**POSITION PAPER**

**International consensus statement** **on core-outcomes and endpoints for clinical trials in children and adolescents with bronchiectasis**

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# **SUMMARY**

Improving paediatric bronchiectasis treatment requires high-quality research containing outcomes that meet study objectives and are meaningful for parents and patients. In the absence of any systematic review or agreement on the health outcomes that should be measured in paediatric bronchiectasis, we established an international, multidisciplinary panel of experts to develop a core-outcome set (COS) incorporating parent and patient perspectives. We first undertook a systematic review from which an outcome list of 21 items was constructed and separate surveys for ranking by parents and patients, and healthcare professionals developed. Theseinternational surveys had 562 respondents (201 parent/patients; 361 healthcare professionals) from 59 countries. The consensus five essential COS were quality-of-life, symptoms, exacerbation frequency, hospitalisations, and unscheduled healthcare visits. This international, parent and patient-informed consensus paediatric bronchiectasis COS should ensure studies have patient-focused outcomes that will facilitate clinical care and research worldwide, and also improve systematic reviews and GRADE-informed guidelines. We now need validated outcome measures for several items in the COS.

**Funding:** The ERS Children’s Bronchiectasis Education, Advocacy and Research Network.

# **KEY MESSAGES**

Rationale and approach

* Bronchiectasis is a neglected condition, particularly in children, for which there is a wide range of outcomes used for research and clinical care.
* As appropriate patient-focused and valid outcomes for intervention studies are important for the study itself and for future clinical practice, we sought to develop a core-outcome set (COS) for paediatric bronchiectasis for use in clinical practice and research settings globally via a systematic review and international surveys that included 201 parents and patients from 17 countries and 361 health professionals from 58 countries who rated the outcomes that they considered most important.

Findings

* Of the 10 highest ranked outcomes, eight were common to both the parent and patient group, and to healthcare professionals.
* Our international consensus-derived COS for paediatric bronchiectasis that is patient-focused derived five essential outcomes (quality-of-life, symptoms, exacerbation frequency, non-scheduled healthcare visits, and hospitalisations) and five important but not essential outcomes (time-to-next exacerbation, lost days from school or work, adverse events, lung function and burden of therapy).

Future directions and implications

* Future intervention studies on paediatric bronchiectasis should include, as a minimum, the patient-focused COS (especially the first 5 rated as essential) thus facilitating clinical care and research, while also allowing better comparisons between studies and improving the quality of systematic reviews and GRADE-informed guidelines.
* The next steps are deriving validated outcome measures for several of the COS items that do not currently exist, eg. paediatric-specific bronchiectasis QoL instruments.

**Search strategy and selection criteria panel for COS**

Our search strategy for the systemic review is outlined in the Appendix, pp 2-3. For the manuscript, we undertook a PubMed search before commencing our project in March 2021. We used the terms “child OR children AND bronchiectasis AND outcomes”. We did not identify any systematic reviews on the outcomes for paediatric bronchiectasis. Prior to manuscript submission, we repeated the search on the COMET and PubMed databases on the 6th of February 2023. There was one published COS for adult bronchiectasis and another study in progress using a COS for airway clearance techniques in adult bronchiectasis. However, no systematic review for outcome or COS were found for paediatric bronchiectasis.

**INTRODUCTION**

Improving children’s lung health is vital for future adult health and is one of the eight essential actions identified by the Forum of International Respiratory Societies to reduce the burden of respiratory disease and to improve global health.1 Bronchiectasis is one such chronic pulmonary disorder affecting both children and adults. It is characterised by a chronic or recurrent wet/productive cough, accompanied by airway infection and inflammation, and abnormal bronchial dilatation on chest computed-tomography (CT) scans.2

