

## CHAPTER 1

# Definition, Epidemiology and Risk Factors

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### OVERVIEW

- Chronic obstructive pulmonary disease (COPD) is defined by relatively fixed airflow obstruction.
- The number of individuals diagnosed with COPD is far less than the actual number thought to be affected. Prevalence increases with age and socioeconomic deprivation.
- Globally, COPD is projected to be the third leading cause of death by 2030 with the majority of deaths likely to be in low-/middle-income countries.
- The impact of COPD, particularly exacerbations, on health service resource is considerable.
- Risk factors for COPD include cigarette smoking, indoor air pollution (particularly close and regular exposure to combustion of biomass fuels), outdoor air pollution, occupational exposure to some dusts, vapours, irritants and fumes and  $\alpha$ 1-antitrypsin deficiency.

### Definition

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease characterised by airflow obstruction and destruction of the lung parenchyma. The widely used definition put forward by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) is that COPD is 'a common preventable and treatable disease characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lungs to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients'.

COPD is the preferred name 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 bronchiectasis and obliterative bronchiolitis. Although these conditions need to be considered in the differential diagnosis of obstructive airways disease, they are not conventionally covered by the definition of

COPD. Although asthma is defined by variable airflow obstruction, there is evidence suggesting 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 and can raise diagnostic uncertainty.

#### Box 1.1 Definitions of conditions associated with airflow obstruction.

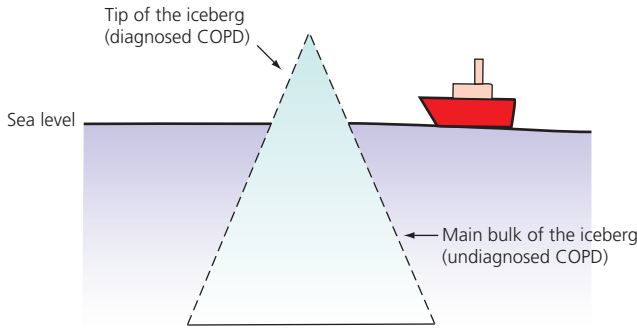
- COPD is a common preventable and treatable disease characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and co-morbidities contribute to the overall severity in individual patients.
- 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 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 widespread narrowing of the bronchial airways which changes in severity over short periods of time, either spontaneously or following treatment.

### Epidemiology

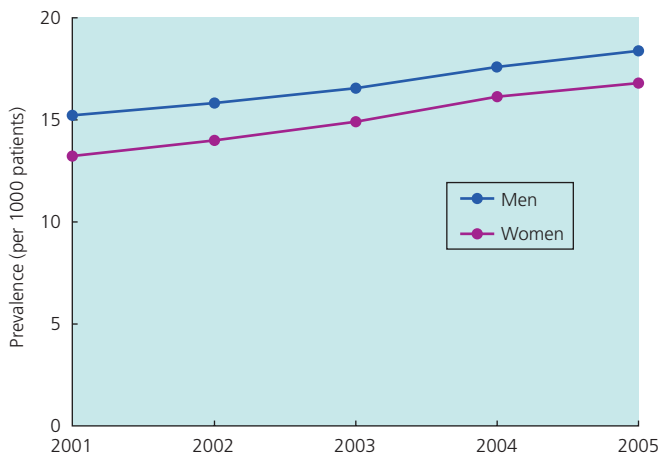
#### Prevalence

The prevalence of COPD varies considerably between epidemiological surveys. While this reflects the variation between and within countries, differences in methodology, diagnostic criteria and analytical techniques undoubtedly contribute to disparities among studies. There is no consensus as to the optimal metric of COPD prevalence. The lower estimates of prevalence are usually

