




# The European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) ERS Clinical Research Collaboration

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The European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) is the ERS Clinical Research Collaboration born to develop scientific, educational and advocacy activities for bronchiectasis at an international level <http://ow.ly/EHr030mxEcC>

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The European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) was established in 2012 as a collaborative group within the Respiratory Infections Assembly of the European Respiratory Society (ERS) with the objective of creating a European bronchiectasis registry, harmonising existing databases, and identifying opportunities to raise the profile of bronchiectasis at an international level [1].

Bronchiectasis has been always described as one of the most neglected respiratory diseases, with no licensed treatments in the face of a substantial burden in terms of poor patient quality of life and increasing healthcare costs [2, 3]. Although the label of “orphan disease” does not apply to bronchiectasis in light of recent epidemiological data, it has been used historically to reflect the lack of interest that scientists, clinicians, regulators and funders had in this disease until one decade ago. As an example, the recommendations from the British guidelines on bronchiectasis published in 2010 were almost exclusively based on expert opinion because of the absence of high-quality evidence [4].

The EMBARC project was born within an environment where many doubted whether bronchiectasis was really a disease, and where most management was based on paradigms developed in cystic fibrosis or

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chronic obstructive pulmonary disease. Research into bronchiectasis was limited and came mainly from the UK, Spain, the USA and Australia. A lack of European patient organisations meant the absence of a clear voice from patients suffering from this disease. Funders did not recognise bronchiectasis as a problem and so rarely provided funding for bronchiectasis research and, finally, there were no internationally recognised standards of care.

6 years since its establishment, EMBARC is now recognised as one of the most successful Clinical Research Collaborations (CRCs) within the ERS [5]. EMBARC has been supported by a large and enthusiastic community of more than 150 centres in more than 40 countries. One of the keys to its success has been the support of the European Lung Foundation, which established a European advisory group of people with bronchiectasis and their caregivers, providing the first “patient voice” for bronchiectasis in Europe, and all EMBARC projects and meetings now involve patient representatives [6]. With the support of international partners and the ERS, the profile of bronchiectasis in Europe and the available evidence have improved. In this article, we list some of the achievements of the EMBARC project.

EMBARC was approved as an ERS CRC in 2013 with the primary objective of developing a pan-European, prospective registry of adults with bronchiectasis following the recommendations from the European Union Committee of Experts on Rare Diseases (study website: [www.bronchiectasis.eu](http://www.bronchiectasis.eu)). The detailed protocol was published in 2016 [7]. More than 14000 patients had been recruited up to September 2018, with up to 4-year follow-up now available for some patients. Research priorities in bronchiectasis were identified in the early phase of the CRC by a Europe-wide group of experts and patients/carers (the EMBARC Roadmap Study Group), with the aim of guiding collaborative research and supporting international stakeholders in designing calls for funding in the field [8]. EMBARC also provided consensus guidance on cross-infection issues in bronchiectasis and led a consensus working group of international experts who worked together for >1 year to develop a simple and operational definition of bronchiectasis exacerbation for use in clinical trials [9, 10]. Further consensus documents on the definitions of bronchiectasis, chronic infection and eradication are planned for 2018 and beyond, with the intention that these will be used in planning clinical trials. More than 10 datasets from different European countries have been aligned and designated as the FRIENDS dataset (Facilitating Research Into Existing National DataSets). Their analysis ended up with >10 original publications evaluating disease severity, ageing, radiology, aetiologies, phenotypes and endotypes, the role of *Pseudomonas* and exacerbations, and the impact of comorbidities in bronchiectasis [11–23]. EMBARC supported the development of an international task force of experts and patients who published in September 2017 the ERS guidelines for the management of adult bronchiectasis [24]. In line with the fact that the registry can provide crucial insights in planning and executing clinical trials, not only in terms of feasibility but also in providing patient input into the trial design and validation of end-points, EMBARC is currently supporting three randomised controlled trials on new drugs in bronchiectasis (one is registered at [ClinicalTrials.gov](http://ClinicalTrials.gov) with identifier NCT03696290) and further trials, including pragmatic ones, are planned. EMBARC promoted three international conferences specifically focused on bronchiectasis, which have been held in Hannover (Germany) in 2016, Milan (Italy) in 2017 and Washington, DC (USA) in 2018. In 2019, EMBARC will host an ERS research seminar in Barcelona (Spain) jointly with the ERS CRC SHARP (Severe Heterogeneous Asthma Research collaboration, Patient-centred), addressing the overlap between bronchiectasis and airways disease [25]. Finally, other investigators from several other countries outside of Europe are developing bronchiectasis research infrastructures using the EMBARC platform; India and Australia are already working collaboratively with EMBARC (with their respective websites at <https://hicservices.dundee.ac.uk/rri> and <https://lungfoundation.com.au/research/our-research/bronchiectasis/>). EMBARC is also central to the European Reference Network (ERN) for rare respiratory diseases (ERN-LUNG) core network for bronchiectasis [26]. Some of the most successful initiatives developed by EMBARC are represented in figure 1.

Although important achievements, especially from a clinical and epidemiological point of view, were reached during the first 3 years of EMBARC, some important research priorities still remain unexplored. Heterogeneity of the disease remains the greatest clinical challenge. There are no licensed therapies for bronchiectasis and clinical trials in bronchiectasis have been inconsistent, perhaps because we have not yet identified the endotypes of bronchiectasis that respond to specific therapies such as inhaled antibiotics, macrolides and mucoactive drugs [27, 28]. Translational and cooperative studies will be needed in the future to investigate the pathophysiology of bronchiectasis, and to identify treatment response endotypes. Some aspects of bronchiectasis, including inflammatory pathways, the microbiome, proteomics and genomics, are not sufficiently studied. Their investigation on a large scale could help to better understand bronchiectasis pathophysiology, to better phenotype patients and individualise their management.