However, unlike bronchiectasis in adults, the abnormal airway dilatation in some children may be reversible if it is detected early when bronchial dilatation is mild and treatment is optimised.2,3,4,5 Programmes designed to improve the clinical outcomes of children with bronchiectasis rely upon its early diagnosis and treatment.3 Once considered rare in this age group, bronchiectasis is now recognised increasingly in both high and low-to-middle income countries.2,6 Nevertheless, despite the resulting high patient burden, needs, treatment costs and the opportunity to stabilise or even reverse bronchiectasis,7,8 it remains a neglected chronic respiratory condition.9,10

Improving the clinical outcomes of children and adolescents with bronchiectasis requires many approaches, including high-quality clinical research (e.g. intervention trials) with appropriate outcomes and endpoints that not only meet study treatment objectives, but are relevant for patients and their families. Outcomes are measurable variables or parameters (e.g. exacerbations), whilst endpoints refer to analysis of these parameters (e.g. exacerbation rate at 12-months post-intervention). Availability of patient-important outcomes and endpoints will improve individual clinical studies and guide treatment decisions. Including a core set of such outcomes (leading to patient and clinician-focused endpoints) for clinical trials is also important as this will improve comparability of findings across trials and allow data to be combined when conducting systematic reviews to inform guideline development and where the ‘Grading of Recommendations, Assessment, Development and Evaluations’ (GRADE) framework is the current gold standard. In GRADE, assignment of ‘high quality-of-evidence’ requires an assessment of certainty of evidence on all critical outcomes for the specific ‘Patient, Intervention, Comparison, Outcome’ (PICO) question, and not just for a subset of the critical outcomes.11 Having common outcomes in studies will enable data to be available for critical outcomes, which will lead to improved quality-of-evidence for PICOs and evidence-based guidelines.

Standardised sets of outcomes, which prescribe the minimum set of study outcomes and endpoint measurements, known as core-outcome sets (COS) are available for several respiratory conditions (e.g. clinical studies of chronic obstructive pulmonary disease exacerbations in adults.12). For adults with bronchiectasis, there is a COS limited to trials of long-term management of bronchiectasis.13 However, currently there are no publications or consensus on outcomes considered important in studies involving children and adolescents with bronchiectasis. The variability in outcomes and/or endpoints used for studies on bronchiectasis was evident in our evidence tables in the European Respiratory Society (ERS) clinical practice guideline (CPG) for the management of children and adolescents with bronchiectasis.9 Furthermore, during the developmental phase of the CPG, it became evident that core outcomes and endpoints important to parents and their children with bronchiectasis were sometimes different to those of clinicians.

To address this gap, an international, multidisciplinary panel of experts, comprising members of the Children’s Bronchiectasis Education, Advocacy and Research Network (Child-BEAR-Net),14 an ERS Clinical Research Collaboration network, aimed to develop a consensus on a set of well-defined patient-relevant outcomes and endpoints for clinical interventions, incorporating the views of people with lived experience of bronchiectasis in the COS-development process. The final COS is intended to inform the planning and conduct of future studies and improve their relevance for children and adolescents with bronchiectasis, unrelated to cystic fibrosis (CF).

# **METHODS**

This project comprised three stages: (1) a systematic review of outcomes for consideration by participants; (2) surveys to rate the selected outcomes; and (3) a consensus meeting to review and develop the final COS. The project was registered on the Core Outcome Measures in Effectiveness Trials (COMET) Initiative database <https://www.comet-initiative.org/Studies/Details/2487>.

# **Study groups and participants**

The scientific panel (the core author group) comprised all 24 committee members of the Children’s Bronchiectasis Education, Advocacy and Research Network (Child-BEAR-Net),14 an ERS Clinical Research Collaboration network, which included a European Lung Foundation (ELF) representative (JB), parent and patient advisory group (PAG) member (ZP), specialists in paediatric respiratory medicine (ABC, AB, AZ,CC, KD, MG, JG,AH, BK, OM, FM, AM, MP, AK), and paediatric experts in infectious disease (KG), radiology (EA), physiotherapy (CW), and lung function (AJC), a scientist and statistician (SY), two global leaders in adult bronchiectasis (ATH, JD), and the Cochrane Airways Group coordinating editor (also a primary care physician**,** RF). All have specific expertise related to bronchiectasis. The project was overseen by the Child-BEAR-Net steering group made up of eight Child-BEAR-Net committee members (ABC, KG, AK, AZ, AB, ATH as well as a PAG member (ZP) and the ELF representative (JB). Conflicts of interest were declared when commencing this project and again when submitting the manuscript.