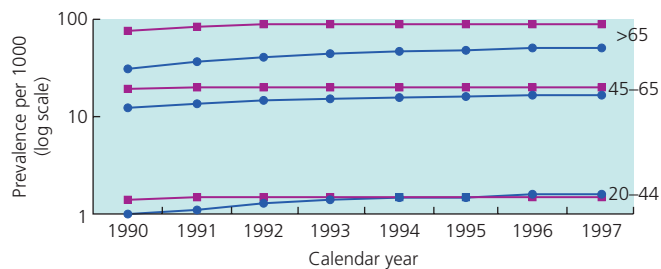
based on self-reported or ‘doctor-confirmed’ COPD and are typically 40–50% of the rates derived when spirometry is used. The underdiagnosis of COPD probably arises because many individuals fail to recognise the significance of symptoms and present relatively late with moderate or severe airflow obstruction (Figures 1.1–1.3).



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



**Figure 1.2** Lifetime prevalence of diagnosed COPD in males and females (per 1000) resident in England 2001–2005. Figure adapted from Simpson CR, Hippisley-Cox J, Sheikh A. Trends in the epidemiology of chronic obstructive pulmonary disease in England: a national study of 51 804 patients. *British Journal of General Practice* 2010; **60**(576): 277–284.

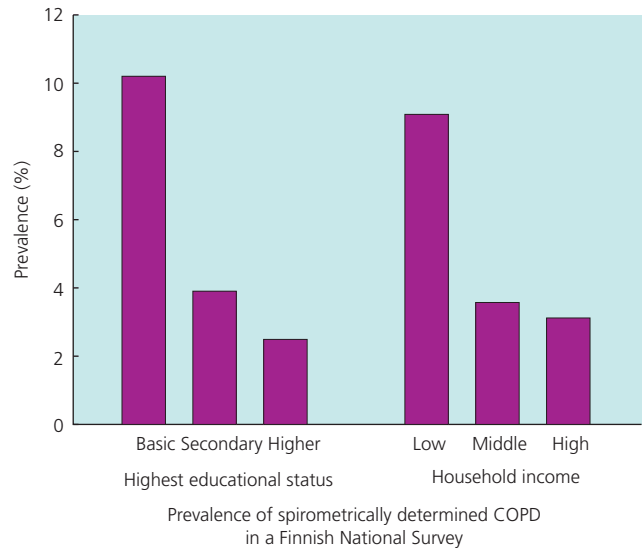


**Figure 1.3** Prevalence (per 1000) of diagnosed COPD in UK men (■) and women (●) grouped by age, between 1990 and 1997. Reproduced from Soriano JB, Maier WC, Egger P et al. *Thorax* 2000; **55**: 789–794, with permission of BMJ Publishing Group.

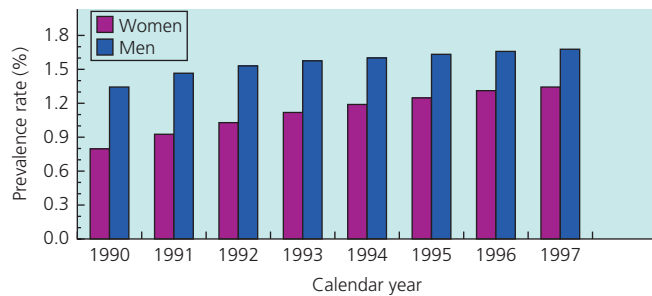
Globally, the World Health Organization (WHO) estimates that 65 million people have moderate to severe COPD. In the UK, a national study reported that 10% of males and 11% of females aged 16–65 had an abnormally low FEV<sub>1</sub>. Similarly, in Manchester, non-reversible airflow obstruction was present in 11% of subjects aged >45 years, of whom 65% had not been diagnosed with COPD. In the UK, an estimated 3 million individuals have COPD but only 1.2 million have a formal diagnosis. In the US, an estimated 24 million have evidence of impaired lung function consistent with COPD, while 12.7 million US adults have diagnosed disease. In a study of 12 countries in Europe, North America, China, Australia, South Africa and the Philippines, the prevalence of COPD in those over the age of 40 years based on lung function criteria was 10.1%, being more common in males (11.8%) than females (8.5%). The prevalence of COPD increases with age, almost doubling with each decade from the age of 40 years. In the UK, the lifetime prevalence of diagnosed COPD has been reported to be increasing and is more common in males than females. In contrast, in the US the prevalence of COPD has been reported to be stable, with the disease being more common in females. COPD is associated with socioeconomic deprivation. In a systematic review, individuals from the lowest socioeconomic strata were at least twice as likely to have COPD when compared with more affluent individuals, regardless of the population studied, metric of socioeconomic status or COPD outcome investigated (Figures 1.4, 1.5).

