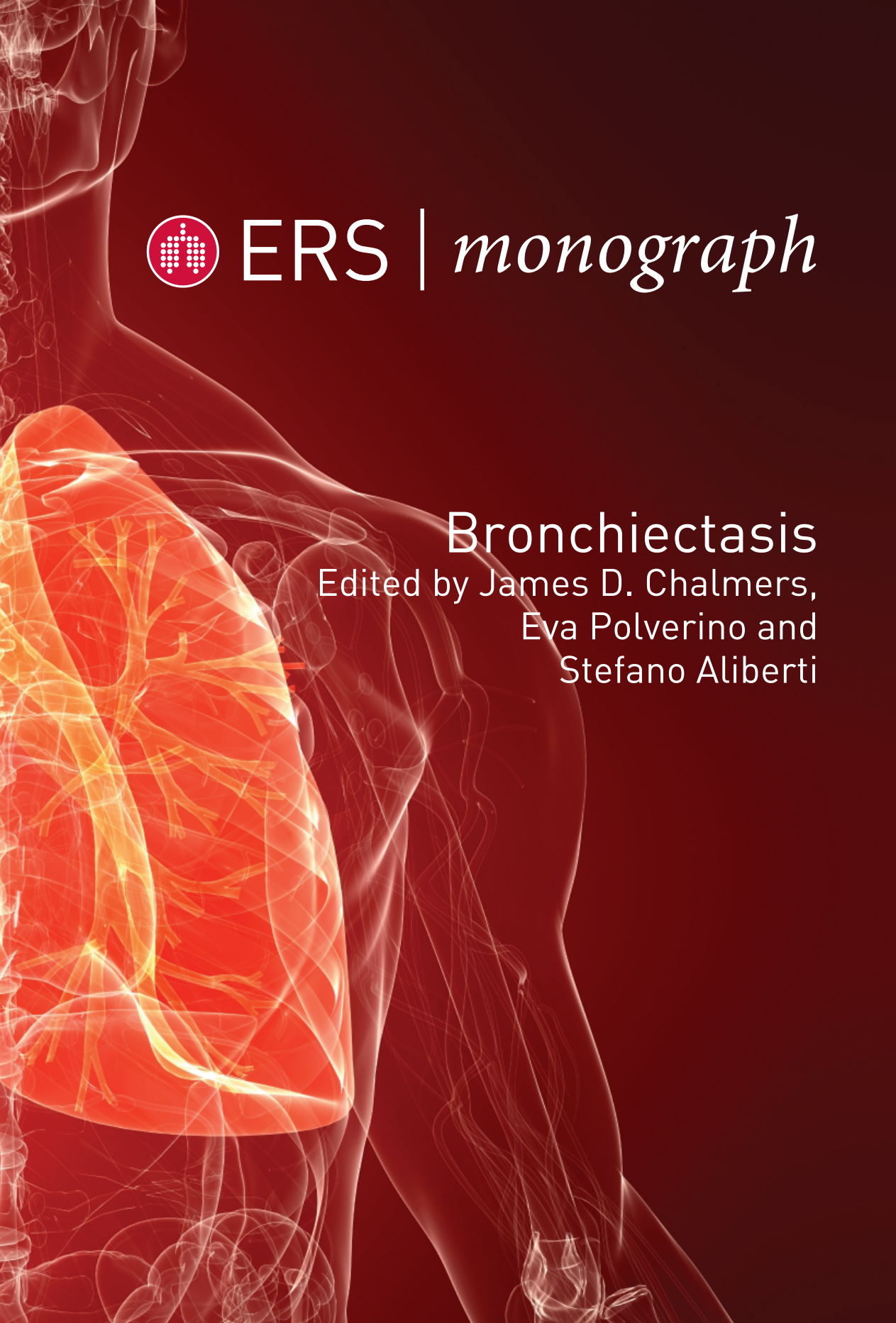




ERS | *monograph*

Bronchiectasis

Edited by James D. Chalmers,
Eva Polverino and
Stefano Aliberti



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and Stefano Aliberti

Editor in Chief
Robert Bals

This book is one in a series of *ERS Monographs*. Each individual issue provides a comprehensive overview of one specific clinical area of respiratory health, communicating information about the most advanced techniques and systems required for its investigation. It provides factual and useful scientific detail, drawing on specific case studies and looking into the diagnosis and management of individual patients. Previously published titles in this series are listed at the back of this *Monograph*.

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Preface

Robert Bals

The disease area of bronchiectasis has experienced something of a renaissance in recent years. The disease's aetiology, as well as the diagnostic and therapeutic approaches have been much better defined. These advances are clinically important as they help the diagnosis and treatment of patients with chronic cough, a frequently reported condition. The recent developments also highlight the heterogeneity of bronchiectasis, which often requires complex diagnostic tests. Therapy is also multilayered and combines strategies learned from conditions such as chronic obstructive pulmonary disease and cystic fibrosis.



