know of their use in other diseases.	The costs of inhaled corticosteroid medications is well known. The balance of costs and benefits and therefore the cost effectiveness is unknown as there are no cost effectiveness studies and no large studies of effectiveness.

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies X No included studies	We did not look for cost effectiveness studies	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced X Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	We did not search for studies on health equity.	ICS are widely available and so if proven to effective can improve equity compared to more expensive therapies.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes X Yes ○ Varies ○ Don't know	Study completion and adherence data suggests that the intervention is acceptable to patient	Acceptability was supported by the patients in the TF. ICS are widely used by clinicians and patients and are well accepted.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes X Yes ○ Varies ○ Don't know	We did not look for studies assessing feasibility	ICS are widely used by clinicians and patients and are therefore feasible to use.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	X	○	○	○

CONCLUSIONS

Recommendation

Recommendation

We suggest not to offer long term inhaled corticosteroids to patients with bronchiectasis who do not have coexisting COPD or asthma (conditional recommendation against the intervention, low certainty of evidence)

Remarks

- Patients with bronchiectasisshould be evaluated for the presence of co-existing asthma and COPD. The presence of bronchiectasis does not alter the recommendation to use inhaled corticosteroids (ICS) in patients with asthma or in a subset of patients with COPD. Suspected asthma or COPD should be appropriately investigated in patients with bronchiectasis.

- There is limited evidence suggesting that ICS may be beneficial in a subgroup of patients with bronchiectasiswith elevated blood eosinophil counts who do not have asthma or other eosinophilic conditions. However, no recommendation on ICS use based on blood eosinophils is currently possible, and we recommend further research in this group.
- The use of ICS should be reevaluated in patients without a clear indication. Discontinuation of ICS may be appropriate in some patients.

Justification

The panel considered there is a lack of evidence of benefit of ICS and a risk of harms associated with this treatment. AEs of ICS are well known and include an increased risk of pneumonia and NTM infection as well as a small but significant increase in systemic adverse effects of corticosteroids. 20-30% of people with bronchiectasis have comorbid asthma or COPD. Treatment with ICS is recommended for most individuals with asthma and for a subset of people with COPD who have elevated blood eosinophils and frequent exacerbations. There is no clear evidence that bronchiectasis should influence the decision to prescribe ICS in these groups.

Blood eosinophils require further investigation in bronchiectasis as a predictor of ICS efficacy. Around 20% of patients with bronchiectasis have blood eosinophil counts >300cells/µl in the absence of asthma or other eosinophilic conditions. There are reports suggesting that in a subset of individuals with elevated blood eosinophils, ICS may be beneficial in improving quality of life and reducing exacerbations but these data are from *post hoc* analyses and observational studies only and prospective trials are needed.

Subgroup considerations

One study shows a benefit on the St Georges respiratory questionnaire in patients with raised blood eosinophils. In other diseases (COPD/asthma) blood eosinophils are a biomarker of response justifying the use of this biomarker on a case by case basis in patients with bronchiectasis.

Implementation considerations

The use of ICS with or without long-acting beta2 agonists (LABA) is widespread in people with respiratory symptoms, and mislabeling of bronchiectasis as asthma or COPD is not uncommon. Newly diagnosed patients with bronchiectasis may thus be already treated with ICS, and the decision to continue or withdraw ICS when bronchiectasis is diagnosed requires consideration. Factors favoring stopping ICS treatment include the absence of asthma or COPD, supported by established criteria and low blood and sputum eosinophils. On the other hand, every effort should be made to correctly identify asthma in people with bronchiectasis as treatment with ICS has been shown to be beneficial in this population. COPD is frequently misdiagnosed in bronchiectasis patients and the ROSE criteria may support appropriate use of this label in patients with bronchiectasis.

Monitoring and evaluation

If ICS are used, a formal evaluation should be performed after a defined period of time and ICS discontinued if they are not effective. Patients receiving ICS should be evaluated for ICS related adverse effects and treatment discontinued if the risks outweigh theoretical benefits.

Research priorities

A randomized controlled trial of inhaled corticosteroids in people with bronchiectasis is needed to establish if they can reduce the frequency of exacerbations. Such a trial should address whether blood eosinophil counts can predict response.