**Mortality**

Globally, COPD was ranked sixth as the cause of death in 1990, but with the ageing of the world population, the epidemic of cigarette smoking in developing countries and reduced mortality from other currently common causes of death (e.g. ischaemic heart disease and infectious diseases), it is expected that COPD will become the third leading cause of death worldwide by 2030. In 2012, an estimated 6%



**Figure 1.4** Prevalence of COPD confirmed by spirometry in a Finnish National Survey: association with metrics of socioeconomic status. Figure derived using data from Kanervisto M et al. Low socioeconomic status is associated with chronic obstructive airway diseases. *Respiratory Medicine* 2011; **105**: 1140–1146.



**Figure 1.5** Prevalence of diagnosed COPD in UK men and women (per 1000) between 1990 and 1997. Reproduced from Soriano JB, Maier WC, Egger P et al. *Thorax* 2000; **55**: 789–794, with permission of BMJ Publishing Group.

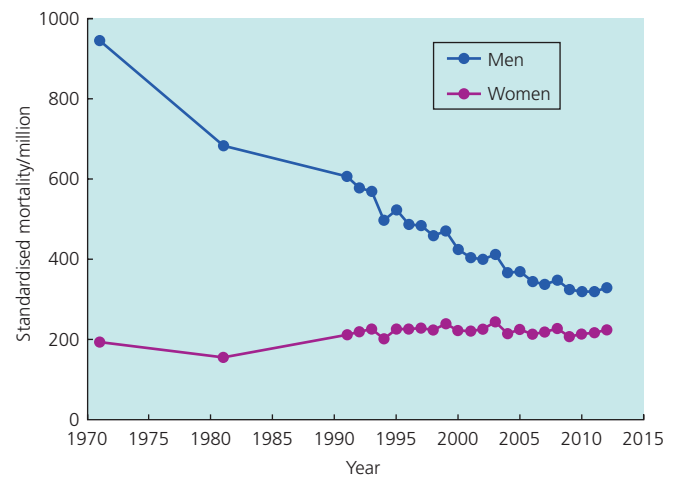
(3 million) of deaths worldwide were attributed to COPD, and more than 90% of these occurred in low- and middle-income countries. In the UK in 2014, there were approximately 30 000 deaths attributed to COPD, with 15 300 of these deaths in males and 14 700 in females. These figures suggest that in the UK, COPD underlies 5.3% of all deaths, 5.5% of male deaths and 5.0% of female deaths. In the US, the most recent data, covering 1999–2013, indicate that 136 000 (5.5%) deaths are a consequence of COPD, and that it is the third leading cause of death behind cancer and heart disease.

In the UK, over the last 40 years, mortality rates due to COPD have fallen in males and risen in females. In the US, the age-adjusted death rate for COPD in males is approximately 1.3 times greater than the rate in females. However, since there are more females in the general US population than males, the actual number of females dying from COPD has exceeded the number of males dying since about 1999. COPD mortality rates increase with age, disease severity and socioeconomic disadvantage. On average, in the UK COPD reduces life expectancy by 1.8 years (76.5 versus 78.3 years for controls). Mild disease reduces life expectancy by 1.1 years, moderate disease by 1.7 years and severe disease by 4.1 years. In the US, it has been estimated that a male smoker at the age of 65 years will have his life expectancy reduced by 0.3, 2.2 and 5.8 years, with mild, moderate and severe disease respectively. For a female smoker at age 65, mild, moderate and severe COPD is associated with reduced life expectancies of 0.2, 2.0 and 6.1 years respectively (Figure 1.6).

