Supplement file

Methods
A working group (WG) was formed representing an expert panel of parents, patient advocates and clinician researchers covering paediatric respiratory medicine, physiotherapy and infectious diseases. The working group consisted of several Clinical Practice Guideline (CPG) authors (AC, LB, ZP, AK, JB, KG, AW, CW) and two additional clinicians with specific expertise in bronchiectasis (IBM, VG). This group worked with the European Lung Foundation (ELF) parent advisory group (PAG) that was initiated as part of the European Respiratory Society (ERS) CPG [1] for managing children and adolescents with bronchiectasis. The CPG consisted of a multidisciplinary group of clinicians with expertise in bronchiectasis and two parents of children with bronchiectasis.

Parents/patients survey on Quality-of-Life (QoL), clinical needs and research priorities
The entire CPG panel was consulted before ELF launched the web-based survey. The English language-based survey was professionally translated by EVS Translations UK Ltd (Nottingham, UK) into nine languages: Italian, French, Spanish, Turkish, German, Portuguese, Greek, Polish and Russian. The link to the survey (on the SurveyMonkey platform) was distributed widely by the ELF and the CPG's panel members' networks, including several Lung Foundations outside of Europe. We used emails and posters to promote the survey that was held open over 7-months (July 2019 to January 2020).

The ELF lead (JB) summarised the participants' responses. The WG then discussed and grouped the priorities into research or clinical entities or both. These were then categorised into themes. The results, groupings and themes were reiteratively discussed with the PAG and the data presented in tabulated form. These groupings and themes were also discussed with the parent group associated with an Australian Centre of Research Excellence for bronchiectasis in children (<www.crelungs.org.au>). Overall, when preparing this document, four web-based conferences were held.

Health Practitioners survey for research priorities
The 49 items for the Health Practitioners survey were based on: (i) research questions raised from our CPG [1] and (ii) items adapted from the adult bronchiectasis research priorities of the ERS [2] and the United States [3]. After several reiterations among the WG members, the link to the web-based survey (only in English) was sent to all the members of the paediatrics assembly of the ERS (~1300 members). In addition, WG members sent the link to non-Europeans/ERS collaborators in the field. The survey was held open between 28 July 2020 and 30 Sept 2020. To make the survey comparable to the ERS adult priorities [2], we used the same five-point scale (1=unimportant, 2=slightly important, 3=moderately important, 4=very important, 5=essential).

As with the parents/patients' survey described above, the ELF lead (JB) summarised the participant responses and the WG then grouped the priorities into research themes, matching the parent/patient-based themes.

Results
Parents/patients survey
The 225 respondents came from 21 countries, with the highest numbers living in Australia (n=32), Italy (n=27), UK (n=26) and New Zealand (n=18,) but included others from lower-middle income countries (Venezuela, Brazil, Turkey, Morocco, Kazakhstan, Morocco, Burkino Faso, Barbados). However, not all responded to every survey question and/or the item(s) were that not applicable to them.

Concerns over their child's health were highest in relation to deterioration of disease over time, protection from infection and ability to conduct a normal life. The most important areas to improve childhood treatment were rated by parents as having an exacerbation action management plan, finding exacerbation

triggers and finding new medicines. Other common issues/factors that affect QoL included lack of knowledge by healthcare professionals, everyday burden of airway clearance, sibling and family relationships, anxiety about the future eg., long-term effects of medication and worries about the transition from paediatric to adult services.

Adults diagnosed as children thought the main treatment improvement should be in educating primary care doctors to prescribe the same dose of antibiotics and course duration as they do in cystic fibrosis (CF). The other highest rated areas were similar to those specified by parents.

Health practitioner survey
There were 258 health practitioners (from 54 countries) of whom 248 (96.1%) managed patients with bronchiectasis unrelated to CF and most (n=187, 72.5%) practiced in a university-based hospital. The mean scores for all the questions were between 3.19 and 4.41 with little variation between practitioners grouped by number of patients with bronchiectasis seen regularly in their clinics (Supplement Figure-1). Of the top six items (two items ranked equal 5th), four related to antibiotics (Table-3), one to airway clearance and the other with factors associated with rapid progression and poor outcomes. The items ranked by mean scores are presented in Supplement Table-1.

Top 10 research priorities and consensus statements
A formal voting process was not undertaken as complete consensus was obtained.