This *ERS Monograph* provides the reader with broad and detailed overview of the biology of and clinical approach to bronchiectasis. It provides in-depth information about multiple aspects of the disease area, and includes chapters covering basic biology and mechanistic areas, as well as microbiome analysis. Diagnostic approaches to comorbidities and specific phenotypes are also discussed, as well as multidisciplinary therapeutic approaches, such as antibiotic therapy, physiotherapy and specific therapies for known causes of bronchiectasis.

The Guest Editors, James D. Chalmers, Eva Polverino and Stefano Aliberti, have brought together leading authors to create a book that will prove an essential resource for those working with bronchiectasis patients or conducting research in this area. I would like to thank them for their hard work; I feel sure that their book will help generate advances in diagnosis and therapy, as well as better care for bronchiectasis patients.

Guest Editors

James D. Chalmers



James D. Chalmers is GSK/British Lung Foundation Professor of Respiratory Research and Honorary Consultant Respiratory Physician at the University of Dundee/Ninewells Hospital (Dundee, UK). He runs a regional specialist clinic for over 600 patients with bronchiectasis and is coordinator of the ERN Lung core network for bronchiectasis. His research group investigates clinical and translational aspects of respiratory infections in bronchiectasis and other difficult airways diseases and he has published widely on different aspects of the disease. He is Chair of EMBARC (European Multicentre Bronchiectasis Registry Audit and Research Collaboration) and chaired the 2017 European Bronchiectasis Guidelines. He is Deputy Chief Editor of the *European Respiratory Journal*. In 2017, he won the Patrick Neil Medal from the Royal Society of Edinburgh (RSE) and the Romain Pauwels award from the European Respiratory Society (ERS) for his contribution to bronchiectasis research.

Eva Polverino



Eva Polverino is an expert in respiratory infections and leads research into bronchiectasis and cystic fibrosis at Vall d'Hebron University Hospital in Barcelona (Spain).

She graduated in Medicine at the University of Naples (Naples, Italy) and went on to specialise in pulmonology at the University of Pisa (Pisa, Italy). After a training period at the Hospital Clinic of Barcelona (Barcelona, Spain) focusing on gas exchange, she gained a PhD in cardiopulmonary pathophysiology at the University of Pisa. In 2007, she moved to the Department of Pulmonology at the Hospital Clinic of Barcelona, to work in the field of respiratory infections. She went on to become Senior Investigator at the Hospital Clinic of Barcelona and Associate Professor at the University of Barcelona (Barcelona, Spain).

Eva Polverino is an active member of several respiratory societies: the European Respiratory Society (ERS), the American

Thoracic Society (ATS), the Sociedad Española de Neumología y Cirugía Torácica (SEPAR) and the Catalan Society of Pulmonology (SOCAP). She is currently Secretary of the ERS Respiratory Infections Assembly, Co-Chair and member of the Steering Committee of EMBARC (European Multicentre Bronchiectasis Registry Audit and Research Collaboration), and Chair of the European task force on adult non-CF bronchiectasis (ERS 2014).

Eva Polverino has been an oral session facilitator and speaker at many European, American, Latin-American and Italian respiratory congresses. She has presented more than 150 oral communications at scientific congresses/courses and more than 200 communications (abstracts, posters, *etc.*).

Eva Polverino's personal research interests focus on respiratory infections and particularly bronchiectasis, cystic fibrosis, pneumonia, infection control and vaccination, and pulmonary physiotherapy.

Stefano Aliberti

Stefano Aliberti is Professor of Respiratory Medicine at the University of Milan (Milan, Italy), and consultant at the Policlinico Hospital in Milan (Milan, Italy). He is the director of the bronchiectasis and primary ciliary dyskinesia programmes at the Policlinico Hospital.

Stefano Aliberti's major clinical and research interests are in both acute and chronic respiratory infections. He has extensive experience in clinical research in pneumonia, gained since early 2000 when he worked at the Division of Infectious Diseases at the University of Louisville (Louisville, KY, USA) as an investigator of the Community-Acquired Pneumonia Organization and a member of the Community-Acquired Pneumonia Inflammatory Study Group.

Stefano Aliberti has extensively published clinical and translational research papers on community-acquired pneumonia, especially in the field of antimicrobial resistance, and he received the Young Researcher Award in Respiratory Infections from the European Respiratory Society (ERS) in 2007. Over the past 10 years he has been heavily involved in bronchiectasis research. He is one of the founders and co-Chairs of EMBARC (the European Multicentre Bronchiectasis Registry Audit and Research Collaboration; www.bronchiectasis.eu). He is also chair of both the Italian Bronchiectasis Registry (IRIDE) and the Italian Registry of Pulmonary Non-Tuberculous Mycobacteria (IRENE; www.registroirene.it).



Stefano Aliberti has had over 170 peer-reviewed articles published in the field of respiratory infections over the past 15 years. He was a member of the task force that produced the ERS Guidelines on adult non-cystic fibrosis bronchiectasis. He is currently an Associate Editor of *ERJ Open Research, Respirology* and *Multidisciplinary Respiratory Medicine*.