For the survey, participants included parents of children and adolescents with bronchiectasis, patients aged >18-years who had bronchiectasis diagnosed during their childhood, and healthcare professionals responsible for the care of children and adolescents with bronchiectasis. Invitations for experts to participate were overseen by the steering group, but included the networks of the entire scientific panel. Specifically, healthcare professionals were invited to participate in the survey by Child-BEAR-Net extended network members and the paediatric members of the ERS via a direct email with a link sent to each members’ email address.Parents and patients were recruited via calls for participants on several websites (ELF, Child-BEAR-Net), ELF emails to parents, and also by Child-BEAR-Net scientific panel members’ networks who encouraged their patients to complete the survey either during the clinic consultation or later through a link provided via a printed quick response (QR) code.

## **Systematic review**

Development of a COS was one of the five initial objectives of Child-BEAR-Net14 that were in the proposal submitted by the Chairs (ABC, AK) to the ERS CRC committee (November 2020). Planning for the project were first discussed at the steering committee’s virtual meeting on 22 March 2021. The plan was then discussed at the virtual meeting (10 June 2021) of the scientific panel who agreed upon the overall approach (Figure-1) and inclusion and exclusion criteria for the systematic review (appendix p2).

We undertook a systematic review to identify outcomes and endpoints that have been used in previous and on-going studies in children with bronchiectasis to inform the surveys. Briefly, we undertook the following. Our database search strategies were randomised controlled trials and observational studies involving children and adolescents aged <18-years with bronchiectasis. Additionally, we reviewed the outcomes used in the ERS CPG.9 The search strategy (appendix pp 2-3) was designed and undertaken by the Cochrane Airways Group information specialist (Elizabeth Stovold). However, we excluded studies published prior to the Year 2000 in line with the availability of chest CT scans for clinical practice, as well as CF-based studies. The search was performed on the 25th of August 2021 by the Cochrane Airways Group’s Information Specialist (Elizabeth Stovold) using the criteria outlined in the appendix, on several databases (OVID MEDLINE, Cochrane Central Library and ClinicalTrials.gov). Its results were uploaded onto Rayyan (<https://rayyan.qcri.org/>).Two panel members (ABC, AJC) independently screened the titles and abstracts. Potentially relevant papers were retrieved and reviewed by the same two panel members. Additional papers and protocol registries were identified from the authors’ databases. Disagreements were resolved by consensus between the same two panel members, and *a priori* a third person (RF) was identified to adjudicate if necessary. Outcomes as reported in the included studies were counted.

Between March 2021 and November 2022, we held eight virtual meetings (two involved the Child-BEAR-Net14 steering group only and the rest were attended by the whole scientific panel) and one face-to-face meeting (on 3rd June 2022 in Bergamo, Italy) in addition to email correspondence. All meetings were chaired by ABC and AK. During these meetings, we reviewed data from the systematic review and made decisions on retaining or excluding outcomes for the surveys based upon whether they were applicable to most studies or only relevant for specific study questions (eg. levels of vitamin D and measures of movement, such as the 6-minute walk test).These decisions were made through iterative review and discussion.

**Surveys**

A pilot survey was undertaken using REDCap hosted by the Queensland University of Technology, and sent to the Child-BEAR-Net’s scientific panel, the extended Child-BEAR-Net network members, and two PAGs (CPG9 and the Australian Centre for Research Excellence for paediatric bronchiectasis; <crelungs.org.au/cre-parent-and-community-advisory-group>). Following feedback, the survey for parents and patients was modified for further clarity and a lay description for each outcome was provided.

