



ERS | *monograph*

# Controversies in COPD

Edited by  
Antonio Anzueto,  
Yvonne Heijdra and  
John R. Hurst

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Antonio Anzueto, Yvonne Heijdra  
and John R. Hurst

Editors in Chief  
Tobias Welte (outgoing Editor)  
Robert Bals (incoming Editor)

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# Preface

Tobias Welte (outgoing Editor in Chief) and  
Robert Bals (incoming Editor in Chief)

After arteriosclerosis and stroke, COPD is one of the most common diseases worldwide. The morbidity, mortality and healthcare costs of COPD are high and will continue to rise due to the demographic changes expected. Since the beginning of the millennium, COPD has become one of the major areas of research. The improvement in quality of life, and perhaps in life expectancy, achieved since then is primarily due to the establishment of non-pharmacological measures, such as standardised smoking-cessation programmes, structured exercise therapy, and infection prevention with influenza and pneumococcal vaccination.

Progress in pharmacological therapy, however, has been low. The essential treatment components, such as  $\beta$ -mimetics, anticholinergics or ICSs, have been available for more than 50 years, and have improved in terms of duration of action, efficacy and mode of administration. However, more than 15 substances with new and different modes of action tested in clinical trials have failed to demonstrate activity and have not been approved for regular treatment. The dynamic development of new therapies for asthma may explain why most of the COPD substances failed. Better phenotyping of asthma patients made targeted pathophysiology-oriented treatment possible. COPD is a heterogeneous disease, and it is indisputable that there are different phenotypes; however, with the exception of  $\alpha_1$ -ATD, these have not been well characterised in the past. Better characterisation of COPD patients using new biomarkers, advanced imaging properties and the whole spectrum of omics technology may stimulate the development of a new generation of drugs.

This issue of the *ERS Monograph* provides a comprehensive overview of the debate in this context, with consideration of the future direction of COPD research and clinical practice. We would like to thank the Guest Editors Antonio Anzueto, Yvonne Heijdra and John R. Hurst for their excellent work in bringing together this interesting and wide-ranging selection of chapters. We hope that both clinicians and scientists will find this book



Tobias Welte



Robert Bals

useful, and that it will stimulate further discussion about the diverse and fascinating disease, COPD.

With this issue Tobias Welte says goodbye after 5 years as Editor in Chief of the *ERS Monograph*. It has been a wonderful time, during which the *Monograph* has continuously developed. I have learned a lot, gained a lot of friends and have always appreciated working with the ERS Publications Office. Many thanks to all who have supported me in the past.

Robert Bals will take over the role of Editor in Chief from now on. Knowing him very well, I am convinced that he will be successful in improving the *ERS Monograph* further. Good luck Robert.



# Guest Editors

## Antonio Anzueto

Antonio Anzueto is currently Professor of Medicine at the University of Texas Health Sciences Center at San Antonio, TX, USA, and the Chief of the Pulmonary Disease Section at The South Texan Veterans Health Care System. He is a faculty member in the Pulmonary Disease and Critical Care Medicine division. He earned his Doctor of Medicine degree at the Universidad de San Carlos de Guatemala, Guatemala City, Guatemala, and completed his training at both Hospital General San Juan de Dios, Guatemala City, and the University of Texas Health Science Center.



Antonio Anzueto is a reviewer for most prestigious scientific journals, including *The New England Journal of Medicine*, *JAMA*, the *European Respiratory Journal* and the *American Journal of Respiratory and Critical Care Medicine*. He is a member of the scientific committee of the Global Initiative for Chronic Obstructive Lung Disease, the 2011 American-European Consensus Conference on ARDS, the European Respiratory Society/American Thoracic Society Acute Exacerbations Task Force, and many other medical institutional and organisational committees.

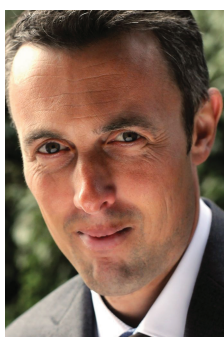
Antonio Anzueto has published over 250 papers in peer-review journals, such as *The New England Journal of Medicine*, *JAMA*, the *European Respiratory Journal*, the *American Journal of Respiratory and Critical Care Medicine*, *Intensive Care Medicine*, the *Lancet* and the *Archives of Internal Medicine*, and has vast experience as an invited speaker and moderator at many scientific meetings. His areas of interest include COPD, pulmonary infections including chronic bronchitis and community-acquired pneumonia, sepsis, and acute respiratory distress syndrome. He is the recipient of a number of awards ranging from the Du Pont/American College of Chest Physicians Young Investigator Award to the Outstanding Teacher Award from the University of Texas Health Science Center.