- Identifying risk and protective factors for bronchiectasis
One of the PAG's top research priorities is to identify how bronchiectasis can be prevented. Our systematic review [1] found very low quality evidence from six studies demonstrating that with appropriate management, early bronchiectasis in some children and young people (CYP) is reversible and thus preventable [4,5,6,7,8,9]. Current limited evidence suggests that factors important for reversibility and/or prevention of bronchiectasis include early identification and treatment of inhaled foreign bodies, preventing early and severe pneumonia, preventing tuberculosis and recurrent protracted bacterial bronchitis (PBB), early recognition and treatment of primary immunodeficiency disorders and human immunodeficiency virus infections causing bronchiectasis, promoting breastfeeding and immunisation, and avoiding tobacco smoke and other pollutants [1].

Consensus statement: Intervention studies that potentially reduce and/or prevent bronchiectasis are required. Examples include vaccinations to prevent early and/or severe childhood pneumonia and long-term azithromycin for recurrent protracted bacterial bronchitis. Additionally, long-term observational studies that delineate currently unidentified risk and protective factors for developing bronchiectasis are required.

- Identifying the underlying aetiologies of bronchiectasis
Bronchiectasis is a heterogenous disease with varying aetiologies across settings, countries and age groups [10]. For example, common aetiologies in children differ from those in adults and aetiologies of bronchiectasis in low-income countries vary from those found in high-income countries, although there are many shared aspects [10]. In-depth investigation contingent on clinical presentation and phenotype is essential for aetiology-based management, such as for primary and acquired immunodeficiency [11]. Of currently known causes, the ERS CPG recommended undertaking a minimum panel of tests that may identify the underlying cause of bronchiectasis as knowing this may alter treatment approaches [1].

However, even following guideline recommendations, an underlying aetiology of bronchiectasis cannot be ascertained in many patients. In the last decade, little new data has been generated with recurrent PBB (>3 episodes within 12-months of initial diagnosis) [12] being the sole exception. Identifying the underlying aetiologies of bronchiectasis may lead to new prevention and/or treatment approaches.

Consensus statement: Studies that further define a standard panel for identifying and/or predicting bronchiectasis are required. Examples include using novel technologies, such as genomics and blood/airway gene expression signatures. Additionally, long-term observational studies to delineate new aetiologies associated with bronchiectasis developing are needed.

- Discovering ways to diagnose bronchiectasis earlier, including ways to increase health practitioner awareness and to facilitate earlier referrals

Diagnosing bronchiectasis requires both clinical awareness of this disorder and undertaking the necessary tests to either confirm or refute this diagnosis. Narrative evidence from the ERS CPG showed the substantial positive impact of diagnosing bronchiectasis, particularly when detected early as with prompt treatment, bronchiectasis can stabilise and can even reverse on occasions [1]. Indeed, several patient cohorts have demonstrated improved lung function with treatment [13,14,15,16], including those with underlying primary immunodeficiency [5,17].

The PAG reported that in their experience, it is not uncommon for there to be long delays in diagnosing bronchiectasis in children, even when classical symptoms are present. Limited published literature supports the PAG's experience where most children and adults have had a wet/productive cough for many years (even decades in adults dating back to childhood) before a diagnosis of bronchiectasis is made [18,19,20,21]. In children and non-smoking adults with bronchiectasis, the duration of chronic cough correlated with poorer lung function and worse radiographic bronchiectasis scores [18,19].

Earlier diagnosis of bronchiectasis in children requires alignment of several factors. These include diligent recognition and treatment of chronic cough (most common symptom of bronchiectasis [22]), patient and health professional awareness, suitable educational resources and health systems that support early and appropriate referrals to specialists with access to diagnostic capability. These capabilities include adopting the ERS CPG recommendation of using multi-detector chest computed tomography (MDCT) routinely with high-resolution computed tomography (HRCT) scans rather than HRCT scans alone and employing the paediatric derived broncho-arterial ratio (BAR, ratio of the inner diameter of the airway to the outer diameter of the adjacent artery) of >0.8 to define abnormality (in contrast to the adult cut-off value of >1-1.5) [1]. Using paediatric-specific rather than adult-derived definitions and early employment of specific diagnostics and management protocols is essential for children with bronchiectasis as this is the period in their lives when their lungs undergo critical growth and developmental phases [5,23].

