ABC of COPD

SECOND EDITION

Edited by Graeme P. Currie

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Second Edition

EDITED BY

Graeme P. Currie

Consultant in Respiratory and General Medicine
Aberdeen Royal Infirmary
Aberdeen, UK

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Editorial Offices: The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Offices: 111 River Street, Hoboken, NJ 07030-5774, USA

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Contributors

Peter J. Barnes
Professor of Respiratory Medicine
Airway Disease Section
National Heart and Lung Institute
Imperial College London
London, UK

David Bellamy
Bournemouth General Practitioner (retired)
Bournemouth, UK

John Britton
Professor of Epidemiology
UK Centre for Tobacco Control Studies
University of Nottingham;
Consultant in Respiratory Medicine
City Hospital
Nottingham, UK

Mahendran Chetty
Consultant in Respiratory Medicine
Aberdeen Royal Infirmary
Aberdeen, UK

Graeme P. Currie
Consultant in Respiratory and General Medicine
Aberdeen Royal Infirmary
Aberdeen, UK

Graham S. Devereux
Professor of Respiratory Medicine
Division of Applied Health Sciences
University of Aberdeen;
Consultant in Respiratory Medicine

Aberdeen Royal Infirmary
Aberdeen, UK

Graham Douglas
Consultant in Respiratory Medicine
Aberdeen Royal Infirmary
Aberdeen, UK

Cathy Jackson
Professor of Primary Care Medicine;
Director of Clinical Studies
Bute Medical School
University of St Andrews
St Andrews, UK

Gordon Linklater
Consultant in Palliative Care Medicine
Roxburghe House
Aberdeen, UK

Brian J. Lipworth
Professor of Allergy and Respiratory Medicine
Asthma and Allergy Research Group
Ninewells Hospital and Medical School
Dundee, UK

William MacNee
Professor of Respiratory and Environmental Medicine
MRC Centre for Inflammation Research
Queen's Medical Research Institute
University of Edinburgh
Edinburgh, UK

Paul K. Plant
Consultant in Respiratory Medicine
St James's University Hospital
Leeds, UK

Jadwiga A. Wedzicha

Professor of Respiratory Medicine
Royal Free and University College Medical School
University College
London, UK

Foreword

Chronic obstructive pulmonary disease (COPD) is a major global epidemic. It already is the fourth commonest cause of death in high income countries and is predicted to soon become the third commonest cause of death worldwide. In the United Kingdom, the mortality from COPD in women now exceeds that from breast cancer. COPD is also predicted to become the fifth commonest cause of chronic disability, largely because of the increasing levels of cigarette smoking in developing countries in conjunction with an ageing population. It now affects approximately 10% of men and women over 40 years in the United Kingdom and is one of the commonest causes of hospital admission. Because of this, COPD has an increasing economic impact, and direct healthcare costs now exceed those of asthma by more than threefold. Despite these startling statistics, COPD has been relatively neglected and is still underdiagnosed in primary care settings. This is in marked contrast to asthma, which is now recognised and well managed in the community. The new NHS National Strategy seeks to improve diagnosis and management of COPD in the community and reduce hospital admissions.

Highly effective treatment is now available for asthma, which has in turn transformed patients' lives. Sadly, this is not the case with COPD, where management is less effective and no drug has so far been shown to convincingly slow progression of the disease. However, we do now have effective bronchodilators and non-pharmacological treatments, which can improve the quality of life of patients. Many patients, however, are not diagnosed or undertreated, so increased awareness of COPD is needed. There are advances in understanding the underlying inflammatory disease, so this may lead to more effective use of existing

treatment and the development of new drugs in the future. In this second edition of the *ABC COPD* monograph, Graeme Currie and colleagues provide a timely update on the pathophysiology, diagnosis, and modern management of COPD. It is vital that COPD is recognised and treated appropriately in general practice where the majority of patients are managed, and this book provides a straightforward overview of the key issues relating to this important condition.