Stefano Aliberti has been heavily involved in the ERS over the past decade as Secretary of the Respiratory Infections Group, Secretary and Head of the Respiratory Infections Assembly, member of both the Research Agency and the Clinical Research Collaborations Working Group, and now as Curriculum Development Director.



Introduction

James D. Chalmers¹, Eva Polverino^{2,3} and Stefano Aliberti^{4,5}

 @ERSpublications

The *ERS Monograph* on Bronchiectasis provides a comprehensive guide to the investigation and management of the disease. This book will be an essential reference for all clinicians caring for bronchiectasis patients. <http://ow.ly/Onzn301rI0>

It is 7 years since the first *ERS Monograph* on Bronchiectasis was published by the European Respiratory Society (ERS). Expertly composed by Dr Floto and Dr Haworth from Cambridge (UK), the book became one of the most successful in the *ERS Monograph* series.

It is exciting and revealing to look back at what has changed in the field since 2011. In that time, bronchiectasis has taken on new importance in the practice of respiratory medicine. Estimates of disease prevalence have risen up to 10 fold and continue to rise. Specialist services for bronchiectasis have developed throughout Europe and beyond, while treatment guidelines have become more widespread, culminating in the 2017 publication of the ERS guidelines for management, the first international recommendations. The disease has been “renamed” with the “non-CF” label abandoned by the majority of authors and international societies.

Perhaps most importantly, there has been a remarkable international collaborative effort to advance clinical care and research. More than 300 investigators have participated in the global European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) project which at the time of writing has recruited more than 12 000 patients. There have been more major publications in leading general and respiratory journals in the past 7 years than in the previous 70 years; of these, studies into the benefits of long-term macrolides and the concept of illness severity have been the most impactful.

But this period has not been without its challenges. Alongside great progress we have met with great disappointments in the form of the repeated failure of clinical trials to consistently reach their primary end-points. Large-scale phase 3 trials into mucoactive drugs and particularly inhaled antibiotics have led to frustration, as drugs which appear

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beneficial in clinical practice fail to reduce exacerbations or improve quality of life in regulatory studies. The heterogeneity of bronchiectasis is almost its characteristic feature and remains the greatest challenge both in clinical care and in designing and interpreting research.

Patients with bronchiectasis urgently need proven therapies and better pathways of care. This *Monograph* brings together a team of leading global experts to discuss the many challenges and opportunities for the disease. Covering topics from pathophysiology, diagnostic testing and management through to critical research topics, such as trial end-points, this book is essential reading for anyone caring for those with the disease or conducting research.

Disclosures: J.D. Chalmers reports receiving the following, outside the submitted work: grants for research into COPD and personal fees from GlaxoSmithKline, Boehringer Ingelheim and Pfizer; grants for research into COPD from AstraZeneca; grants for research into bronchiectasis and personal fees from Bayer Healthcare and Grifols; and personal fees for consulting from Napp. E. Polverino reports receiving honoraria for speeches from Bayer, Ismed, Grifols and Chiesi, during the current work. E. Polverino received grants and personal fees from Chiesi, outside the submitted work. S. Aliberti reports receiving the following outside the submitted work: grants and personal fees from Bayer Healthcare, Aradigm Corporation, Grifols, Chiesi and INSMED; personal fees from AstraZeneca, Basilea, Zambon, Novartis, Raptor, Actavis UK Ltd and Horizon.

List of abbreviations

ABPA	allergic bronchopulmonary aspergillosis
ACT	airway clearance technique
BACI	Bronchiectasis Aetiology Comorbidity Index
BAL	bronchoalveolar lavage
BCI	Bronchiectasis Comorbidity Index
BCOS	bronchiectasis–COPD overlap syndrome
BHQ	Bronchiectasis Health Questionnaire
BMI	body mass index
BSI	Bronchiectasis Severity Index
CF	cystic fibrosis
CFTR	cystic fibrosis transmembrane conductance regulator
COPD	chronic obstructive pulmonary disease
CT	computed tomography
E-FACED	severe exacerbation FACED
FACED	FEV ₁ (>50%=0 points, ≤50%=2 points), age (≤70 years=0 points, >70 years=2 points), chronic colonisation (no <i>Pseudomonas aeruginosa</i> =0 points, <i>P. aeruginosa</i> =1 point), extension (less than or equal to two lobes affected=0 points, more than two lobes affected=1 point), dyspnoea (<2 on the modified Medical Research Council dyspnoea scale=0 points, ≥2 on Medical Research Council scale=1 point)
FeNO	fractional exhaled nitric oxide
FEV ₁	forced expiratory volume in 1 s
FVC	forced vital capacity
HRCT	high-resolution computed tomography
IBD	inflammatory bowel disease
IFN	interferon
Ig	immunoglobulin
IL	interleukin
MAC	<i>Mycobacterium avium</i> complex
MRI	magnetic resonance imaging
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
NTM	nontuberculous mycobacteria
PCD	primary ciliary dyskinesia
PEP	positive expiratory pressure
RCT	randomised controlled trials
TB	tuberculosis
TNF- α	tumour necrosis factor- α