



Children's Bronchiectasis Education Advocacy and Research Network (Child-BEAR-Net): an ERS Clinical Research Collaboration on improving outcomes of children and adolescents with bronchiectasis

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A newly funded ERS Clinical Research Collaboration network (Child-BEAR-Net) will create vital infrastructure to progress education, advocacy and research collaboration in paediatric bronchiectasis <https://bit.ly/3ku2Xbx>

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Introduction

Child-BEAR-Net (Children's Bronchiectasis Education, Advocacy and Research Network) is a new European Respiratory Society (ERS)-funded Clinical Research Collaboration (CRC). Child-BEAR-Net is an international collaboration whose overall aim is to enhance the lives of children and young people (henceforth referred to as children) with bronchiectasis, including their parents, through education, advocacy and research.

Worldwide, bronchiectasis contributes to chronic respiratory morbidity in both affluent [1, 2] and low-to-middle income countries (LMICs) [3]. Despite an increasing recognition and renewed interest in bronchiectasis in adults, the ERS [4] describes bronchiectasis as "one of the most neglected diseases in respiratory medicine". Bronchiectasis describes the final common pathway for multiple disorders, and it is critical to diagnose any underlying disease, especially where specific treatments are available [5, 6].

In children, the burden of bronchiectasis is particularly high among disadvantaged Indigenous populations in affluent countries (~1 in every 63–68 children [7]) and LMICs (where it is being diagnosed increasingly [8]). Bronchiectasis is also being recognised more frequently in affluent countries [6, 9]. However, there are few reliable prevalence estimates and extrapolating published data suggests its incidence ranges widely (0.2–735 per 100 000 children) [9]. Globally, aetiology also varies between countries. For example, bronchiectasis associated with HIV is prevalent in countries like South Africa, while post-infectious bronchiectasis is more common in other LMICs [9, 10].

Although bronchiectasis in adults and children have features in common, such as chronic cough, lower airway infection and inflammation, there are important differences in airway microbiology and approaches

to management and prognosis [6]. A challenge for paediatricians is how to prevent bronchiectasis and/or its progression [6], especially as many adults diagnosed with bronchiectasis have had symptoms from childhood [11, 12]. Indeed, retrospective [13, 14] and prospective [15] data demonstrate lung function improves significantly with optimal care and can even be normalised, despite often challenging clinical settings as in Indigenous Australian children with bronchiectasis living in remote-rural communities [16]. In contrast, when access to optimal care is limited, the morbidity and mortality of bronchiectasis remains high [17].

While the clinical focus in adults is on symptom control and preventing hospitalisation, in children it is on reversing the disease when possible and halting its progress [6]. Cylindrical airway dilation in children is reversible if treated promptly [6, 10, 18]. This may seem counter-intuitive when the definition of bronchiectasis includes "irreversibility", which was coined before computed tomography scans became available. However, more than half a century ago, astute paediatricians recognised that childhood bronchiectasis can be prevented, and even reversed [19, 20], in many treated cases, while those with persistent lower airway infection (manifested by chronic wet cough [21]) developed chronic lung disease.

Thus, in children, early diagnosis and research-informed treatment are vital for reducing the future burden of bronchiectasis. Education strategies alerting primary care physicians and parents to the significance of chronic wet cough and its management, will facilitate earlier diagnosis and even in some cases prevent bronchiectasis developing. Advocacy is also necessary for promoting optimal services and to reduce the current inequity afforded to children with bronchiectasis as well as their families.

Child-BEAR-Net will begin with projects, endorsed by the European Lung Foundation (ELF) parent advisory group, that address questions and issues raised from the ERS paediatric bronchiectasis clinical practice guideline (CPG) [5]. Child-BEAR-Net, like our CPG, encompasses all causes of bronchiectasis other than cystic fibrosis (CF). Our five specific objectives (table 1) align with the ERS CRC's articulated aims [22]. Child-BEAR-Net is supported by the paediatric assembly and is one of several paediatric ERS CRCs (e.g. SPACE [23]). We are linked with the ERS adult bronchiectasis CRC [24] and other external groups focused on paediatric bronchiectasis (figure 1).

Rationale for our objectives

Quality standards for managing children with bronchiectasis

The quality of care patients receive is important in clinical practice. For bronchiectasis, the quality of bronchiectasis care is inequitable and most marked when comparing outcomes between Australian Indigenous and non-Indigenous adults, where the former group die approximately 22 years earlier than the latter [17]. There is also reported inequity [25] between children with bronchiectasis and those with CF. Indeed, in many countries, children with bronchiectasis are still managed as an "add-on" to CF centres, where they may receive care that does not address their particular needs. For instance, some centres use DNase, an inhaled medication that is beneficial for people with CF, but causes harm in those with bronchiectasis unrelated to CF [5]. The issues of combined clinics and poor accessibility to various health experts (particularly chest physiotherapists with specific paediatric expertise) were highlighted by the parent advisory group members.