Peter J. Barnes FRS, FMedSci
Head of Respiratory Medicine
National Heart & Lung Institute
Imperial College London
London, UK

1

Definition, Epidemiology and Risk Factors

Graham S. Devereux

Division of Applied Health Sciences, University of Aberdeen, Aberdeen, UK and Aberdeen Royal Infirmary, Aberdeen UK

Overview

- Chronic obstructive pulmonary disease (COPD) is characterised by largely irreversible airflow obstruction and an abnormal inflammatory response within the lungs
- It is the fourth leading cause of death in the United States and Europe
- Cases of known COPD are likely to only represent the ‘tip of the iceberg’ with as many individuals undiagnosed
- Other conditions also cause progressive airflow obstruction and these need to be differentiated from COPD
- COPD is usually caused by cigarette smoking, but pipe, cigar and passive smoking, indoor and outdoor air pollution, occupational exposures, previous tuberculosis and repeated early life respiratory tract infections have all been implicated in its development
- The prevalence of COPD in never smokers (estimated to be between 25 and 45% worldwide) is higher than

previously thought; the use of biomass fuel (mainly in developing countries) is one of the main risk factors

Definition

Chronic obstructive pulmonary disease (COPD) is a progressive disease characterised by airflow obstruction and destruction of lung parenchyma. The current definition as suggested by the American Thoracic and European Respiratory Societies is as follows:

> *COPD is a preventable and treatable disease state characterised by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces significant systemic consequences.*

COPD is the preferred term for the airflow obstruction associated with the diseases of chronic bronchitis and emphysema (Box 1.1). A number of other conditions are associated with poorly reversible airflow obstruction—for example, cystic fibrosis, bronchiectasis and obliterative bronchiolitis. These conditions need to be considered in the differential diagnosis of obstructive airway disease, but are not conventionally covered by the definition of COPD. Although asthma is defined by variable airflow obstruction, there is evidence that the airway remodelling processes associated with asthma can result in irreversible progressive airflow obstruction that fulfils the definition for COPD. Because of the high prevalence of asthma and COPD, these conditions co-exist in a sizeable proportion of individuals resulting in diagnostic uncertainty.

Box 1.1 Definitions of conditions associated with airflow obstruction

- COPD is characterised by airflow obstruction. The airflow obstruction is usually progressive, not reversible and does not change markedly over several months. The disease is predominantly caused by smoking.
- Chronic bronchitis is defined as the presence of chronic productive cough on most days for 3 months, in each of 2 consecutive years, in a patient in whom other causes of productive cough have been excluded.
- Emphysema is defined as abnormal, permanent enlargement of the distal airspaces, distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis.
- Asthma is characterised by reversible, widespread and intermittent narrowing of the airways.

Epidemiology

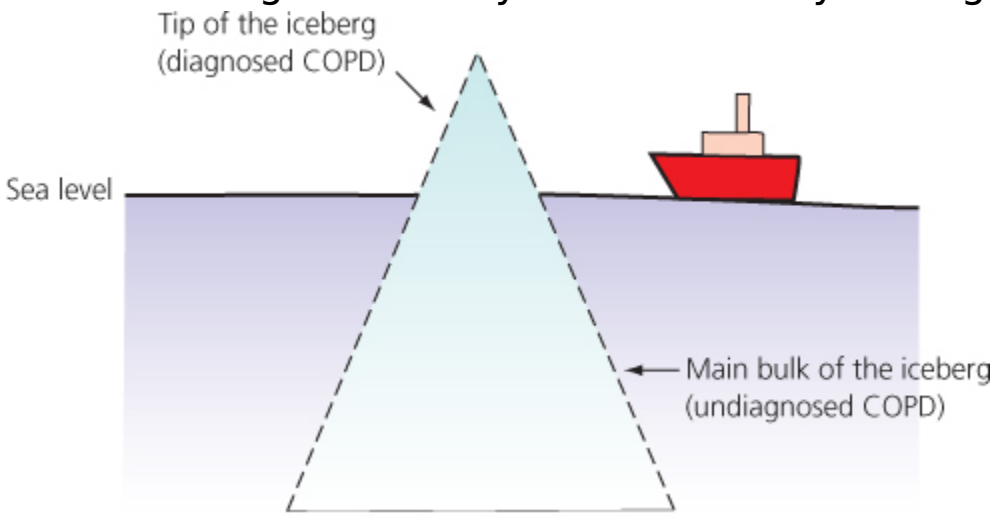
Prevalence

The prevalence of COPD varies considerably between epidemiological surveys. While this reflects the variation in the prevalence of COPD between and within different countries, differences in methodology, diagnostic criteria and analytical techniques undoubtedly contribute to disparities between studies.