The ELF representative (JB) then developed two versions of the survey, one for parents and patients, and another for healthcare professionals. Both surveys (Appendix, p32-39) included access to the systematic review data. The surveys were available in seven languages (English, German, Italian, Portuguese, Russian, Turkish, and Ukrainian) and was open from April to December 2022. Respondents were asked to rate the importance of each of the outcomes using a Likert-type scale with scores ranging from 1 to 5 (1=don’t know/no opinion, 2=not very important, 3=important, 4=very important, and 5=essential). For simplicity, the order of presentation was the same for all outcomes.

**Consensus meetings**

The results of both surveys were presented to the ELF PAG on the 8th of December 2022 at one of their regular meetings. The agenda for the meeting included a discussion of the results of the surveys**.** We held a final scientific panel meeting on the 18th of January 2023 virtually, chaired by ABC and AK to agree upon the core, intervention-specific, and discovery outcome measures. The outcomes for the COS were decided at the final meeting by selecting the top 10, as rated in the surveys. We did not apply any cut-off thresholds, but had agreed a-priori that we considered parents and patients selection were more important and the top 10 would be determined contingent upon their general applicability for studies on paediatric bronchiectasis. The number of outcomes in the COS was not decided a priori; the scientific panel discussed in the meeting and voting was undertaken. The healthcare professionals’ survey results contributed to the selection of the top 10 outcomes by providing a sense of importance of the outcomes from a practitioner’s perspective and used in the general discussion when selecting the final COS.

As full consensus was obtained, a second round of voting/ranking was not undertaken. The COS items were then categorised into ‘essential’, ‘important but not essential,’ and ‘limited importance’ by the scientific panel and the Australian PAG, based upon voting. The votes were undertaken using the same grading method for selecting outcomes during the development of the CPG9 for managing children and adolescents with bronchiectasis. Each panel member filled a template on an excel sheet and marked their score for each of the outcomes where scores of 1 to 3 were ‘limited importance’,
4-6=‘important but not critical’, and 7-9=’critical’. For the PAG, these were openly discussed without a formal voting process.

The process for selecting intervention-specific and discovery outcome measures were based on (a) not fulfilling selection of the top 10 (as described above), (b) whether the measures were applicable to all studies, and (c) whether or not the biomarkers currently exist in the current literature. The last two criteria were based on the included studies (Table S1, appendix p5) and the scientific panel’s knowledge and experience. The items selected for the ‘discovery outcomes’ were based upon biological samples and endpoints used commonly in bronchiectasis studies in the absence of currently available validated biomarkers for bronchiectasis. Measurements for the outcomes were based on the data available from the systematic reviews and the scientific panel’s knowledge and endorsed by email discussions.

**Data analysis**

Only fully completed surveys were accepted. The ‘weighted average score’ of each outcome was calculated (using Survey Monkey). The ‘weighted average score’ takes into account the number of responses to each option and multiplies that by the weighted number for each choice (numbered 1 to 5 in our survey), totals were added together, and then divided by the overall number of respondents i.e. (No. of responses x 1) + (No. of responses x 2) + (No. of responses x 3) + (No. of responses x 4) + (No. of responses x 5) / total number of responses. We used descriptive statistics to present the age of the person with bronchiectasis and when their bronchiectasis was diagnosed, and graphs to display the weighted averages for each outcome, stratified by survey group, produced using Excel (Microsoft Office),to participants at the consensus meetings. Risk of bias was deemed not applicable for our systematic review and survey results,and statistical analyses for these were not undertaken.

Role of funder

The study was partially funded by the ERS as part of Child-BEAR-Net. The funder had no role in the study design; collection, analysis, and interpretation of data; writing of the report; or the decision to submit the paper for publication.