Since ICS is widely used in bronchiectasis, an alternative study design to investigate the efficacy of ICS is to perform a withdrawal trial in which patients are randomized to withdrawal or continuation of ICS.

Further studies are required to understand the role of T2 inflammation in bronchiectasis (not exclusively limited to blood eosinophils) and whether T2 biomarkers can guide treatment.

PICO QUESTION 8

Should pulmonary rehabilitation be used (compared to no pulmonary rehabilitation) in adults with bronchiectasis?	
POPULATION:	Adults with bronchiectasis
INTERVENTION:	Pulmonary rehabilitation
COMPARISON:	No pulmonary rehabilitation
MAIN OUTCOMES:	Exacerbations (critical) Quality of Life (critical) Symptoms measured using symptom questionnaires or other validated methods (critical) Mortality (critical) Severe exacerbations/ Hospitalisations (critical) Exercise capacity (important) Activities of daily living (critical) Breathlessness (critical)
SETTING:	**OUTPATIENTS WITH BRONCHIECTASIS**
PERSPECTIVE:	**CLINICAL RECOMMENDATIONS FOR INDIVIDUAL PATIENTS**
BACKGROUND:	Pulmonary rehabilitation is a structured exercise and education intervention to improve quality of life in people with chronic lung disease. All possible modalities for delivering pulmonary rehabilitation programs were included (home / telerehabiliatation/ hospital).
CONFLICT OF INTERESTS:	None reported

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	It is important to know if pulmonary rehabilitation is an effective intervention for people with bronchiectasis	This intervention is widely used in some countries for people with bronchiectasis

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Trivial o Small X Moderate o Large o Varies o Don't know	The pooled data shows an improvement in exercise capacity which is clinically significant at the end of the intervention and an improvement in quality of life. Exacerbations are also reduced based on one study. The improvements predominantly do not persist after the intervention is stopped	Exercise is known to have beneficial effects on general health

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ○ Trivial ○ Varies X Don't know	We did not specifically look for adverse events as these were not pre-specified outcomes by the panel. This is because exercise and the other components of rehabilitation are not typically associated with adverse events. Worsening of patients condition would be captured through other outcomes including exacerbations and worsening of quality of life. Adverse changes on these outcomes were not observed.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
X Very low ○ Low ○ Moderate ○ High ○ No included studies	Based on GRADE assessment the certainty of evidence is rated as very low.	Overall the data is highly complex because of different questionnaires, exercise tests and other outcomes used to assess the efficacy of the intervention. Certainty of evidence is low or very low for many outcomes due to risk of bias, inconsistency and imprecision.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability X No important uncertainty or variability	We did not search for studies assessing patient values	Patients and clinicians regard exercise capacity, quality of life and exacerbations as very important and there is no uncertainty about this.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

X Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison o Probably favors the intervention o Favors the intervention o Varies o Don't know	There are clear beneficial effects of the intervention with improved quality of life and exercise capacity, both above the minimum clinically important difference, and a significant reduction in exacerbations. There is no evidence of downsides to the intervention.	Although pulmonary rehabilitation places a burden on participants and this was considered by the panel, the patient members of the panel considered that the benefits generally outweigh the burden.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings oVaries X Don't know	We did not look for data on resources required	Proper delivery of pulmonary rehabilitation requires access to appropriate facilities or technological equipment and trained staff and therefore has resource implications

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High X No included studies	We did not look for evidence on resource required	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison o Probably favors the intervention o Favors the intervention o Varies X No included studies	We did not look for studies assessing cost-effectiveness	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced oProbably reduced o Probably no impact o Probably increased o Increased o Varies X Don't know	We did not look for studies assessing health equity	As there are important resource implications for PR, there is a risk that a recommendation for PR for bronchiectasis patients would increase health inequalities

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no X Probably yes o Yes o Varies o Don't know	We did not look for studies assessing acceptability	Patients in general are supportive of PR but not all patients wish to participate particularly associated with logistic barriers (time commitment, social factors,geographic inconvenience,etc)

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no X Probably yes o Yes o Varies o Don't know	We did not search for studies assessing feasibility	Most studies utilized existing PR services designed for patients with COPD and therefore it is clearly feasible to deliver the intervention in some settings Not all countries have widespread access to PR

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	X

CONCLUSIONS

Recommendation

Recommendation

We recommend that patients with breathlessness and/or impaired exercise capacity should be offered pulmonary rehabilitation (strong recommendation for the intervention, very low certainty of evidence)

Remarks

- The educational component of pulmonary rehabilitation (PR) should ideally be bronchiectasis specific and include discussion of airway clearance strategies.