The lowest estimates of prevalence are usually based on self-reported or doctor-confirmed COPD. These estimates are usually 40–50% of the prevalence rates derived from spirometric indices. This is because COPD is underdiagnosed due to failure to recognise the significance of symptoms and relatively late presentation of disease (Figure 1.1).

Estimates of the prevalence of spirometric-defined COPD using UK criteria are less than the estimates based on European and US criteria (Chapter 4).

Figure 1.1 Known cases of COPD may represent only the 'tip of the iceberg' with many cases currently undiagnosed.



In the United Kingdom, a national study reported that 10% of males and 11% of females aged 16–65 years had an abnormally low forced expiratory volume in 1 second (FEV_1). Similarly, in Manchester, non-reversible airflow obstruction was present in 11% of subjects aged >45 years, of whom 65% had not been diagnosed with COPD. In Salzburg, Austria, doctor-confirmed COPD was reported by 5.6% of adults aged ≥40 years in a population survey; however, on evaluation using spirometric indices, 10.7% fulfilled UK criteria and 26.1% fulfilled European/US criteria. In the United States, the reported prevalence of airflow obstruction with an FEV_1 < 80% predicted was 6.8%, with 1.5% of the population having an FEV_1 < 50% and 0.5% of the population having more severe airflow obstruction (FEV_1 < 35% predicted). As in the United Kingdom, around 60% of subjects with airflow obstruction had not been formally diagnosed with COPD.

In England and Wales, it has been estimated that there are about 900,000 patients with diagnosed COPD. However, after allowing for underdiagnosis, the true number of individuals is likely to be about 1.5 million, although a figure as high as 3.7 million has been suggested. The mean age of diagnosis in the United Kingdom is around 67 years, and the prevalence of COPD increases with age (Figure 1.2). It is also more common in males and is associated with socio-economic deprivation. In the United Kingdom, the prevalence of COPD in females is increasing (Figures 1.3 and 1.4). For example, it was considered to be 0.8% in 1990 and had risen to 1.4% in 1997. In males, the prevalence appears to have plateaued since the mid-1990s. Similar trends have been reported in the United States. These time trends in prevalence probably reflect the gender differences in cigarette smoking since the 1970s.

Figure 1.2 Prevalence (per 1000) of diagnosed COPD in UK men (▪) and women (▪) grouped by age, between 1990 and 1997. (Reproduced with permission from Soriano JB, Maier WC, Egger P, *et al. Thorax* 2000; **55**: 789–794)

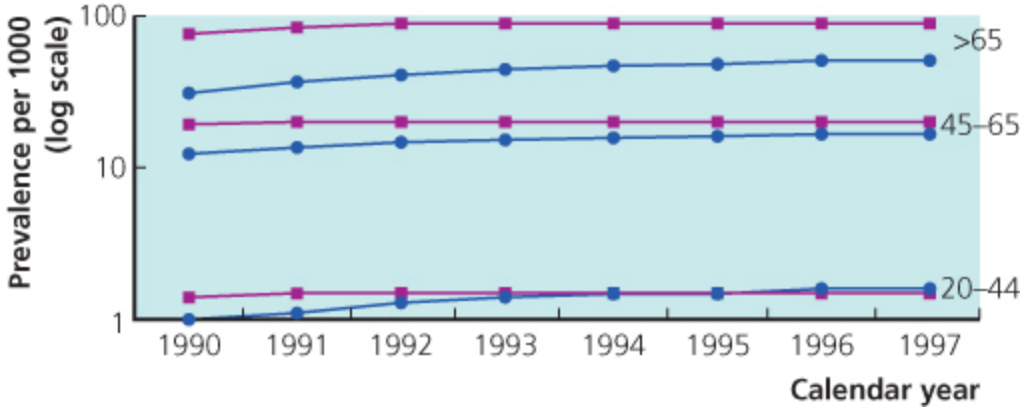


Figure 1.3 Prevalence of diagnosed COPD in UK men and women (per 1000) between 1990 and 1997. (Reproduced with permission from Soriano JB, Maier WC, Egger P, *et al. Thorax* 2000; **55**: 789–794)