Access to high-quality paediatric care for children with bronchiectasis is imperative for helping to prevent pulmonary decline, improving quality-of-life, outlook and lung function [13, 16], and reducing respiratory exacerbations. It should include identifying aetiologies with specific treatment requirements, comorbidities and environmental/lifestyle and psychological factors (i.e. treatable traits) [6, 26]. Implementing

TABLE 1 Objectives of Child-BEAR-Net

- 1) Build a collaborative international network of consumers, clinicians, clinical researchers and biomedical scientists with expertise in paediatric bronchiectasis to lead clinically important research priorities in Europe and beyond;
- 2) Create standardised multinational bronchiectasis registries relevant in both affluent and low-to-middle income countries;
- 3) Develop a "quality standards" document based on the ERS paediatric clinical practice guideline for managing bronchiectasis in children and young people [5];
- 4) Establish a standardised definition of respiratory exacerbations for clinical research; and
- 5) Establish a consensus of core outcomes/endpoints for evaluating interventions relevant to consumers and considered important by clinicians.

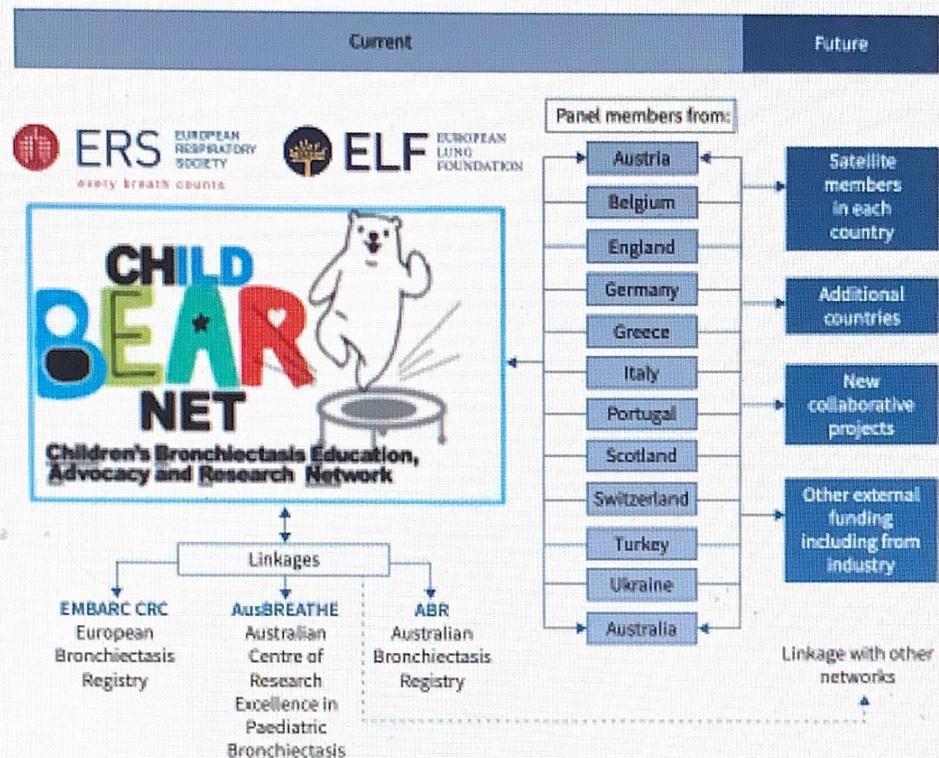


FIGURE 1 Current and future schematic representation of Child-BEAR-Net. Weblinks are: Child-BEAR-Net: www.improveBE.org; EMBARC CRC: <https://www.bronchiectasis.eu/>; AusBREATHE: <https://crelungs.org.au/>; ABR: <https://lungfoundation.com.au/research/our-research/bronchiectasis/>. We also hope to build future links with other networks.

standardised care and having available “quality standards” are important steps for future policy development and benchmarking practice.

A consensus definition of respiratory exacerbations for clinical research

Managing exacerbations is a key component of bronchiectasis care and one of the three top issues identified by parents (in an ELF patient survey) [27]. Exacerbations are particularly important as they are associated with increased respiratory symptoms and psychological stress, impaired quality of life, accelerated lung function decline (-1.9 forced expiratory volume in 1 s % predicted per hospitalised exacerbation) and substantial healthcare costs [14, 28]. Exacerbation rates are an indirect way of evaluating bronchiectasis management. Furthermore, respiratory exacerbations are one of the most important clinical outcomes and are included in every intervention in our CPG [5]. Importantly, these outcomes for our CPG were based on voting by the parent advisory group and task force panel.