- Patients with bronchiectasis should be encouraged to undertake regular physical activity, given its multiple health benefits.

Justification

The recommendation is justified by consistent evidence of improvements in quality of life and exercise capacity. Despite the very low certainty of evidence, the strong recommendation is supported by the unequivocal improvement in functional capacity, and consistent results despite small sample sizes. Implementing PR requires substantial investment in resources and trained health professionals, which significantly increases the overall program costs.

Subgroup considerations

No subgroup considerations were identified

Implementation considerations

There are other guidelines describing the proper implementation of pulmonary rehabilitation - 10.1513/AnnalsATS.202102-146ST and DOI: 10.1164/rccm.202306-1066ST

Monitoring and evaluation

In order to monitor rehabilitation quality and patient evolution, an official ATS/ERS policy statement advises that clinical outcomes must be measured for individual patients and include a standardized assessment of a patients' functional exercise capacity, dyspnea, and health status. Additionally, an evaluation of other outcomes are suggested such as the impact pulmonary rehabilitation has on psychological comorbidity and measurement of the patients' experience.

Research priorities

Future studies should focus on how we can individualize pulmonary rehabilitation in different settings (home-based, outpatient clinics, hospital-based, community-based and tele-rehabilitation) as well as evaluating digital tools that could replace face to face rehabilitation. Research should also try to tackle the impact of pulmonary rehabilitation applied during or immediately after an acute exacerbation. Finally, evaluating pragmatic strategies

PICO QUESTION 6

Should eradication treatment be used for patients with isolation of a new pathogenic microorganism compared with no eradication treatment?	
POPULATION:	Patients with a new or recurrent isolation of a pathogenic microorganism
INTERVENTION:	Eradication treatment for a new pathogenic microorganisms
	No eradication treatment (symptomatic treatment only)
MAIN OUTCOMES:	Exacerbations (critical) Quality of life (critical) Symptoms measured using symptom questionnaires or other validated methods (critical) Mortality (critical) Adverse events (critical) Severe exacerbations/hospitalization (critical) Resistance (important) Sputum culture conversion (defined as sputum culture becoming negative for the target pathogen) (critical)
SETTING:	**PRIMARY OR SECONDARY CARE**
PERSPECTIVE:	**CLINICAL RECOMMENDATIONS FOR INDIVIDUAL PATIENTS**
BACKGROUND:	Current practice is to give eradication treatment at first isolation
CONFLICT OF INTERESTS:	None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	Chronic Pseudomonas infection is associated with poor clinical outcomes therefore preventing chronic Pseudomonas is a priority	Patients are aware of *P. aeruginosa* as a clinical problem and see its treatment and prevention as a key consideration.

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Trivial o Small X Moderate o Large o Varies o Don't know	The pooled estimate from our meta-analysis of eradication is 41.5% clear of Pseudomonas at 1 year. This is clinically important. Interpretation of this data is limited by the lack of a control group and therefore not knowing what the clearance rate would be in a control group	There is limited data for other outcomes of interest such as exacerbations and longer term outcomes over 5 or 10 years are not reported in any studies.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Large X Moderate o Small o Trivial o Varies o Don't know	Studies did not report adverse events in any interpretable way	Antibiotic treatments have a high treatment burden, a high risk of antibiotic resistance and other side effects

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
X Very low o Low o Moderate o High o No included studies	Based on GRADE assessment	The evidence base is limited to a small number of before and after studies which indirectly suggest PA eradication is possible

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or variability o Possibly important uncertainty or variability o Probably no important uncertainty or variability X No important uncertainty or variability	We did not search for studies assessing patient values	Exacerbations, clearance of PA, hospitalisations etc are all regarded as important by clinicians and patients.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favors the comparison o Probably favors the comparison o Does not favor either the intervention or the comparison X Probably favors the intervention o Favors the intervention o Varies	The evidence base is so poor that this is a difficult question to answer but as the impact of chronic PA is known to be severe, and the data suggests that clearance is possible in approximately 40% of cases,	This is also informed by feedback from patients on the importance of the goal of this treatment and their views on the risks vs benefits and treatment burden. We feel most patients would choose to try eradication rather than to take standard care alone. This is reflected in previous recommendations from guidelines as well as indirect evidence from cystic fibrosis.