A second phase of EMBARC as an ERS CRC (namely EMBARC2) has been funded from 2017 to 2020 and is keen to have on board the highest number of ERS members possible. EMBARC2 aims to phenotype

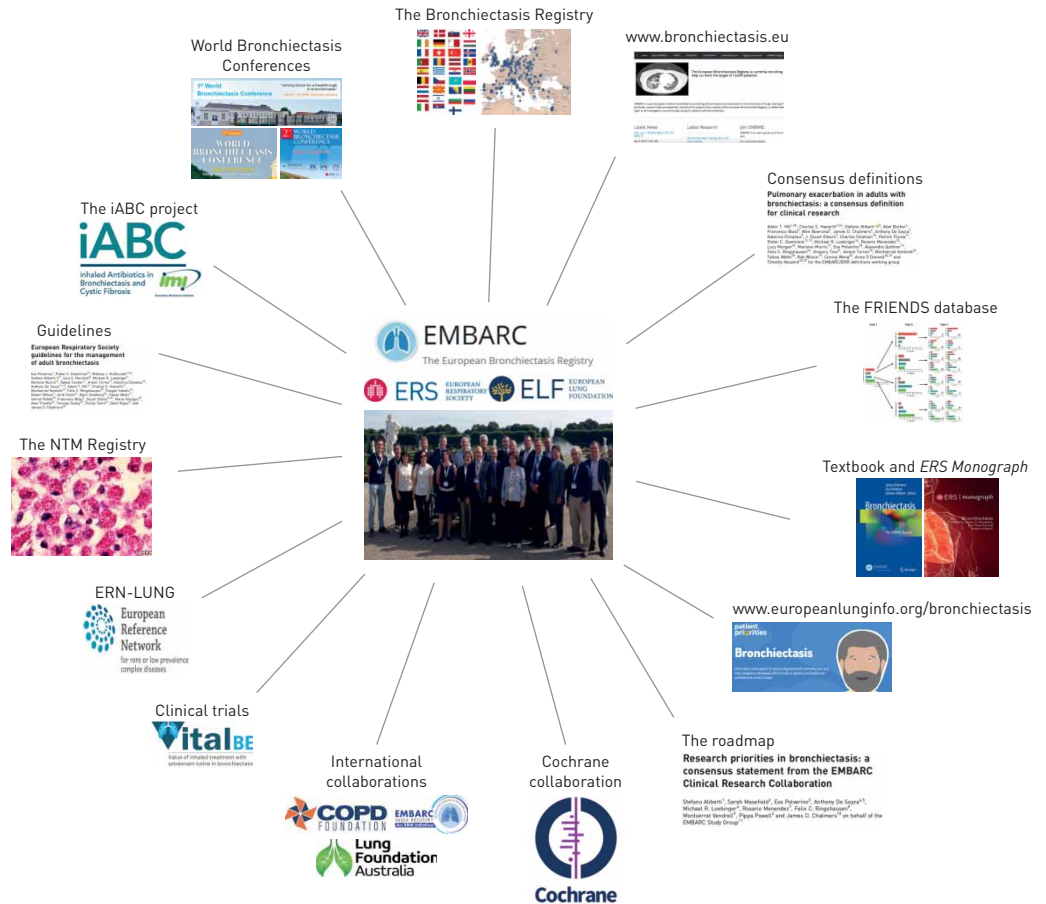


FIGURE 1 Initiatives developed by the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) up to 2018. iABC: Inhaled Antibiotics in Bronchiectasis and Cystic Fibrosis; NTM: nontuberculous mycobacteria; ERN: European Reference Network; FRIENDS: Facilitating Research Into Existing National DataSets.

and endotype bronchiectasis, developing strategies for more successful clinical trials and personalised medicine, and for reducing disease heterogeneity. The core of this project will be the development of an international bioresource, using the registry as a backbone to build a repository of blood, DNA, sputum and other biological materials for use in translational research. This project will include a deep evaluation of local and systemic inflammation, microbiota and genomics in bronchiectasis, in order to address relevant research questions on its pathophysiology. EMBARC2 has also the ambition to generate recommendations for design and conduct of bronchiectasis trials, for end-points to be used in those trials and for the research priorities in each area.

Specific work packages have been designed on the research priorities identified previously, including the European Bronchiectasis Registry, the EMBARC-BRIDGE study, the Bronchiectasis and Airways Disease “overlap” and on clinical trials support and feasibility. The role of nontuberculous mycobacteria in the pathogenesis and progression of bronchiectasis will also be a key topic [29, 30]. The BRIDGE (Bronchiectasis Research Involving Databases, Genomics and Endotyping to match the right treatment to the right patient) study will be an observational, cohort study aiming at determining the molecular endotypes of bronchiectasis during the stable state, as well as the causes and inflammatory profiles of exacerbations, validating biomarkers to use in stratified medicine, and performing *in vivo* or *in vitro* proof-of-concept studies using phenotypic data to identify patient populations likely to benefit in future randomised controlled trials. The kick-off meeting of work package leaders and EMBARC2 management board was recently held in Paris (France) during the ERS International Congress.

EMBARC has made an important contribution to bronchiectasis research, care and increasing the awareness of a disease that is no longer an “orphan”. Over the next 3 years, EMBARC2 will make a substantial contribution to the epidemiology, clinical and translational research, advocacy and education in bronchiectasis and we open a call to all the ERS members to be part of that.

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