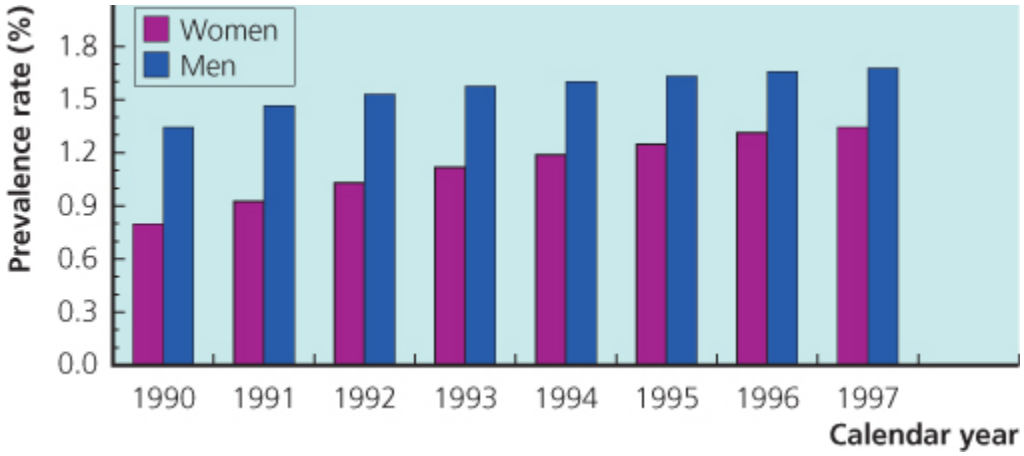
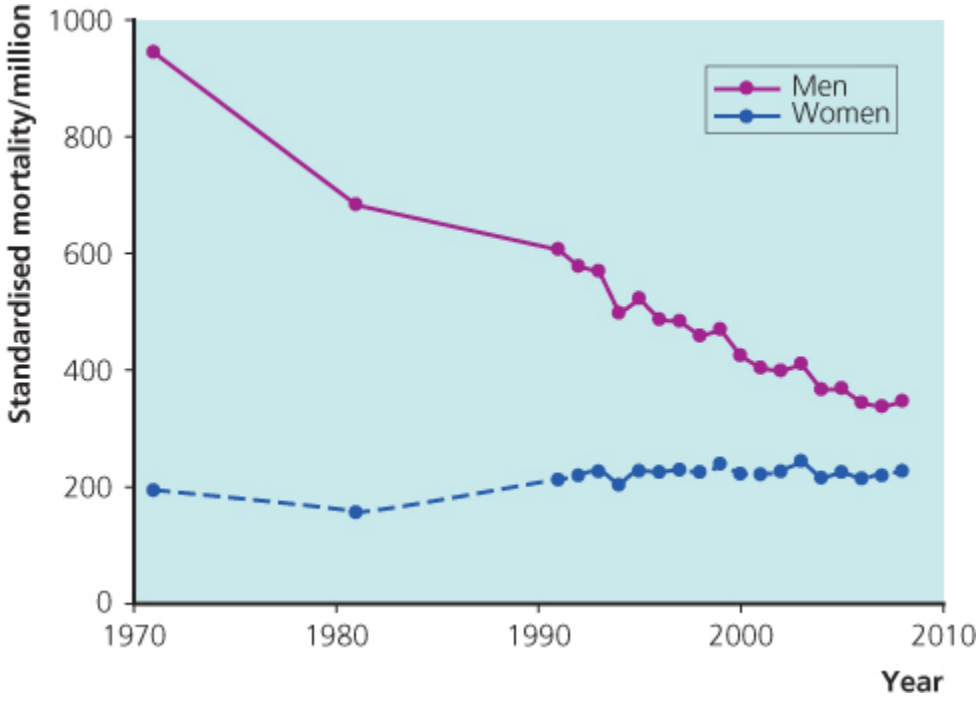


Figure 1.4 UK death rates from COPD since 1971. Age-standardised mortality rates per million: based on the European Standard Population. Figure derived with data from Death registrations, selected data tables, England and Wales 2008. Office for National Statistics, London. http://www.statistics.gov.uk/downloads/theme_health/DR2008/DR_08.pdf. (Accessed 12/09).