○ Don't know		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○Varies X Don't know	We did not search for studies on required resources	The most effective intervention seems to include inhaled antibiotics and this requires some cost and infrastructure. The costs are not insignificant.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High X No included studies	We did not search for studies on required resources	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the	We did not search for studies on cost-effectiveness	There is no cost effectiveness analysis and as treatment can consist of oral antibiotics, IV antibiotics or inhaled antibiotics the costs will vary dramatically depending on the type of intervention used.

intervention o Varies X No included studies		

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased o Varies X Don't know	We did not look for studies addressing health equity	No additional considerations

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no X Probably yes o Yes o Varies o Don't know	We did not search for studies on acceptability	Patients are able to take this treatment and some may want to do so. Poor adherence to inhaled antibiotics in particular suggests it is not acceptable to all patients. IV antibiotics may require an inpatient stay which will not be acceptable to all patients.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes X Yes o Varies o Don't know	We did not search for studies on feasibility	This is an intervention that is widely practiced.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies

	JUDGEMENT						
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
Cost effectiveness	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	X	○

CONCLUSIONS

Recommendation

Recommendation

We suggest to offer eradication treatment to patients with a new isolation of *Pseudomonas aeruginosa* (conditional recommendation for the intervention, very low certainty of evidence)

Remarks

- A new isolation of *P.aeruginosa* may refer to the first time a patient has *P. aeruginosa* isolated or a further isolation following a prolonged period during which *P. aeruginosa* was not detected.
- Eradication practices vary both among panel members and globally. Some clinicians prescribe systemic antibiotics (e.g 2-week course) followed by a repeat sputum culture, discontinuing antibiotics if the sample is negative. Others would add inhaled antibiotics for 4 weeks to 3 months, without rechecking sputum cultures. The 2017 ERS guidelines provide examples of different antibiotic strategies.

Justification

Despite limited available data, there is overwhelming evidence that chronic infection with *P. aeruginosa* is associated with increased mortality, exacerbations, hospitalisations and worse quality of life. Preventing chronic *P. aeruginosa* infection is, therefore, of high benefit to patients, and this was confirmed by our panel members with lived experience. The conditional recommendation reflects both the very low certainty of evidence and the concern that while 40% achieve eradication with the current treatments, it is unknown how many patients would achieve spontaneous clearance due to the lack of control groups across studies. The eradication treatment carries burden, particularly if inhaled antibiotics are used, and antibiotic use is associated with a risk of antimicrobial resistance and side effects.

No evidence was identified for the eradication of organisms other than *P. aeruginosa* and implicit in the above recommendation is that eradication is not recommended routinely for pathogens other than *P. aeruginosa*

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Subgroup considerations

The recommendation applies exclusively to eradication of Pseudomonas aeruginosa as no data was identified for other microorganisms. The panel does not practice eradication of other microorganisms.

Implementation considerations

The 2017 ERS guidelines provides examples of antibiotic regimens for eradication which typically consist of 2 weeks of oral or IV antibiotics followed by 6 weeks to 3 months of inhaled antibiotics. Practice varies in terms of the antibiotics used, and whether some clinicians will check sputum cultures after the systemic antibiotic phase and discontinue treatment if sputum is negative, while some clinicians will use inhaled antibiotics regardless of whether initial culture conversion is achieved after systemic antibiotics.

Monitoring and evaluation

Patients who undergo an eradication regimen should have sputum samples performed after the eradication treatment is completed and at 1 year to confirm if eradication has been successful. Patients who fail to achieve eradication should be treated as chronic *P. aeruginosa* infection.