Consensus statement: Implementation science-based studies are needed to increase: (a) health practitioner awareness and (b) use of guidelines that facilitate earlier bronchiectasis diagnosis and referrals. We encourage research on novel diagnostic techniques, including those that that can reduce human variability in diagnosis (e.g. artificial intelligence) and/or provide alternate/complementary methods to current standards relying upon chest CT-scans. Additionally, research is required to identify and promote the early symptoms and signs of underlying bronchiectasis and develop simple biomarkers to allow local physicians and paediatricians to recognise this disorder promptly and reduce the risk of irreversible damage to the developing airways of young children.

- Identifying triggers/prevention factors and optimal antibiotic treatment for acute exacerbations

Acute respiratory exacerbations in children with bronchiectasis are particularly important as they are associated with increased psychological stress, impaired QoL [24], lung function decline (forced expiratory volume in 1-scond percentage predicted of -1.9% per hospitalised exacerbation) [17], lost school/work-days [25] and substantial healthcare costs [26]. Despite being high on the clinical priority list of parents/patients (Table 1), few data exist on finding triggers of exacerbations [27,28]. Indeed, the only trigger studied in children with bronchiectasis is viral-associated infections whereby respiratory viruses were detected during 48% of exacerbations in a small prospective study of 69 children over 900 child-months [29]. Compared with virus-negative exacerbations, children with virus-positive exacerbations were more likely to require hospitalisation (59% vs 32.5%, p=0.02) and have fever (odds ratio (OR) 3.1, 95%CI 1.2 to 11.1), hypoxia (OR

25.5, 95%CI 2.0 to 322.6), chest signs (OR 3.3, 95%CI 1.1 to 10.2) and raised C-reactive protein (OR 4.7, 95%CI 1.7 to 13.1) [29]. This study [29] was limited however, as viral studies were only undertaken during an exacerbation and not when in a stable clinical state.

Currently, all bronchiectasis guidelines [1,30,31,32] recommend antibiotics for respiratory exacerbations in both children and adults. This leads to high antibiotic consumption, which is associated with increased anti-microbial resistance. A multi-centre study found that the rate of antibiotic use for bronchiectasis was 50 per 100 child-months of observation [25]. Yet, the sole placebo-controlled, double-dummy, randomised controlled trial (RCT) (BEST-1) on antibiotics for non-hospitalised exacerbations found that these resolved by Day-14 in a substantial proportion (43%) of children in the placebo arm [33]. Nevertheless, those whose exacerbations resolved had a longer duration of illness after starting therapy when given placebo compared with those allocated antibiotics. It is therefore apparent that a subset of children with bronchiectasis-related exacerbations do not require antibiotics. Thus, studies are needed to obtain novel data that can identify those who will benefit from antibiotics and those in whom such treatment is unnecessary. Obtaining biomarkers that predict exacerbation outcomes are needed.

Consensus statement: Large prospective studies are needed to identify triggers of respiratory exacerbations and those at risk of these episodes. It is also important to generate novel data to differentiate between children with exacerbations requiring antibiotics from those where they are unnecessary. Such studies should include identifying systemic and/or airway biomarkers that may predict exacerbation outcomes.

- Finding new and optimal airway clearance techniques (ACT)

The ERS CPG [1] strongly recommended that patients are taught and receive regular ACT or manoeuvres. Although the evidence for its efficacy is low, the recommendation was based on balancing the time-consuming effects of performing ACT and the risk of harm if ACT is not undertaken [1]. Parents/PAG give high value to airway clearance as a therapeutic modality and valued individual and age-targeted ACTs to reduce lost school/workdays, duration of symptoms, exacerbation rate, any hospitalisation, QoL, lung function and other adverse events. However, placebo RCTs are currently not feasible as ACT is advocated universally.

Importantly, the PAG highlighted the lack of access to high-quality therapists, including access to paediatric respiratory physiotherapists and education on appropriate ACT in some settings. There are many different types of ACTs that are suitable for the various developmental stages of childhood and adolescence and cognitive ability of individuals. Thus, ACT targeted for individual CYP taught by physiotherapists with expertise in paediatric respiratory care is recommended by the ERS CPG [1]. Most of these techniques are indicated empirically, usually based on the experience and skills of physiotherapists. In the context of these factors and that ACT was the highest rated aspect affecting the children's QoL (Figure 2a), there is an obvious need to find new and optimal ACT during both the stable state and when experiencing exacerbations.

Consensus statement: We advocate multicentre studies of CYP with bronchiectasis to determine the efficacy of ACT based on their frequency and utility of various methods. Innovative techniques that increase the efficiency and/or efficacy of ACTs and reduce the time burden on patients and their carers are needed.