# **RESULTS**

The search identified 1603 potential publications; 98 full-text articles were retrieved, and 79 articles fulfilled the inclusion criteria. The PRISMA diagram is depicted in the appendix (appendix Figure-S1, p4). The 79 included articles are summarised in the appendix (Appendix Table-S1 pp 5–31) and grouped by: (A) randomised controlled trials (RCTs) that are either published (appendix subheading A1, pp 5-10) or in progress (appendix subheading A1, pp 11-13), and (B) observational studies that are either published (appendix subheading B1, pp 14-29), or in progress (appendix subheading B1, p30). 52 individual outcomes were reported in these studies.

Consensus discussion of the results of the systematic review among the scientific panel members at the virtual and face-to-face meetings **l**ed to the identification of 21 outcomes that were considered relevant for further development of the COS from the possible 52 outcomes used in the included studies (Table-S1, appendix pp 5-31). The frequency of the use of the 21 outcomes in the included studies are presented in Table-1. The agreed set of 21 outcomes was used for inclusion and rating in the pilot survey followed by the two (parents and patients, and health professionals) international surveys.

There were 484 respondents to the parent and patient version of the survey, of whom 217 were excluded (as they were neither a parent of a child or adolescent with bronchiectasis nor an adult who was diagnosed with bronchiectasis as a child). This resulted in 267 eligible respondents of whom 201 from 17 countries completed all sections of the survey (appendix, p39). The median age of the persons with bronchiectasis was 9·0 years (IQR 5·9, 13·0) and their bronchiectasis had been diagnosed 4·2 (IQR 2·0, 8·0) years earlier (from time survey was answered). In addition, 447 responded to the healthcare professional survey version, of whom 37 were excluded (as they were not responsible for the care of either children or adolescents with bronchiectasis), leaving 410 eligible respondents of whom 361 healthcare professionals from 58 countries completed all sections of the survey (see appendix, p39).

The weighted average of the outcomes for both surveyed groups are presented in Figure-2 (and in tabular form, appendix, Table-S2, p41). Of the 10 highest ranked outcomes (Table-2), eight were common to both the parent and patient group, and to healthcare professionals. However, for the remaining two items, the parent and patient group included ‘adverse events’ and ‘non-scheduled healthcare visits’ in their top 10, whereas healthcare professionals included ‘sputum microbiology’ and ‘validated cross-sectional imaging’. Nonetheless, the three highest ranked outcomes were common to both groups (quality-of-life [QoL], exacerbations, and hospitalisations), although not in the same order. Four outcomes (blood [e.g. C-reactive protein, Interleukin-8], sputum [e.g. neutrophil elastase], and breath biomarkers, and nasal swab microbiology) were rated <3·00 by both groups. The rest of the outcomes were rated >3·00. The order of the other outcomes also varied between the parent and patient group, and healthcare professional surveys.

The ELF-PAG meeting was attended by seven people whilst 25 participants attended the final consensus meetings: 19 scientific panel members and 6 Australian PAG members. Our choice of the COS was based upon the top 10 (three grouped into a single exacerbation group) outcomes chosen by parents and patients **in** the surveys. We achieved total consensus by voting in the meeting(s) upon the outcomes that made up the COS. These were then later rated into essential/important but not essential categories by each scientific panel member returning their e-paper based vote which was collated and then summarised (by ABC)**.** We grouped the rest of the remaining outcomes into ‘selected outcomes based upon intervention type’ and ‘discovery outcomes’ (Table-3).

# **DISCUSSION**

We have developed an international-derived, patient-focused consensus COS for paediatric bronchiectasis for use in clinical practice and research settings globally. Ideally, these are also used for clinical monitoring of the patient’s bronchiectasis health status and response to interventions. In addition, we have suggested other outcomes (‘selected outcomes based upon intervention type’ and ‘discovery outcomes’) and provided a description of the measurements for the core outcomes. All these outcomes were informed by a systematic review and ranking by 562 survey respondents that included parents of children and adolescents with bronchiectasis, adults who had bronchiectasis diagnosed during childhood, and clinicians with expertise in paediatric bronchiectasis.