Research priorities

A randomized controlled trial of *P. aeruginosa* eradication vs symptomatic treatment only should be performed to establish the long term efficacy and safety of this practice.

Studies utilising molecular techniques to detect *P. aeruginosa* should be performed to identify if the organism is truly eradication or just suppressed.

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Evidence to Decisions (EtD) framework

Narrative question 2

Question: What diagnostic tests and interventions are currently recommended/used for managing exacerbations?

Domain	Judgement	Research evidence	
Priority **Is the Problem a priority**	○ No ○ Probably no ○ Probably yes **x** Yes ○ Varies ○ Don't know	Exacerbations are a cause of significant morbidity and sometimes mortality, and are desirable to prevent. Patients regard exacerbations as highly distressing and important to prevent and treat. There is some heterogeneity in the definition of exacerbations. Therefore, diagnostic tests are important in the management of exacerbations and as they impact morbidity and mortality, interventions are also very important.	The patient members of the guideline panel identified the management of exacerbations as one of the most impactful aspects for their daily lives.
Certainty of evidence	What is the overall certainty of the evidence of effects? X Very Low ○ Low ○ Moderate ○ High ○ No included studies	The certainty of evidence is very low. We did a narrative review of the evidence. The included guidelines are mainly based on expert opinion and good clinical practice for the diagnostic questions.	
Current practice		Current practice is to diagnose exacerbations based on an acute worsening of respiratory symptoms in patients with bronchiectasis (with no uniform definition used globally) and to treat with 14 days of antibiotics. Sputum culture is recommended by all guidelines that address this topic and they suggest to do this baseline with modification of therapy based on isolated microbes and sensitivity results.	In real life clinical practice some exacerbations, particularly when mild or associated with antibiotic sensitive pathogens (e.g S. pneumoniae) are treated with 7 days of antibiotic treatment with good results. Sputum culture is frequently not available and so most prescribing is empirical based on prior results or on what has “worked” for patients in the past.

Values	Is there important uncertainty about or variability in how much people value the main outcomes? ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○Probably no important uncertainty or variability ○ Not important uncertainty or variability **X** No known undesirable outcomes	All recommendations and all data suggest that there is consensus that the main outcome of exacerbation management and the diagnostics and interventions used are valued highly in the overall management. The fact that exacerbation is a main outcome in almost every clinical trial accentuates this.	A survey of patients performed by EMBARC in 2015/16 found 70% or more of patients regard exacerbations as difficult or very difficult with less than 10% of patients reporting this as not an issue. People with bronchiectasis who were part of the guideline panel confirmed that exacerbations are important to them, and that the management of exacerbations is one of the major interactions they have with healthcare. Patients reported variable management of exacerbations as well as difficulty in accessing appropriate treatment.
Summary of evidence/ Benefits and harms	How substantial are the benefits of the intervention compared to harms? ○ Trivial ○ Small ○ Moderate **X** Large ○ Varies ○ Don't know	Recommendations in current guidelines regarding diagnostics focus on timing of sputum sampling, clinical examination and additional investigations that might help to assert the diagnosis of an exacerbation. They include a statement on the definition of an exacerbation as well as recommendations on how to recognize severe exacerbations.Recommendations in current guidelines regarding interventions are focused on antibiotics, mainly their timing, duration, administration and type.	
Equity	What would be the impact on health equity?	The recommendations in current guidelines literature are easily applied across different settings both geographically and economically. One guidelines even specifically targets remote and	…

	○ Reduced ○ Probably reduced ○ Probably no impact **X** Probably increased ○ Increased ○ Varies ○ Don't know	economically poorer regions. In that respect, health equity is being considered in the current guideline literature.	
Acceptability	Is the intervention acceptable to key stakeholders? ○ No ○ Probably no ○ Probably yes **X** Yes ○ Varies ○ Don't know	Stakeholders currently accept the guidelines as trials designed by healthcare providers or industry include many aspects of the guidelines (sputum collection at exacerbation, definition of exacerbation, investigations to determine severe exacerbation, antibiotic choice, etc) in their policies, trials and local guidelines. Other aspects of exacerbation diagnostics and interventions are accepted as they are a vital aspect of the disease that needs adequate management and involvement by all stakeholders.	