- Defining optimal antibiotic therapy for eradicating specific pathogens (eg. *P. aeruginosa*) and for suppressing bacteria once chronic infection is established

The association between chronic lower airway *P. aeruginosa* infection and worsening clinical state in adults with bronchiectasis is well recognised, especially in those with frequent exacerbations [34]. Although *P. aeruginosa* is relatively uncommon in children with bronchiectasis, when detected it is often in the presence of multi-lobar disease and serious underlying co-morbid disorders [35]. These observations raise important questions over whether, in the absence of effective vaccines [36], it is possible to prevent chronic *P. aeruginosa* infections becoming established and furthermore, once chronic infection is established by either

P. aeruginosa or other respiratory bacterial pathogens whether long-term antibiotics reduce the risk of recurrent exacerbations.

Health practitioners rated highly the importance of determining if eradicating bacterial pathogens, especially *P. aeruginosa*, improves clinical outcomes and if so, which eradication regimen provides the best results. However, currently there are no published paediatric data, while three small studies in adults with bronchiectasis whose primary outcomes were eradication of pathogens from sputum were limited to participants with *P. aeruginosa* infections. Two were observational studies [37,38]. The third was a single-blinded, placebo-controlled RCT of intravenous ceftazidime and tobramycin in those with a first detection of *P.* aeruginosa, followed by nebulised tobramycin for 3-months versus intravenous ceftazidime and tobramycin and then 3-months of nebulised normal saline [39]. In the nebulised tobramycin group, 5/16 (31.3%) withdrew because of bronchospasm, while by 15-months 6/11 (54.5%) were free of *P. aeruginosa* compared with 5/17 (29.4%) receiving nebulised saline. The mean number of exacerbations and hospital admissions were also significantly lower in the tobramycin group. Despite the paucity of supporting data, the ERS CPG recommends eradication therapy following an initial or new detection of *P. aeruginosa* in children with bronchiectasis [1]. This decision was heavily influenced by eradication treatment being standard practice in CYP with CF, even though it may fail in 10–40% of patients [40]. It light of these factors it is unlikely that placebo-controlled *P. aeruginosa* eradication trials will take place as it is current standard clinical practice in most settings. Therefore, future well-designed studies comparing various eradication regimens (eg. oral versus inhaled anti-pseudomonal antibiotics, alone or in combination, or parenteral antibiotics as single or dual agents, and varying treatment course duration) to improve the available evidence are required. Studies should document potential effect modifiers (eg. age, aetiology and severity of underlying bronchiectasis, co-morbidities, bacterial load, co-pathogens, exacerbation frequency) in order to identify key subgroups who may gain either the most benefit or be harmed by the intervention. Patient-important outcomes (eg. eradication, exacerbations, hospitalisations, QoL, symptoms, days of school/work lost, antibiotic resistance and careful monitoring of lung function) will need to be measured. In the absence of clinical data, trials are also needed to determine if eradicating other bacterial pathogens associated with chronic infection in bronchiectasis is possible and beneficial.

Health practitioners also wanted to know when, in whom and which antibiotics to prescribe for how long to induce or maintain clinical stability in CYP with bronchiectasis. This too was also important for parent/patient groups. Currently, the trigger for commencing long-term suppressive antibiotic therapy is the frequency of exacerbations. ERS adult guidelines recommend long-term antibiotics in those with $\geq$3 exacerbations per year [32]. Inhaled antibiotics are recommended for those with chronic *P. aeruginosa* infection, while oral macrolides are prescribed if *P. aeruginosa* is not present or inhaled antibiotics are not tolerated. In contrast, the ERS CPG recommends long-term oral macrolides for at least 6-months in those who have had >1 hospitalised or $\geq$3 non-hospitalised exacerbations in the previous 12-months [1]. This recommendation was based on only three RCTs [41,42,43], all of which involved macrolide antibiotics and only one [41] was judged to be of high-quality (determined externally i.e. not by the authors). Nevertheless, the findings were consistent with RCTs in adults [44] and the clinical experience of the CPG panel. Despite the recommendations from both ERS guidelines, considerable knowledge gaps remain. RCTs are still required to identify CYP with bronchiectasis who are most likely to benefit from long-term antibiotics (eg. number of exacerbations/year), as well as to define which antibiotic (eg. macrolide versus inhaled antibiotics) to prescribe, the optimum duration of treatment, describe how long these beneficial effects persist, and establish the clinical significance of antibiotic-resistant respiratory bacterial pathogens. Studies should record important effect modifiers (eg. age; aetiology and severity of underlying bronchiectasis, co-morbidities, bacterial load, co-infections [including microbiota], exacerbation frequency) while outcome measure should include both clinical and patient-important factors such as: time-to-next exacerbation, hospitalisations, QoL, days of school/work lost, adverse events and induction of anti-microbial resistance.