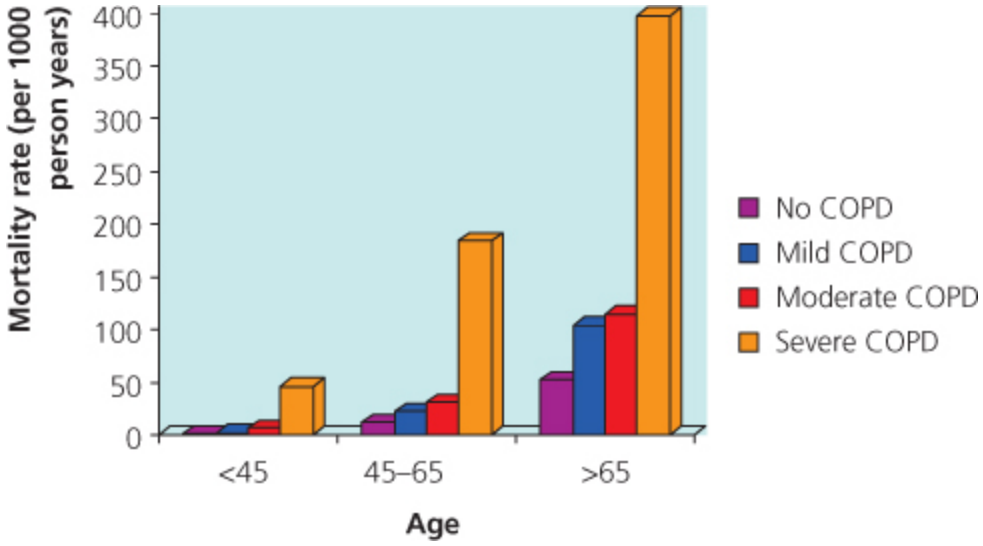
Mortality

COPD is the fourth leading cause of death in the United States and Europe. Globally, COPD was ranked the sixth most common cause of death in 1990; however, with increases in life expectancy and cigarette smoking, particularly in developing countries, it is expected that COPD will be the third leading cause of death worldwide by 2020. In the United Kingdom in 2008, there were approximately 25,000 deaths due to COPD; 13,000 of these deaths were in males and 12,000 in females. These figures suggest that COPD underlies 4.9% of all deaths (5.4% of male deaths and 4.4% of female deaths) in the United Kingdom.

In the United Kingdom, over the last 30 years, mortality rates due to COPD have fallen in males and risen in females. However, it seems likely that in the near future, there will be no gender difference. In the United States, the most recent data between 2000 and 2005 suggest that 5% of deaths are a consequence of COPD. Although overall, the age-standardised mortality rate was stable at about 64 deaths per 100,000, the death rate in males fell from 83.8/100,000 in 2000 to 77.3/100,000 in 2005 and increased in females from 54.4/100,000 to 56.0/100,000.

Mortality rates increase with age, disease severity and socio-economic disadvantage (Figure 1.5). On average, in the United Kingdom, COPD reduces life expectancy by 1.8 years (76.5 vs 78.3 years for controls); mild disease reduces life expectancy by 1.1 years, moderate disease by 1.7 years and severe disease by 1.4 years.

Figure 1.5 UK deaths from COPD (per 1000 person years) by age and severity of COPD. Figure derived with data from Soriano JB, Maier WC, Egger P, *et al.* Recent trends in physician diagnosed COPD in women and men in the UK. *Thorax* 2000; **55**: 789–794.



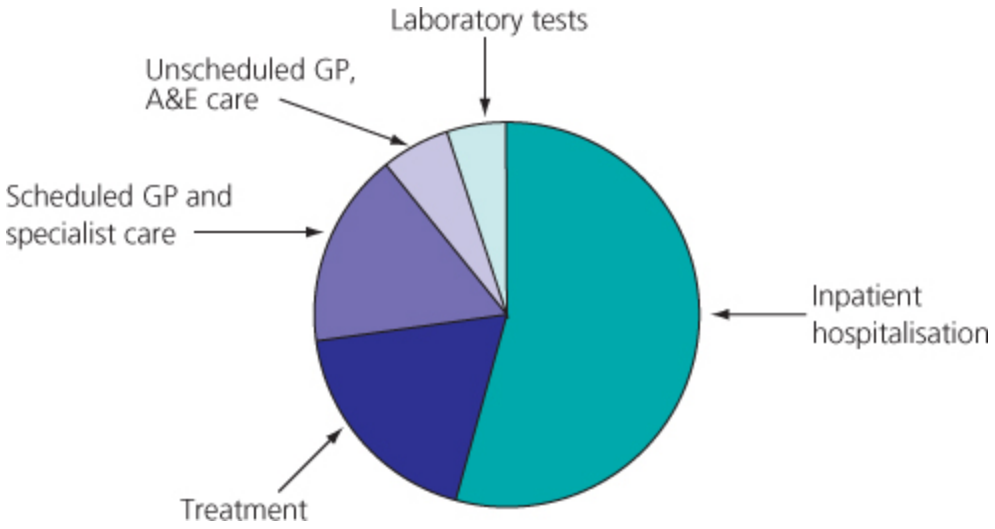
Morbidity and Economic Impact

The morbidity and economic costs associated with COPD are very high, generally unrecognised and more than twice that associated with asthma. The impact on quality of life is particularly high in patients with frequent exacerbations, although even those with mild disease have an impaired quality of life.