Narrative question:

TYPE OF RECOMMENDATION	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the alternative	Conditional recommendation for the interventions	Strong recommendation for the intervention
	o	o	o	X	o

Recommendation	**We suggest the following diagnostic tests be performed during exacerbations (conditional recommendation for the intervention, very low certainty of evidence based on a narrative review of evidence):** **Recommendations in current guidelines regarding diagnosis and treatment of exacerbations endorsed by the panel:** • An exacerbation is defined as a worsening of symptoms that exceeds day-to-day variability and requires a change in management. Core symptoms of exacerbation include a change in cough, sputum volume and/or consistency, sputum purulence, dyspnea and/or exercise intolerance, fatigue or malaise and haemoptysis. Addition clinical features are fever, wheezing, general discomfort, anorexia, weight loss, pleuritic chest pain and changes on chest examination.

	• Features of a severe exacerbation (defined as requiring hospitalization or intravenous antibiotic treatment) may include tachypnoea, acute or acute on chronic respiratory failure, a significant decline in oxygenation or respiratory acidosis, hypercapnia, hemoptysis, new onset of cyanosis, new signs of *cor pulmonale*, hemodynamic instability, and/or impaired cognitive function. • At the onset of an exacerbation, a sputum sample for microbiology should ideally be obtained before initiating antibiotic treatment. • Sputum culture should be repeated, where possible, if there is no response to the initial antibiotic treatment. **We suggest the following interventions to be performed during exacerbations (conditional recommendation for the intervention, very low certainty of evidence based on a narrative review of evidence):** **Recommendations in current guidelines regarding interventions endorsed by the panel:** • Antibiotics should be prescribed for an exacerbation, guided by previous microbiology results, local susceptibility patterns, and clinical severity. • An adult bronchiectasis self-management plan should include guidance on recognising exacerbations. Providing selected patients the ability to self-administer antibiotics at home with appropriate instruction and education, may allow more prompt treatment. • Patients not responding promptly to oral antibiotics or showing signs of a severe exacerbation, should be reviewed to determine if there is a need for a change in treatment, intravenous antibiotic treatment and/or hospitalization. • Airway clearance regimens may need to be adapted in frequency, intensity, and technique during an exacerbation. • In general, a 14-day antibiotic course is considered standard, especially in severe exacerbations or in patients with *P. aeruginosa infection.* Shorter courses may be appropriate in patients with mild bronchiectasis, those with infection due to pathogens more sensitive to antibiotics (e.g. *S. pneumoniae*), or patients with a rapid return to baseline symptoms during treatment.
Justification	Despite the very low quality of evidence, the recommendations are justified as many of the suggested practices are already routinely implemented in hospitals managing patients with bronchiectasis. While specific antibiotic regimens are not detailed due to variations in local practice and resistance patterns, general principles for management of exacerbations can still be established to guide clinical decision-making.
Subgroup considerations	Subgroup consideration are mentioned in current guideline literature, targeting patients with *Pseudomonas aeruginosa*, patients who fail to respond to oral antibiotic treatment and patients with severe exacerbations.
Implementation consideration	The implementation of these recommendations is expected to be straightforward, as they are generally inexpensive and already widely integrated into clinical practice. Given their broad acceptance and routine use in most settings, additional resource allocation or infrastructural changes are unlikely to be necessary for widespread adoption.
Monitoring and evaluation	Exacerbations are common and important events in the natural history of bronchiectasis. Monitoring and evaluation should prioritise assessing their frequency, severity, and response to interventions. Prevention of exacerbations is a major priority and therefore in addition to the acute management of exacerbations patients should be reviewed to determine if they are at high risk of future exacerbations, and preventative measures implemented to reduce future risk.
Research priorities	Future research should be focused on the following topics: i) Assessing the presence, severity, and evolution of bronchiectasis exacerbations; ii) Determining the optimal antibiotic management, especially regarding monotherapy *versus* dual antibiotics and evaluating the role of inhaled antibiotics during exacerbations; iii) Investigating the role of non-antibiotic treatments and identifying causes of exacerbations other than bacterial infection; iv) Establishing the optimal duration of antibiotic treatment particularly for outpatients v) identification of biomarkers that can allow shortening or individualising of antibiotic treatment duration.