Our study is the first to undertake a systematic review of the outcomes used for paediatric bronchiectasis studies (RCTs and observational studies), and the first to derive a COS, and other outcomes and endpoints, for this chronic pulmonary disorder in children and adolescents. The absence of consistent important outcomes, including a COS for studies on bronchiectasis in children and adolescents, has been a clinical research gap, which was evident when we undertook writing the ERS CPG for managing bronchiectasis in this age group.9 Our study fills this gap, and its importance is enhanced by not only our international approach, but also from the combined views of parents, patients, and healthcare professionals. The need for outcomes that reflect parent and patient priorities is recognised increasingly19 and is one of the key elements recommended by the COMET initiative (https://www.comet-initiative.org/).

Having a COS to inform the choice of endpoints in intervention studies will also benefit future systematic reviews for GRADE-based guidelines. For example, in one of our CPG’s PICO questions, there was high certainty of evidence that using long-term macrolides reduces respiratory exacerbations,20 yet the recommendation was graded as low. This was because grading is based upon the quality of certainty of evidence for all critical outcomes for the PICO and, in this particular RCT,20 data were missing for three of the PICO’s essential outcomes (lost days of work, time-to-next exacerbation, and QoL).9

Endpoints in clinical trials need to be “clinically relevant, sensitive to treatment effect, and measurable and interpretable”.21 Currently, although validated paediatric cough-specific QoL questionnaires have been used in paediatric bronchiectasis RCTs,22,23 there are no validated paediatric QoL instruments that are specific for bronchiectasis. Moreover, despite cough being the most common feature of bronchiectasis, cough-specific QoL measures are generic rather than disease-specific. Since disease-specific QoL instruments are more sensitive than generic ones,17 development of a paediatric bronchiectasis QoL tool is an important clinical research gap.

Respiratory exacerbations (including hospitalisations) were ranked highly by both parents and patients, and healthcare professionals. This is unsurprising as several aspects of exacerbations featured prominently in our previous international survey on clinical and research priorities for children and adolescents with bronchiectasis that involved 225 parents of children with bronchiectasis and patients with bronchiectasis diagnosed in childhood.7 Respiratory exacerbations can be measured relatively easily, although adherence to a standardised definition is needed. Fortunately, there is now an ERS-endorsed paediatric-specific definition of bronchiectasis respiratory exacerbations for clinical research.18 This development was in response to our previous work showing marked variability in definitions of respiratory exacerbations used in clinical studies. Except for ‘burden of therapy’, other outcomes (symptom duration/profile, adverse events, lung function and lost days from school/work) that are part of our developed COS are also measured relatively easily and used previously in paediatric bronchiectasis RCTs assessing short22,23 and long-term interventions.20 The two outcomes that were in the top ten of the health professionals’ survey, but not in the top ten of the patients/parents’ survey were sputum microbiology and validated cross-sectional imaging (Table-2). Both these outcomes are objective and thus important for some, but not all types of studies. Microbiology is arguably important for antibiotic, mucolytic or anti-inflammatory-based interventions, but not for other interventions, such as exercise. Validated cross-sectional imaging data will only be applicable in relatively long (≥12-months) interventions as such changes take time to occur and involve additional radiation. Based upon science and clinical foundations, these were considered by the scientific panel as belonging in the second tier of outcomes.

An adult bronchiectasis COS for long-term treatment studies is also available.13 The adult proposal consists of 18 outcomes (appendix, p42), but it is still incomplete despite the large numbers already proposed. Irrespectively, a paediatric-specific COS is necessary to advance the field and our COS is applicable for both short and long-term intervention studies in paediatric bronchiectasis. It is now recognised that while paediatric bronchiectasis shares features with the disease in adults, there are also important differences.2 Indeed, as children differ from adults in their physiological, pharmacological, developmental, social, and psychological characteristics, there is an increasing appreciation of the need for paediatric-based trials instead of extrapolating from adult data.24 Furthermore, in bronchiectasis, unlike current data in adults, recent research has shown that paediatric bronchiectasis may be reversible over time if detected early in the course of the disease and treated effectively.2,5,9 Other important disease-specific differences include significantly different pathogen profiles (bacterial25 and microbiota26), age-related immunological responses,27 common underlying aetiologies,5 and definition of bronchiectasis exacerbations.18 The argument for paediatric-specific studies in all diseases is now mature24 and includes paediatric bronchiectasis.7