Consensus statement: RCTs are needed to identify those benefiting from long-term antibiotics as well as the optimal antibiotic regimens (including oral or inhaled formulations) and their duration for eradicating

bacterial pathogens (eg. P. aeruginosa) and reducing exacerbations. Both clinical and patient-focused benefits and harm should be identified in these trials. Studies on the safety and efficacy of inhaled antibiotics in CYP and determining risk factors and clinical impact of anti-microbial resistance are also required.

- Finding new medications and/or techniques for managing bronchiectasis

Despite the burden of bronchiectasis being recognised increasingly, there are still no licenced long-term therapies available for bronchiectasis [10,45]. Treatments at present are usually extrapolated from the CF literature, sometimes with adverse results when later subjected to high-quality RCTs [46]. There is an obvious need to identify evidence-based therapies for people with bronchiectasis.

Consensus statement: Investment in developing and/or assessing new therapeutics that can improve the lives of children and adolescents with bronchiectasis are needed. This includes investment from both commercial and research funding bodies to accelerate the conduct of basic scientific studies and multi-centre clinical trials to allow the identification and licensing of beneficial therapeutic agents.

- Identifying lung function tests/indices that predict outcomes

Tools that can monitor disease and predict outcomes are important for managing chronic diseases. Such prognostic/severity tools have been developed in adults with bronchiectasis and include the FACED score [47] and bronchiectasis severity index [48]. However, tools that include data on lung function, lower airway microbiology and self-reported subjective questionnaires are limited in some settings [49,50,51] and cannot be applied to children. A combined Australian and New Zealand study found that while Indigenous Australian adults had mild disease according to their FACED scores, their prognosis was much poorer than non-Indigenous adults with higher FACED scores [50]. The reasons these tools are not applicable in children include the differences between children and adults in their disease prognosis [22], airway microbiology, especially related to *P. aeruginosa* [52], and being unable to obtain reliable spirometry data in young children.

Consensus statement: We require tools and indices that can be used to effectively monitor disease severity and predict outcomes for CYP with bronchiectasis. Longitudinal studies should be conducted in CYP with bronchiectasis to monitor lung function and other indices to identify specific monitoring parameters that can predict outcomes.

- Understanding the relationship between causes and co-morbidities of bronchiectasis with clinical outcomes

Bronchiectasis is a heterogenous condition associated with multiple underlying aetiologies, co-existing diseases and overlap syndromes as it is the 'final common pathway' of a pathobiological process involving impaired airway clearance, chronic lower airway infection and inflammation. These various underlying aetiologies and co-morbidities (eg. concurrent asthma, gastroesophageal disease, airway malacia) potentially represent paediatric phenotypes and 'treatable traits' [22] that require further investigation. Classifying adults with bronchiectasis using latent class-analysis suggests phenotypes (eg. frequent exacerbators, *P. aeruginosa* infection) exist and endotypes (eg. airway eosinophilia with neutrophilia) have also been proposed [53]. There are no such data for children who differ from adults in many aspects including clinical (eg. reversibility of bronchiectasis and aetiologies of adult-onset bronchiectasis [10,22]) and bacteriology (e.g. lower airway microbiota [54] and prevalence of non-tuberculous mycobacteria and *P. aeruginosa* [35,52]). However, so far, there are only limited data on paediatric bronchiectasis phenotypes or treatable traits. With no publications to date, this represents a large knowledge gap. Such knowledge is needed to understand how these concepts would improve short-term clinical outcomes and long-term prognosis in children.

Consensus statement: Well-characterised large cohorts of CYP with bronchiectasis that advance the concept of phenotypes and 'treatable traits' are required. This includes utilising mathematical modelling methods and multiparametric immunophenotyping.