Evidence to Decisions (EtD) framework

Narrative Question 3: What investigations and treatments are currently recommended in a patient with bronchiectasis who is rapidly deteriorating in terms of symptoms or exacerbations?

Domain	Judgement	Research evidence	
Priority **Is the Problem a priority**	○ No ○ Probably no ○ Probably yes **X** Yes ○ Varies ○ Don't know	Rapidly deteriorating patients are a group that is rarely explicitly mentioned in the current guidelines. Most guidelines indirectly mention guidance in patients who are deteriorating. However current guidelines in literature are a priority as substantial mortality follow from patients who are rapidly deteriorating.	The patient members of the panel considered rapid deterioration a priority
C 3ertainty of evidence	What is the overall certainty of the evidence of effects? **X** Very Low ○ Low ○ Moderate ○ High ○ No included studies	The evidence is based on a narrative review of existing guideline recommendations, many of which are based on expert opinion or extrapolation for other clinical situations. Therefore the certainty of evidence as a whole is considered very low, even if individual components of the interventions recommended may have a stronger evidence base.	
Current practice		Current practice for rapidly deteriorating patients is based on an acute worsening of respiratory symptoms in patients with bronchiectasis (with no uniform definition used globally). Currently, patients with rapid deterioration, are advised to be referred to a specialist clinic. A reevaluation of treatment is performed and critically appraised. Serious symptoms or end-stage disease are managed accordingly and are in line with the recommendations mentioned in this summary.	Based on the discussion with the task force panel, current practice for rapidly deteriorating patients is inconsistent between different healthcare providers. There is no uniform definition of what represents deterioration or disease progression.

Values	Is there important uncertainty about or variability in how much people value the main outcomes? ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○Probably no important uncertainty or variability **X** Not important uncertainty or variability ○ No known undesirable outcomes	All relevant stakeholders acknowledge the importance of rapid disease deterioration as it causes significant mortality and morbidity. Therefore there is no important uncertainty of variability in how much people/stakeholders value these outcomes.	Patients expect that if their health status is rapid worsening they would receive expedited investigations and treatment.
Summary of evidence/ Benefits and harms	How substantial are the benefits of the intervention compared to harms? ○ Trivial ○ Small ○ Moderate **X** Large ○ Varies ○ Don't know	The current guidelines in literature on investigations in deteriorating patients focuses on a good baseline characterization to able to assess deterioration in the future. This also entails reevaluation of etiology, current treatment and preventive measures in case of deterioration. In terms of recommendations in current guideline literature on treatments, referral to a specialist clinic is key where current treatment will be reassessed. Also timely referral for hospitalization in case of deterioration of severe exacerbation or if surgery or transplantation needs to be considered, is essential.	Large is selected here partly based on patient feedback that it would be completely inappropriate to not intervene in a patient who is rapidly worsening.
Equity	What would be the impact	The recommendations in current guidelines literature are easily applied across different settings both geographically and economically. Especially the	…

	on health equity? ○ Reduced ○ Probably reduced ○ Probably no impact **X** Probably increased ○ Increased ○ Varies ○ Don't know	timely referral in deteriorating patients to specialist bronchiectasis centers could improve health equity.	
Acceptability	Is the intervention acceptable to key stakeholders? ○ No ○ Probably no ○ Probably yes **X** Yes ○ Varies ○ Don't know	Deterioration of symptoms is a vital aspect of the disease that needs adequate management and involvement by all stakeholders. Current guidelines in literature involve different stakeholders. Both investigations and treatments for deteriorating patients with bronchiectasis is a multidisciplinary endeavor where all stakeholders are involved.	Patients expect that is their health status is deteriorating rapidly that there would be immediate intervention to identify the cause and provide treatment.

Narrative question:

TYPE OF RECOMMENDATION	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the alternative	Conditional recommendation for the intervention	Strong recommendation for the intervention
	o	o	o	X	o

Recommendation	**We suggest the following investigations and management in a deteriorating patient (conditional recommendation for the intervention, very low certainty of evidence based on a narrative review of evidence):** **Recommendations in guideline literature on investigations in the deteriorating patient endorsed by the panel:** • Clinical deterioration including increasing exacerbation frequency and/or severity, worsening of symptoms and/or rapid decline in lung function, should result in a comprehensive re-evaluation of the patients and their treatment.