In line with the current guidelines for managing bronchiectasis for both children9,28 and adults,28-30 we did not consider the possible different aetiologies (other than excluding CF) when developing the COS as we believe the attitude towards QoL for bronchiectasis would be universal. Furthermore, there are far too many aetiologies to consider and in children the most commonly ascribed cause is either idiopathic or post-infectious.2

Our study does however have some limitations. First, while 562 people completed all survey sections, many others responded, but did not fully complete the surveys (appendix, p39). Thus, we are unaware whether the ranking of the items would differ if more people had completed these surveys. Second, numbers of respondents from individual countries were limited and may not be representative of the broader community of patients with bronchiectasis, their families or healthcare professionals responsible for their care. Third, older children and adolescents aged <18-years were not surveyed directly, and while their parents may have sought their opinions, this could not be measured and as such**, there is potential skewing in parent versus patient responses.** Fourth, the priorities of participating parents may have changed over time depending upon the clinical state and developmental stage of their child. Fifth, while adverse events were ranked highly by parents and patients, this was not reflected in the rankings of healthcare professionals. This was unexpected given that reporting adverse events is required in all intervention studies. We therefore included adverse events in the COS as we prioritised patient/parent responses. Furthermore, reporting of adverse events is required in all intervention studies. Sixth, although our study was registered with the COMET initiative, we did not submit a protocol prior to initiating this project. Finally, we did not discuss grouping our COS into domains (eg. physiological or clinical, life impact, etc) as undertaken in a recent COS article for COVID-19 studies.31

While we have derived an international consensus for paediatric bronchiectasis studies, we now need to develop the appropriate tools for all the COS measures. As outlined in Table-3, not all the COS currently have validated measurement tools. Of utmost importance is the development of a paediatric-specific bronchiectasis QoL, the highest ranked priority outcome of parents and patients. Also, we recognise the potential hurdles for implementing our COS; for example, requiring study participants to have sufficient health knowledge to report outcomes such as exacerbation symptoms, and the resource implications for collecting data in studies with limited funding. Nevertheless, the minimum COS, which includes the 5 outcomes categorised as ‘essential’ (Table-3), is inexpensive to collect and achieved relatively easily by training both parents and research staff.

Bronchiectasis remains one of the most neglected pulmonary disorders32 especially so in children.10 There is also marked inequality in service delivery between various chronic respiratory diseases, including bronchiectasis, which may impact adversely upon outcomes.33 Indeed, the need for better health services and research for improving the lives and outcomes of children and adolescents with bronchiectasis, as well as improving the QoL of their families, was highlighted recently by an international parent and patient survey on their clinical needs.7 By adopting this internationally-derived, patient-focused COS (Table-3) there is an opportunity to help advance the field and satisfy the demands of regulatory authorities as “clinical trials are only as credible as their outcomes”.34 Widespread adoption of this COS will mean that children with bronchiectasis and their families will benefit from healthcare informed by evidence from higher-quality studies that utilise patient-important outcomes and endpoints and have reduced reporting bias.35 Moreover, use of the COS will reduce heterogeneity in the paediatric bronchiectasis literature, leading to more robust meta-analyses and clinical practice guidelines,36 and reduced research wastage.35

Author Contributions

This position statement was conceived by ABC who co-designed it with other members of the Child-BEAR-Net steering group (AK, KG, AB, JB, ZP, AZ, ATH). ABC was responsible for the day-to-day management/running of the project including organisation of the consensus meetings.ABC and AJC screened the literature searches for the systematic review bronchiectasis outcomes with planned adjudication by RF, with the data summarised by ABC. JB set-up the Survey Monkey questionnaires, analysed and summarised the results, and prepared all the figures for the results. **All authors recruited survey participants and contributed to meeting discussions** The manuscript was drafted by ABC and edited by KG and AK. All authors have full *access* to all the data reported in the study, further edited and approved the manuscript. ABC and KG accessed and verified the data. ABC, KG and AK accept responsibility to submit for publication.