- Identifying factors associated with worse bronchiectasis outcomes

Bronchiectasis, previously defined as irreversible bronchial dilatation [31], is now defined as abnormal bronchial dilatation on chest CT scans with the phenotype of chronic or recurrent wet/productive cough and pulmonary exacerbations [10,22]. The outcomes of bronchiectasis are varied and indeed it is now accepted that mild radiographic bronchiectasis in children is reversible when optimal treatment is begun early in the course of the disease, thereby avoiding the later progressive decline in lung function [22]. Identifying factors that likely influence progression of the illness are important as these represent potential intervention points i.e. secondary prevention. While some of these factors have been described [22], the evidence is limited. Identifying factors associated with disease deterioration based on host genetic or environmental factors may lead to new pharmacological agents.

Consensus statement: Long-term observational studies in large cohorts across multiple settings to further delineate factors influencing outcomes of CYP with bronchiectasis are required. These include genetic and environmental factors that predispose some patients to chronic infections (e.g. with P. aeruginosa) and/or frequent exacerbations. Studies with innovative treatment protocols based on patient phenotypes are also needed.

Discussion

In addition to the main manuscript, we highlight the following points. Firstly, while availability of paediatric-focused registries was ranked number 11 in the health practitioner survey, this item did not appear in the parents/patients survey. Following the process outlined in main text, it could therefore not be included among the top 10 research priorities.

Secondly, as biomarkers were not ranked highly (mean scores of 3.68 and 3.58; Supplement Table 1), they were not listed as one of the top 10 priorities. However, our consensus statements included mention of biomarkers as the panel considered that from a research perspective, biomarkers are necessary to help address the patients/parents research priorities of identifying those at risk of bronchiectasis, including exacerbations and disease progression.