In the United Kingdom, emergency hospital admissions for COPD have steadily increased as a percentage of all admissions from 0.5% in 1991 to 1% in 2000. In 2002/2003, there were 110,000 hospital admissions for an exacerbation of COPD in England with an average duration of stay of 11 days, accounting for 1.1 million bed days. At least 10% of emergency admissions to hospital are as a consequence of COPD and this proportion is even greater during the winter. Most admissions are in individuals over 65 years of age with advanced disease who are often admitted repeatedly and use a disproportionate amount of resource. Approximately 25% of patients diagnosed with COPD are admitted to hospital and 15% of all patients are admitted each year.

The impact in primary care is even greater, with 86% of care being provided exclusively in that setting. It has been estimated that a typical general practitioner's list will include 200 patients with COPD (even more in areas of social deprivation), although not all will be diagnosed. On average, patients with COPD make six to seven visits annually to their general practitioner. It has been estimated that each diagnosed patient costs the UK economy £1639 annually, equating to a national burden of £982 million. For each patient, annual direct costs to the National Health Service (NHS) are £819, with 54% of this being due to hospital admissions and 19% due to drug treatment (Figure 1.6). COPD has further societal costs; about 40% of UK patients are below retirement age and the disease prevents about 25% from working and reduces the capacity to work in a further 10%. Annual indirect costs have been estimated at £820 per patient and encompass the costs of disability, absence from work, premature mortality and the time caregivers miss work. Within Europe, it has been estimated that in 2001 the overall cost of COPD to the economy was €billion; this comprised of €billion for ambulatory care, €billion for drugs, €billion for inpatient care and €billion for lost working days.

Figure 1.6 An analysis of the direct costs of COPD to the National Health Service. A&E, accident and emergency; GP, general practitioner. Figure derived with data from Britton M. The burden of COPD in the UK: results from the Confronting COPD survey. *Respiratory Medicine* 2003; **97**(suppl C): S71–S79.



Risk Factors

Smoking

In developed countries, cigarette smoking is clearly the single most important risk factor in the development of COPD, with studies consistently reporting dose–response associations. Cigarette smoking is also associated with increased probability of COPD diagnosis and death. Pipe and cigar smokers have significantly greater morbidity and mortality from COPD than non-smokers, although the risk is less than that with cigarettes. Approximately 50% of cigarette smokers develop airflow obstruction and 10–20% develop clinically significant COPD. Maternal smoking during and after pregnancy is associated with reduced infant, childhood and adult ventilatory function, days, weeks and years after birth, respectively. Most studies have demonstrated that the effects of antenatal environmental tobacco smoking exposure are greater in magnitude and independent of associations with post-natal exposure.

Other Factors

In the last 5 years, an increasing number of risk factors other than smoking have been linked to the development of COPD, particularly in developing countries. These include indoor (biomass) and outdoor air pollution, occupational exposures and early life factors such as intra-uterine growth retardation, poor nutrition, repeated lower respiratory tract infections and a history of pulmonary tuberculosis. Many of these risk factors are inter-related. For example, biomass smoke exposure is associated with intrauterine growth retardation and repeated early life lower respiratory tract infections. Accumulating evidence suggests that the prevalence of COPD worldwide in never smokers may be as high as 25–45% worldwide (Figure 1.7) with many risk factors and associations identified (Table 1.1).

Figure 1.7 Proportion of patients with COPD who are non-smokers worldwide. ECRHS, European Community Respiratory Health Survey. (Figure reproduced with permission from Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009; **374**: 733–743. *Australia, Belgium, Denmark, France, Germany, Iceland, Ireland, Italy, Netherlands, New Zealand, Norway, Spain, Sweden, Switzerland, United Kingdom and United States)