Non-recognition of exacerbations risks delayed treatment, which may be harmful, whilst adequate treatment of exacerbations helps to maintain lung function. Increased awareness among physicians of well-defined symptoms and signs of exacerbations is required to ensure prompt intervention. Thus, our CPG included a definition of exacerbations for clinical use, which is substantially different from the adult-derived consensus definition [29] with respect to symptom duration and assessment type, as the adult definition is only for research purposes. However, a consensus definition of pulmonary exacerbations for research purposes in children is now needed, given the importance of exacerbations as an outcome measure in clinical trials. This will complement our CPG-defined clinical exacerbation [5] and is also an objective of another ERS task force (TF-2020-17).

A consensus of core outcomes/endpoints for evaluating interventions

A set of consensus-driven and patient-relevant outcomes/endpoints for clinical interventions will improve the relevance of future studies. The variability of the outcomes used in studies is evident in our evidence

tables in the ERS paediatric bronchiectasis CPG [5]. Moreover, when developing the CPG, it became evident that core outcomes and endpoints important to parents/children with bronchiectasis were not always aligned with those of clinicians. Thus, one of Child-BEAR-Net's objectives is to develop a consensus on a set of well-defined patient-relevant outcomes/endpoints for clinical interventions that will inform future trials.

Create standardised multinational bronchiectasis registries

The importance of bronchiectasis registries is demonstrated by the successful ERS CRC-supported adult bronchiectasis registry (EMBARC) [24], reflected in its extensive collaboration networks and publications. Currently, the only bronchiectasis registry to include children is the Australian Bronchiectasis Registry (ABR) [30]. The ABR, initially embedded within EMBARC (with additional fields created), has now transferred its platform to REDCap, a web-based system that is widely used. Availability of a registry will promote identification of underlying causes of bronchiectasis. Our planned registry allows each leader in their country to create and own their national registry that can be easily combined, or compared, with registries of other countries, pending ethical clearances. Data points with field dictionaries will be agreed upon by the group; these fields will include underlying aetiologies, microbiology, lung function and treatment aspects. Future aims will be outlined on the website.

Our team, further information and the future

Our panel is both inclusive and multidisciplinary, and includes young researchers across 11 countries, whilst remaining Europe-focused in this current phase. Many in the team were members of the paediatric bronchiectasis CPG [5]. Child-BEAR-Net has an eight-member steering committee, a scientific manager and an additional 15 core members (www.improveBE.org). We plan for future satellite members from the panel's respective countries (figure 1). Pending further funding, future projects could include biobanking of specimens. We hope to engage industry partners and experts from other countries whose interests align with Child-BEAR-Net's aims and that they will join us and build their local teams with support from the steering group. To join Child-BEAR-Net as a satellite member or to obtain support in improving patient care, please contact your country's leader/co-leader listed on the website. To join as a new country leader, please contact kidslungresearch@qut.edu.au

Summary

Child-BEAR-Net will create vital infrastructure to progress education, advocacy and research collaboration in paediatric bronchiectasis (see www.improveBE.org). With the ELF and parent advisory group, our initial planned projects respond to identified needs and complement the ERS paediatric bronchiectasis CPG [5]. Our CRC will advance bronchiectasis by raising awareness and encouraging an evidence-based approach to diagnosis and management. In doing so, this will improve the lives of the many children at risk of, or affected by, bronchiectasis.

Other network members: Efthymia Alexopoulou, Leanne Bell, James D. Chalmers, Andrew Collaro, Carolina Constant, Kostas Douros, Rebecca Fortescue, Matthias Giese, Jonathan Gigg, Andreas Hector, Bulent Karadag, Oleksandr Mazulov, Fabio Midulla, Alexander Möller, Marijke Proesmans and Christine Wilson.

Conflict of interest: A.B. Chang reports grants from National Health and Medical Research Council, Australia (NHMRC) during the conduct of the study; and that they are an independent data monitoring committee member for an unlicensed vaccine (GlaxoSmithKline), and advisory member of study design for unlicensed molecule for chronic cough (Merck), and an independent data monitoring committee member for a COVID-19 vaccine for children (Moderna), outside the submitted work. J. Boyd is an employee of the European Lung Foundation. A. Bush has nothing to disclose. K. Grimwood reports grants from National Health and Medical Research Council, Australia (NHMRC), during the conduct of the study. A.T. Hill has nothing to disclose. Z. Powell has nothing to declare. S. Yerkovich has nothing to disclose. A. Zacharasiewicz has nothing to disclose. A. Kantar has nothing to disclose.

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