	• Adherence to both airway clearance techniques and/or pharmacological treatment should be evaluated. • Underlying diseases other than bronchiectasis should be reviewed to ensure they are being adequately treated. • Investigation for specific conditions known to be associated with deterioration (e.g ABPA, NTM infection or infection with a new pathogen) should be considered. • Early diagnosis of bronchiectasis, accurate identification and treatment of its underlying cause, adequate management of chronic airway infection, and interventions to prevent exacerbations and control disease may delay disease progression. • Repeat chest CT imaging can help to identify several potential causes of deterioration. • Repeat testing for NTM should be performed when there are suggestive clinical or radiologic features of NTM infection, particularly in those who deteriorate despite appropriate antibiotics. **Recommendations in guideline literature on treatments endorsed by the panel:** • Deteriorating patients who are not already under the care of a bronchiectasis specialist should be referred to a respiratory clinic with expertise in bronchiectasis. • Current treatment should be reviewed and optimised using a "treatable traits" approach. This includes, but is not limited, to treatment directed at the underlying aetiology of the patients bronchiectasis, airway clearance and mucoactive treatments, vaccination status, long-term (inhaled or oral) antibiotic treatment, *P. aeruginosa* eradication treatment, long-term inhaled bronchodilator and corticosteroid treatment, pulmonary rehabilitation, oxygen therapy and non-invasive ventilatory support where appropriate. • Lung resection may be considered in highly selected patients with localised disease whose symptoms are not controlled by medical treatment optimised by a bronchiectasis specialist. • Early referral for lung transplantation is essential in patients with progressive disease despite optimal medical management. This may include rapidly declining FEV1 or FEV1 <30%predicted, and/or PaCO2 >50mmHg.
Justification	Rapid deterioration in patients with bronchiectasis represents a critical aspect of the disease spectrum, necessitating timely recognition and appropriate management. While most current guideline literature, with the exception of the British Thoracic Society guidelines, do not provide specific guidance for the deteriorating patient, many existing recommendations are applicable to those experiencing increasing exacerbations or worsening symptoms and we therefore extracted these recommendations. These include guidance on follow-up strategies, treatment optimisation, and prevention measures to mitigate disease progression. The accumulated evidence supports early investigation and proactive treatment of patients who have deterioration. By applying these general principles from existing guidelines, clinicians can ensure that deteriorating patients receive timely and individualised management, potentially reducing morbidity and improving long-term outcomes.
Subgroup considerations	Current subgroup recommendations are made for patients with specific deterioration of a symptom, such as significant increase in hemoptysis, significant shortness of breath with need for oxygen or non-invasive ventilation as well as recurrent infections due to chronic infection.
Implementation consideration	As with all aspects of bronchiectasis care the approach to the deteriorating patient must be personalised and adapted based on the nature of the deterioration, the signs and symptoms presenting and the patients treatable traits. The approach to deteriorating symptoms and reduced lung function may be different as will specific situations such as, a marked increase in haemoptysis, worsening shortness of breath requiring oxygen or non-invasive ventilation, and recurrent exacerbations due to chronic bacterial infections.
Monitoring and evaluation	Monitoring and evaluation should focus on early identification and timely intervention for patients experiencing disease deterioration, as this is a common feature of bronchiectasis. Regular clinical assessment, symptom tracking, and objective investigations should be prioritized to detect worsening conditions and guide appropriate treatment. Key aspects of monitoring include evaluating exacerbation frequency, respiratory function decline, increased need for oxygen or ventilatory support, and persistent infections
Research priorities	Future research should focus on: - Improving diagnostic tools to enable faster identification, severity assessment, and objective follow-up of deteriorating patients with bronchiectasis. - Determining the optimal timepoint for hospitalisation referral, as well as referral for surgery or lung transplantation. - Establishing strategies for measure end-of-life care and palliative management in patients with advanced bronchiectasis.