### Morbidity and economic impact

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

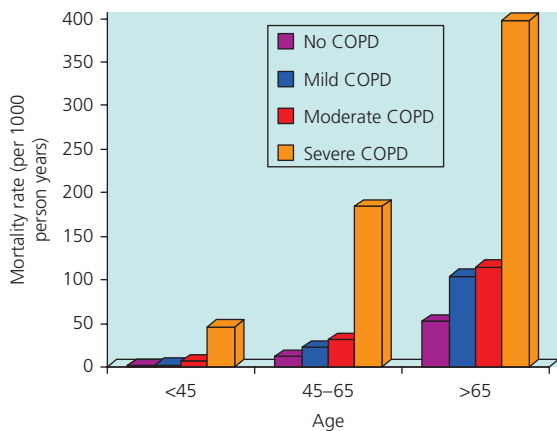
In the UK, emergency hospital admissions for COPD have steadily increased as a percentage of all admissions, from 0.5% in 1991 to 1% in 2000 and 1.5% in 2008–2009. In 2008–2009, COPD exacerbations resulted in 164 000 hospital admissions in the UK, with an average duration of stay of 7.8 days, accounting for 1.3 million bed-days. COPD is the second largest cause of emergency admission to hospital in the UK and is one of the most costly inpatient conditions treated by the National Health Service (NHS). At least 10% of emergency admissions to hospital are as a consequence of COPD



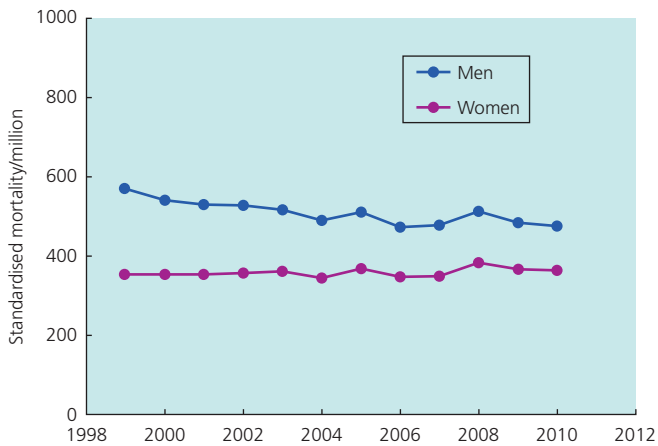
**Figure 1.6** UK death rates from COPD since 1971. Mortality age-standardised rates per million, based on the European Standard Population. Figure derived using data from death registrations, selected data tables, England and Wales 2013. Office for National Statistics, London. [www.ons.gov.uk/ons/datasets-and-tables/index.html?pageSize=50&sortBy=none&sortDirection=none&newquery=standardised+mortality+by+cause+and+age+DR+series](http://www.ons.gov.uk/ons/datasets-and-tables/index.html?pageSize=50&sortBy=none&sortDirection=none&newquery=standardised+mortality+by+cause+and+age+DR+series).

and this proportion is even greater during the winter. Approximately 25% of individuals diagnosed with COPD are admitted to hospital and about 15% of all patients are admitted each year. In the US in 2010, there were an estimated 715 000 hospital discharges with COPD as the first-listed condition, while in contrast to the UK, the number and rate of COPD hospitalizations remained unchanged between 1999 and 2010. In both the US and the UK, there has been an increase in the proportion of COPD admissions that are female. In the UK, similar proportions of males and females are admitted with exacerbations of COPD, but in the US since 1993 COPD discharge rates for females have been higher than for males.