## Yvonne Heijdra



Yvonne Heijdra studied medicine at the Radboud University Medical Centre (RUMC), Nijmegen, the Netherlands, where she obtained her medical degree. Thereafter, she specialised in internal medicine, followed by pulmonary medicine, combined with a PhD research project on respiratory muscle function and nocturnal oxygenation in COPD patients. She obtained her PhD in 1995 and registered as a pulmonologist in 1997. She became a staff member at the pulmonary department of the RUMC. In addition to her clinical activities, she was head of the pulmonary function department. In 2000, she worked for 1 year at Saint Elisabeth Medical Centre, a Tufts University-affiliated hospital, in Boston, MA, USA, to perform COPD-related research in the field of dynamic hyperinflation with Prof. Bartolome Celli. In 2006, she became an associate professor at the RUMC. Her fields of professional interest include COPD, pulmonary hypertension and clinical physiology. She leads the research performed in the field of COPD, especially related to (dynamic) hyperinflation. Her research aims to improve physical activity in COPD patients, which may result in an increased health status. She has published over 100 peer-reviewed papers. She was scientific secretary of the board of the Netherlands Society of Physicians in Pulmonary Medicine and Tuberculosis (NVALT) in 2011. In 2013, she was made president of the NVALT, and since 2015, she has served as vice president of the NVALT.

## John R. Hurst



John R. Hurst graduated from the University of Edinburgh Medical School, Edinburgh, UK, in 1997 and was appointed Senior Lecturer, then Reader in Respiratory Medicine at University College London, London, UK, in October 2007. He has a research interest in the mechanisms of exacerbation susceptibility and cardiovascular risk as applied to COPD and bronchiectasis. This extends to  $\alpha_1$ -ATD, lung disease in primary immunodeficiency and the adult consequences of prematurity. He was awarded the 2012 European Respiratory Society COPD research prize. His h-index is 21 with 76 citations listed on PubMed. His clinical work at Royal Free London NHS Foundation Trust focuses on the Specialist COPD and Bronchiectasis services, and he has an active role in undergraduate and postgraduate medical education. A previous Associate Editor at *Thorax*, he was appointed to the Editorial Board of the *American Journal of Respiratory and Critical Care Medicine* in 2012.



# Introduction

Antonio Anzueto<sup>1</sup>, Yvonne Heijdra<sup>2</sup> and John R. Hurst<sup>3</sup>

COPD is common but that does not mean it is easy to understand and manage. Our patients deserve excellent care, wherever they live. We define excellent as world-class, patient-centred, evidence-based and cost-effective multidisciplinary care from diagnosis to death.

The complexity of COPD is now more widely recognised, and with that comes care directed towards each patient's specific demographic and clinical characteristics (phenotype) or, more likely, phenotypes. We all face, in our everyday practice, areas of controversy in COPD. Evidence-based medicine is often not available. For example, how would you alter the management for a COPD patient with  $\alpha_1$ -ATD? Can COPD arise as a consequence of premature birth? How should ACOS and COPD-bronchiectasis overlap syndrome be managed? What is the value of CT in COPD? Is there a difference between a COPD exacerbation and pneumonia?

It is timely, then, to consider where the current controversies in COPD may lie. Developed from an idea discussed at the European Respiratory Society International Congress in 2014, we are delighted to present this *ERS Monograph* at the 2015 Congress. Our international expert authors have produced a monograph that addresses the key current controversies in a way that we hope is both relevant to the clinician through the use of case vignettes, whilst illustrated by state-of-the-art science and clinical evidence.

We hope you enjoy reading this *Monograph* recognising the described controversies and that you take these concepts back to the clinic to improve the care of patients with COPD. Fundamentally, that is why we all do what we do.

We would like to take this opportunity to thank all the authors, reviewers and ERS Publications staff for their commitment and enthusiasm for the project.

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# List of abbreviations

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<b>6MWD</b>	6-min walk distance
<b>6MWT</b>	6-min walk test
<b><math>\alpha_1</math>-AT</b>	$\alpha_1$ -antitrypsin
<b><math>\alpha_1</math>-ATD</b>	$\alpha_1$ -antitrypsin deficiency
<b>ACOS</b>	Asthma-COPD overlap syndrome
<b>AECOPD</b>	Acute exacerbations of COPD
<b>AHR</b>	Airway hyperresponsiveness
<b>BMI</b>	Body mass index
<b>BODE</b>	BMI, airflow obstruction, dyspnoea, exercise capacity
<b>CF</b>	Cystic fibrosis
<b>COPD</b>	Chronic obstructive pulmonary disease
<b>CRP</b>	C-reactive protein
<b>CT</b>	Computed tomography
<b><i>D</i><sub>LCO</sub></b>	Diffusing capacity of the lung for carbon monoxide
<b>FEF<sub>25-75%</sub></b>	Forced expiratory flow at 25–75% of FVC
<b><i>F</i><sub>e</sub>NO</b>	Exhaled nitric oxide fraction
<b>FEV<sub>1</sub></b>	Forced expiratory volume in 1 s
<b>FFM</b>	Fat-free mass
<b>FVC</b>	Forced vital capacity
<b>HRCT</b>	High-resolution computed tomography
<b>ICS</b>	Inhaled corticosteroid
<b>IL</b>	Interleukin
<b>ILD</b>	Interstitial lung disease
<b><i>K</i><sub>co</sub></b>	Transfer coefficient of the lung for carbon monoxide
<b>MRI</b>	Magnetic resonance imaging
<b>PET</b>	Positron emission tomography
<b>PR</b>	Pulmonary rehabilitation
<b>PPM</b>	Potentially pathogenic microorganism
<b>QALYs</b>	Quality-adjusted life-years
<b>TNF</b>	Tumour necrosis factor