Acknowledgment

Child-BEAR-Net is funded by a ERS Clinical Research Collaboration grant. ABC is supported by an Australian National Health Medical Research Council Senior Practitioner (NHMRC) Fellowship (APP1154302). AJC is supported by a NHMRC Postgraduate Scholarship (APP2003334). The funding sources had no involvement in the study including its design, methodology or manuscript.

We thank Elizabeth Stovold, Information Specialist from the Cochrane Airways Group, for designing and undertaking the literature searches. We are grateful to PAGs from the ELF and the Cough and Airways Group (Brisbane) for their reflections and advice on several occasions. We also thank all the people who responded to the survey. We appreciate the support for Child-BEAR-Net from the ERS CRC office, Elise Heuvelin, Celine Genton and Prof Joanna Pepke-Zaba. All authors have access to all the data reported in the study.

Declaration of Interest statement

Drs Alexopoulou, Bush, Constant, Douros, Fortescue, Hector, Karadag, Hill, Kantar, Mazulov, Midulla, Proesmans, Yerkovich have nothing to disclose. Ms Boyd, Powell and Wilson, and Mr Collaro also have nothing to disclose. Drs Chang and Grimwood report grants from the NHMRC and NHMRC managed grants (Medical Research Futures Fund), Australia, during the conduct of the study. Dr Chang is also an independent data management committee member for clinical trials for Moderna (COVID-19 vaccine) and of an unlicensed vaccine (GlaxoSmithKline), and monoclonal antibody (AstraZeneca), received fees to the institution for consulting on study designs for Zambon and Boehringer Ingelheim, airfares for travel from the ERS and Boehringer Ingelheim, and personal fees for being an author of two UpToDate chapters that are outside the submitted work. Dr Chalmers reports personal consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Insmed, Grifols, Pfizer, Jansen, Antabio and Zambon that are outside the submitted work but related to bronchiectasis in adults. Dr Chalmers reports grants from AstraZeneca, Boehringer Ingelheim, Novartis, GlaxoSmithKline, Gilead Sciences, Insmed, Grifols and Genetech that are outside the submitted work but related to bronchiectasis in adults. Dr Grigg reports unrestricted grants from OM Pharma and Mariomed Biotech, and receiving wheeze detection equipment without cost from OMRON. Dr Grigg also reports personal fees for advisory board membership from OM Pharma, GlaxoSmithKline and AstraZeneca, being a trial investigator for AstraZeneca, lecture from Sanofi and expert testimony for medical advice to a London coroner regarding the case of a child who died of asthma, outside the submitted work. Dr Zacharasiewicz reports personal fees for lectures from AstraZeneca, Chiesi, Vertex Pharmaceuticals, and Sanofi and travel from Vertex, that are outside the submitted work. Dr Moeller reports grants to his institution from Vertex. Dr Griese reports personal consulting fees and honoria for lectures/presentations and advice in an adjudication board from Boehringer Ingelheim and for advice on study development from Roche, outside the submitted work.

**FIGURE LEGENDS
Figure-1**: Overall approach for developing our international consensus.

PAG = Parent Advisory Group.

**Figure-2**: Weighted average scores\* for both parent and patient, and healthcare professional (HCP) surveys. BMI=body-mass index; CT=computed tomogram; MRI=magnetic resonance imaging. \*Weighted average scores were calculated by Survey Monkey which takes into account the number of responses to each option and multiplies that by the weighted number for each choice (numbered 1 to 5 in our survey), totals were added together, and then divided by the overall number of respondents i.e. (No. of responses x 1) + (No. of responses x 2) + (No. of responses x 3) + (No. of responses x 4) + (No. of responses x 5) / total number of responses.

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