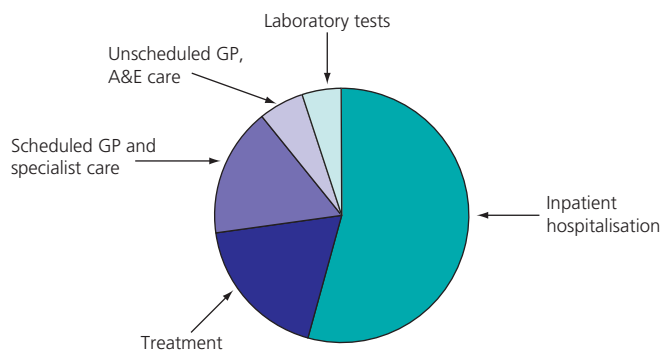
The impact in primary care is even greater in that 86% of care is exclusively provided by primary care. It has been estimated that an average general practitioner's list will include 200 patients with COPD (even more in areas of social deprivation), although not all will be diagnosed. It has also been estimated that COPD is responsible for 1.4 million GP consultations annually and that each diagnosed patient costs the UK economy £1639 each year, equating to a national burden of £982 million. For each patient, annual direct costs to the NHS are £819, with 54% of this due to hospital admissions and 19% due to drug treatment. 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 of COPD have been estimated at £820 per patient and consist of 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 European economy was €38.7 billion (€4.7 billion for ambulatory care, €2.7 billion for drugs, €2.9 billion for inpatient care and €28.4 billion for lost working days). In the US, the National Heart Lung and Blood Institute estimated that the national annual cost to the US economy of COPD in 2010 was \$49.9 billion (\$29.5 billion in direct healthcare expenditure, \$8.0 billion in lost productivity and \$12.4 billion in lost productivity attributable to premature deaths) (Figures 1.7–1.9).



**Figure 1.7** UK deaths from COPD (per 1000 person-years) by age and severity of COPD. Figure derived using data from Soriano JB, Maier WC, Egger P et al. *Thorax* 2000; **55**: 789–794. Reproduced with permission of BMJ Publishing Group.



**Figure 1.8** COPD mortality in the United States of America, 1999–2010, expressed as standardised mortality per million. Figure redrawn with data from [www.cdc.gov/copd/pdfs/graph\\_copd\\_death\\_rates\\_united\\_states1999\\_2010.pdf](http://www.cdc.gov/copd/pdfs/graph_copd_death_rates_united_states1999_2010.pdf).



**Figure 1.9** An analysis of the direct costs of COPD to the NHS. 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 the single most important risk factor in the development of COPD, with studies consistently reporting dose–response associations and accelerated decline

in lung function. Current smoking is also associated with an increased diagnosis and death. Pipe and cigar smokers have significantly greater morbidity and mortality from COPD than non-smokers, although the risk is less than for cigarettes. Approximately 50% of cigarette smokers develop airflow obstruction and 10–20% develop clinically significant COPD. The risk of developing lung function evidence of COPD increases by 20% for each 10 pack-years of smoking. Although smoking is the dominant risk factor, it is not a prerequisite. It is now increasingly apparent that 5–12% of people with diagnosed COPD have never smoked and based on spirometry, 20–40% of individuals with COPD have either never smoked or have a minimal cumulative smoking history.

Maternal smoking during and after pregnancy is associated with reduced infant, childhood and adult lung 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 postnatal exposure.

### Other factors

An increasing number of risk factors other than smoking have been associated with COPD, particularly in developing countries (Box 1.2). These non-smoking risk factors include indoor (biomass) and outdoor air pollution, occupational exposures and early life factors such as intrauterine growth retardation, poor nutrition, repeated lower respiratory tract infections and a history of pulmonary tuberculosis.

#### Box 1.2 Non-smoking risk factors associated with the development of COPD.

##### Indoor air pollution

- Smoke from biomass fuel: plant residues (wood, charcoal, crops, twigs, dried grass) animal residues (dung)
- Smoke from coal

##### Occupational exposures

- Crop farming: grain dust, organic dust, inorganic dust
- Animal farming: organic dust, ammonia, hydrogen sulphide
- Dust exposures: coal mining, hard rock mining, tunnelling, concrete manufacture, construction, brick manufacture, gold mining, iron and steel founding
- Chemical exposures: plastic, textile, rubber industries, leather manufacture, manufacture of food products
- Pollutant exposure: transportation and trucking, automotive repair

##### Treated pulmonary tuberculosis

##### Repeated childhood lower respiratory tract infections

##### Chronic asthma

##### Outdoor air pollution

- Particulate matter (<10 $\mu$ m or <2.5 $\mu$ m diameter)
- Nitrogen dioxide
- Carbon monoxide

##### Poor socioeconomic status

##### Low educational attainment

##### Poor nutrition

Reproduced with permission from Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009; **374**: 733–743.