Supplement Table-1: Results of health practitioner survey ranked by mean score
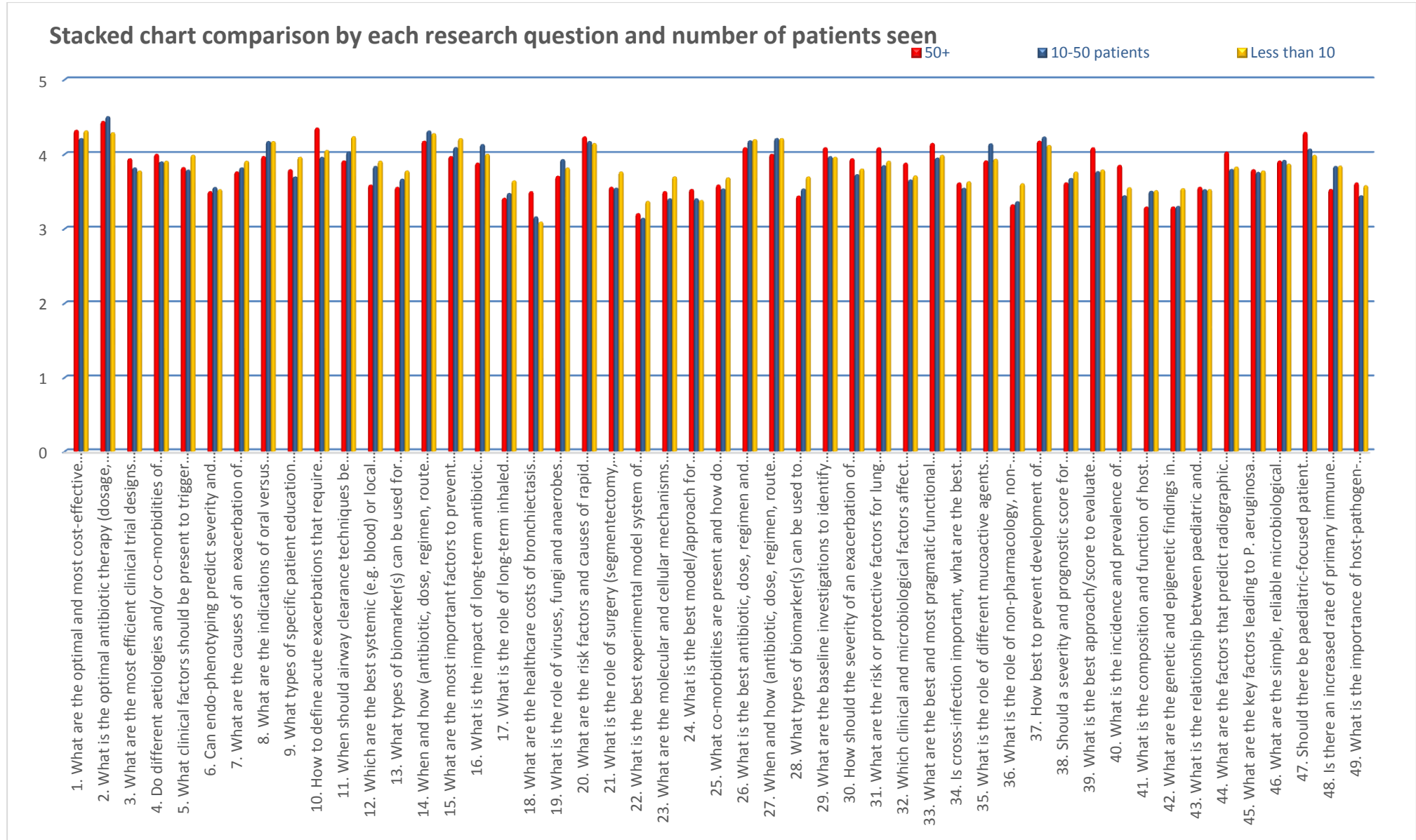
In children and young people with bronchiectasis (unrelated to cystic fibrosis):	Mean Score
What is the optimal antibiotic therapy (dosage, how many antibiotics, type, oral versus intravenous versus inhaled/nebulised and length of therapy) for an exacerbation of bronchiectasis	4.41
When and how (antibiotic, dose, regimen, route [intravenous, oral or inhaled/nebulized] and duration) should pathogens other than *P. aeruginosa* be eradicated, and do patient outcomes improve afterwards?	4.27
What are the optimal and most cost-effective airway clearance techniques?	4.26
When and how (antibiotic, dose, regimen, route [intravenous, oral or inhaled/nebulized] and duration) should *Pseudomonas aeruginosa* be eradicated, and do patient outcomes improve afterwards?	4.18
What is the best antibiotic, dose, regimen and duration for long-term oral antibiotic therapy in patients with bronchiectasis (according to the presence or absence of *P. aeruginosa* or other pathogens)?	4.17
What are the risk factors and causes of rapid progression of lung disease and poor outcomes (e.g. hospitalisation, lung transplantation and mortality)?	4.17
How best to prevent development of bronchiectasis?	4.16
What are the indications of oral versus inhaled/nebulised long-term suppressive antibiotic treatment?	4.14
What are the most important factors to prevent acute exacerbations?	4.12
When should airway clearance techniques be started in patients with bronchiectasis, and how often should it be done during the stable state and for exacerbations?	4.09
Should there be paediatric-focused patient registries?	4.06
How to define acute exacerbations that require additional treatment?	4.05
What is the impact of long-term antibiotic therapy on anti-microbial resistance?	4.03
What is the role of different mucoactive agents (e.g. inhaled hypertonic or isotonic saline, mannitol, oral erdosteine or N-acetyl cysteine)?	4.03
What are the best and most pragmatic functional tests (such as carbon monoxide diffusing capacity, 6-min walk test, lung clearance index, endurance shuttle walk, incremental exercise tests or accelerometers) as markers for severity of the disease, outcomes and end-points for the clinic?	4.00
What are the baseline investigations to identify underlying aetiologies of bronchiectasis?	3.98
Do different aetiologies and/or co-morbidities of bronchiectasis predetermine microbiological characteristics, and affect severity, patients' quality of life and disease progression?	3.92