Many of these risk factors are interrelated; for example, biomass smoke exposure is associated with intrauterine growth retardation and repeated early life lower respiratory tract infections.

### Air pollution

Urban air pollution may be involved in lung function development and consequently be a risk factor for COPD. Cross-sectional studies have demonstrated that higher levels of atmospheric air pollution are associated with cough, sputum production, breathlessness and reduced lung function. Exposure to particulate and nitrogen dioxide air pollution has been associated with impaired lung function in adults and reduced lung growth in children.

Worldwide, approximately 3 billion individuals are exposed to indoor air pollution from burning biomass fuel (wood, charcoal, animal waste) in open fires or poorly functioning stoves for cooking and heating. It has been estimated that biomass smoke exposure underlies about 50% of COPD in developing countries. Exposure to biomass smoke is a particular problem for females and young children who are heavily exposed during food preparation. Exposure to biomass smoke has been reported to increase the risk of COPD 2–3-fold.

### Occupation

Some occupational environments with intense prolonged exposure to irritating dusts, gases and fumes can cause COPD independently of cigarette smoking. However, smoking appears to enhance the effects of occupational exposure by increasing the risk of COPD development. It has been estimated that about 15–20% of diagnosed cases are attributable to occupation, and in life-long non-smokers this proportion increases to about 30%. Occupations that have been associated with a higher prevalence of COPD include coal mining, hard rock mining, tunnel working, concrete manufacture, construction, farming, foundry working, the manufacture of plastics, textiles, rubber, leather and food products, transportation and trucking (Figure 1.10) The increasing recognition that occupation can contribute to the development of COPD emphasises the importance of taking a full chronological occupational history.

### $\alpha$ 1-Antitrypsin deficiency

The best documented genetic risk factor for COPD is  $\alpha$ 1-antitrypsin deficiency. However, this is rare and is present in only 1–2% of patients with COPD.  $\alpha$ 1-Antitrypsin is a glycoprotein responsible for the majority of antiprotease activity in serum. The  $\alpha$ 1-antitrypsin gene is highly polymorphic, although some genotypes (usually ZZ) are associated with low serum levels. Severe deficiency of  $\alpha$ 1-antitrypsin is associated with premature and accelerated development of COPD in smokers and non-smokers, although the rate of decline is accelerated in those who smoke. The  $\alpha$ 1-antitrypsin status of patients with severe COPD who are less than 40 years of age should be determined since over 50% have  $\alpha$ 1-antitrypsin deficiency. The detection of such cases identifies family members who require genetic counselling and patients who might be suitable for future potential treatment with  $\alpha$ 1-antitrypsin replacement or lung transplantation.



**Figure 1.10** This patient (with minimal smoking history) was found to have chronic obstructive pulmonary disease, with his occupation (coal miner) being the main risk factor. The image shows coal dust tattoos on his back.

### Further reading

- American Lung Association. Trends in COPD (Chronic Bronchitis and Emphysema): Morbidity and Mortality. Available at: [www.lung.org/assets/documents/research/copd-trend-report.pdf](http://www.lung.org/assets/documents/research/copd-trend-report.pdf) (accessed 20 February 2017).
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- Gershon AS, Dolmage TE, Stephenson A, Jackson B. Chronic obstructive pulmonary disease and socioeconomic status: a systematic review. *Journal of COPD* 2012; **9**: 216–226.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD. Available at: <http://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/> (accessed 20 February 2017).
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- Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009; **374**: 733–743.