What are the risk or protective factors for lung function decline in patients with bronchiectasis?	3.91
What are the simple, reliable microbiological tests for determining lower airway infection?	3.90
What clinical factors should be present to trigger referring a child for a chest CT scan to diagnose bronchiectasis?	3.87
What is the role of viruses, fungi and anaerobes (as single agents and/or polymicrobial infections), during both the stable state and exacerbation, and what is their impact upon patient severity and outcomes?	3.85
What are the causes of an exacerbation of bronchiectasis?	3.84
What are the factors that predict radiographic reversibility (on HRCT scan)?	3.84
What are the most efficient clinical trial designs and measurable outcomes?	3.83
Which are the best systemic (e.g. blood) or local (e.g. sputum) inflammatory markers for the diagnosis, management and follow-up for an exacerbation?	3.82
What is the best approach/score to evaluate radiographic severity?	3.82
What types of specific patient education packages, self-management plans and patient support groups improve outcomes?	3.81
What are the key factors leading to *P. aeruginosa* acquisition and infection?	3.78
How should the severity of an exacerbation of bronchiectasis be assessed and what is its impact on long-term outcomes?	3.78
Is there an increased rate of primary immune defects (e.g. mannose-binding lectin deficiency, common variable immunodeficiency, IgM or IgA deficiency, or complement deficiency)?	3.78
Which clinical and microbiological factors affect macrolide efficacy?	3.71
Should a severity and prognostic score for children that is useful in clinical practice be developed?	3.70
What types of biomarker(s) can be used for predicting bronchiectasis exacerbation?	3.68
What is the role of surgery (segmentectomy, lobectomy or pneumonectomy) and when should it be undertaken?	3.62
What co-morbidities are present and how do they influence bronchiectasis severity?	3.59
Is cross-infection important, what are the best strategies and is strict patient segregation required?	3.59
What types of biomarker(s) can be used to monitor bronchiectasis severity during stable state, so as to define the subgroup who will benefit from more intensive treatment?	3.58
What is the incidence and prevalence of different aetiologies of bronchiectasis across the world?	3.55
Can endo-phenotyping predict severity and outcomes in children?	3.54
What is the relationship between paediatric and adult bronchiectasis?	3.54
What is the role of long-term inhaled corticosteroids?	3.53

What is the importance of host-pathogen-environment interactions?	3.53
What are the molecular and cellular mechanisms and pathobiological pathways of bronchiectasis development, exacerbations and progression?	3.52
What is the composition and function of host microbiomes, both during the stable state and exacerbation, and does it impact directly disease severity and progression?	3.48
What is the role of non-pharmacology, non-airway clearance technique-based therapeutics, such as singing exercise, wind instruments, and yoga during stable states and acute exacerbations?	3.45
What is the best model/approach for transferring an adolescent with bronchiectasis to adult services?	3.42
What are the genetic and epigenetic findings in patients with bronchiectasis compared to healthy controls, and what is their role in acquisition of specific pathogens and patients' outcomes?	3.39
What is the best experimental model system of bronchiectasis?	3.24
What are the healthcare costs of bronchiectasis management across the world?	3.19

Supplement Figure-1: Scores from the health practitioner survey grouped by number of patients with bronchiectasis they under their care

Stacked chart comparison by each research question and number of patients seen

Legend: 50+ (red), 10-50 patients (blue), Less than 10 (yellow)

X-axis categories:
1. What are the optimal and most cost-effective...
2. What is the optimal antibiotic therapy (dosage,...
3. What are the most efficient clinical trial designs...
4. Do different aetiologies and/or co-morbidities of...
5. What clinical factors should be present to trigger...
6. Can endo-phenotyping predict severity and...
7. What are the causes of an exacerbation of...
8. What are the indications of oral versus...
9. What types of specific patient education...
10. How to define acute exacerbations that require...
11. When should airway clearance techniques be...
12. Which are the best systemic (e.g. blood) or local...
13. What types of biomarker(s) can be used for...
14. When and how (antibiotic, dose, regimen, route...
15. What are the most important factors to prevent...
16. What is the impact of long-term antibiotic...
17. What is the role of long-term inhaled...
18. What are the healthcare costs of bronchiectasis...
19. What is the role of viruses, fungi and anaerobes...
20. What are the risk factors and causes of rapid...
21. What is the role of surgery (segmentectomy...
22. What is the best experimental model system of...
23. What are the molecular and cellular mechanisms...
24. What is the best model/approach for...
25. What co-morbidities are present and how do...
26. What is the best antibiotic, dose, regimen and...
27. When and how (antibiotic, dose, regimen, route...
28. What types of biomarker(s) can be used to...
29. What are the baseline investigations to identify...
30. How should the severity of an exacerbation of...
31. What are the risk or protective factors for lung...
32. Which clinical and microbiological factors affect...
33. What are the best and most pragmatic functional...
34. Is cross-infection important, what are the best...
35. What is the role of different mucoactive agents...
36. What is the role of non-pharmacology, non-...
37. How best to prevent development of...
38. Should a severity and prognostic score for...
39. What is the best approach/score to evaluate...
40. What is the incidence and prevalence of...
41. What is the composition and function of host...
42. What are the genetic and epigenetic findings in...
43. What is the relationship between paediatric and...
44. What are the factors that predict radiographic...
45. What are the key factors leading to P. aeruginosa...
46. What are the simple, reliable microbiological...
47. Should there be paediatric-focused patient...
48. Is there an increased rate of primary immune...
49. What is the importance of host-pathogen-...

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