CHRONIC RESPIRATORY DISEASES

4. Chronic Disease Epidemics

KEY MESSAGES

- **Chronic disease epidemics take decades to become fully established.**
- **Chronic diseases often begin in childhood.**
- **Because of their slow evolution and chronic nature, chronic diseases present opportunities for prevention.**
- **Many different chronic diseases may occur in the same patient (e.g. chronic respiratory diseases, cardiovascular disease and cancer).**
- **The treatment of chronic diseases demands a long-term and systematic approach.**
- **Care for patients with chronic diseases should be an integral part of the activities of health services, alongside care for patients with acute and infectious diseases.**

Chronic respiratory diseases are a group of chronic diseases affecting the airways and the other structures of the lungs. Common chronic respiratory diseases are listed in Table 2, as they appear in ICD-10. Common symptoms of the respiratory tract are also listed in ICD-10 (Table 3).

Table 2 Common chronic respiratory diseases

Diseases	International Classification of Diseases (ICD-10)
Asthma	J44[a] –46
Bronchiectasis	A15–16[b], J44, J47, Q32–33
Chronic obstructive lung disease, including chronic obstructive pulmonary disease, bronchitis and emphysema	J40–44
Chronic rhinosinusitis	J32–33
Hypersensitivity pneumonitis	J66–67
Lung cancer and neoplasms of respiratory and intrathoracic organs	C30–39
Lung fibrosis	B90, J69, J70, J84, P27

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TABLE 2 (CONTINUED)

Diseases	International Classification of Diseases (ICD-10)
Chronic pleural diseases	C38, C45, D38, J92
Pneumoconiosis	J60–65
Pulmonary eosinophilia	J82
Pulmonary heart disease and diseases of pulmonary circulation including pulmonary embolism, pulmonary hypertension and cor pulmonale	I26–28
Rhinitis	J30–31, J45 [a]
Sarcoidosis	D86
Sleep apnea syndrome	G47

[a] Codes depicted are not exclusive of the disease listed. All codes mentioning the specific diseases were included.
[b] In patients with tuberculosis.
Source: reference *29.*

Table 3 Symptoms and signs involving the respiratory system

Respiratory symptoms	International Classification of Diseases (ICD-10)
Haemorrhage from respiratory passages ■ Epistaxis ■ Haemoptysis	R04 ■ R04.0 ■ R04.2
Cough	R05
Abnormalities of breathing ■ Dyspnoea ■ Stridor ■ Wheezing ■ Hyperventilation ■ Sneezing	R06 ■ R06.0 ■ R06.1 ■ R06.2 ■ R06.4 ■ R06.7
Pain in the throat and chest	R07
Other symptoms and signs involving the circulatory and respiratory systems ■ Asphyxia ■ Pleurisy ■ Respiratory arrest (cardiorespiratory failure) ■ Abnormal sputum	R09 ■ R09.0 ■ R09.1 ■ R09.2 ■ R09.3
Source: reference *29*.	

Hundreds of millions of people around the world suffer from preventable chronic respiratory diseases. The prevalence estimates shown in Table 4 are likely to be conservative. This report focuses on the following preventable chronic respiratory diseases and their risk factors:

- Asthma and respiratory allergies.
- Chronic obstructive pulmonary disease (COPD).

- Occupational lung diseases.
- Sleep apnea syndrome.
- Pulmonary hypertension.

Table 4 Estimates of the prevalence of preventable chronic respiratory diseases

Chronic respiratory disease	Year of estimation	Prevalence	Reference
Asthma	2004	300 million	*15*
Chronic obstructive pulmonary disease	2000	210 million	*30–32*
Allergic rhinitis	1996–2006	400 million	*33–37*
Other respiratory diseases	2006	>50 million	*38–44*
Sleep apnea syndrome	1986–2002	>100 million	*45–48*

Respiratory symptoms are among the major causes of consultation at primary health care centres. Surveys in nine countries, in 76 primary health care facilities, among which 54 (71.1%) involved medical officers and 22 (28.9%) nurses only. The number of primary health care facilities, involving 29 399 respiratory patients, showed that the proportion of patients with respiratory symptoms, among those over 5 years of age, who visited primary health care centres ranged from 8.4% to 37.0% (Table 5).

Table 5 Proportion of patients with respiratory symptoms among all patients (aged 5 years and older) who visited primary health care facilities for any reason

	Males	Females
Argentina	36.1%	32.2%
Guinea	20.6%	28.7%
Morocco (1st survey)	31.0%	21.4%
Morocco (2nd survey)	37.0%	28.7%
Nepal	17.1%	11.3%
Thailand	9.8%	8.4%

Source: reference *49*.

5. Asthma

KEY MESSAGES

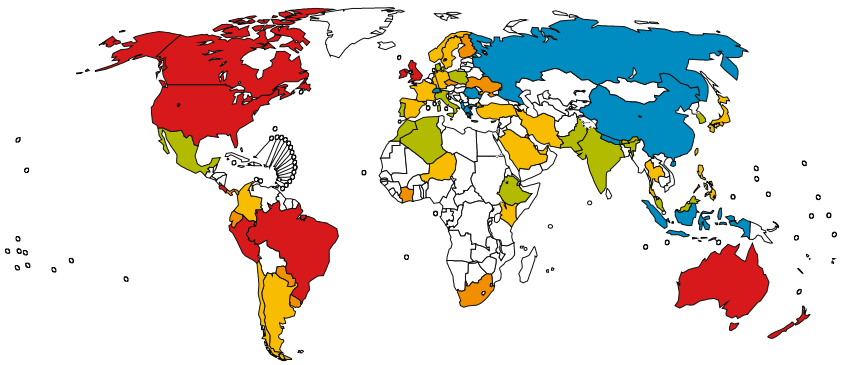
- **300 million people of all ages worldwide have asthma.**
- **The prevalence of asthma has increased following changes to a modern, urban lifestyle.**
- **Globally, 250 000 people die of asthma every year.**
- **Asthma deaths are related to lack of proper treatment.**
- **Treatment for asthma is not available to all people who have asthma.**

Asthma is a chronic inflammatory disorder of the airways, usually associated with airway hyper-responsiveness and variable airflow obstruction, that is often reversible spontaneously or under treatment (*50*). Allergen sensitization is an important risk factor for asthma. Asthma is often associated with rhinitis, an inflammation of the nasal mucosa (*51*).

Prevalence

Asthma affects both children and adults. Using a conservative definition, it is estimated that as many as 300 million people of all ages and all ethnic backgrounds suffer from asthma. Two large multinational studies have assessed the prevalence of asthma around the world: the European Community Respiratory Health Survey (ECRHS) in adults (*52*) and the International Study of Asthma and Allergies in Childhood (ISAAC) in children (*33*). The world map of the prevalence of asthma (Figure 4) is based on these two studies (*15*).

Figure 4 World map of the prevalence of clinical asthma



Proportion of population (%)

- ≥10.1
- 7.6–10.0
- 5.1–7.5
- 2.5–5.0
- 0–2.5
- No standardized data available

Source: reference *15*.

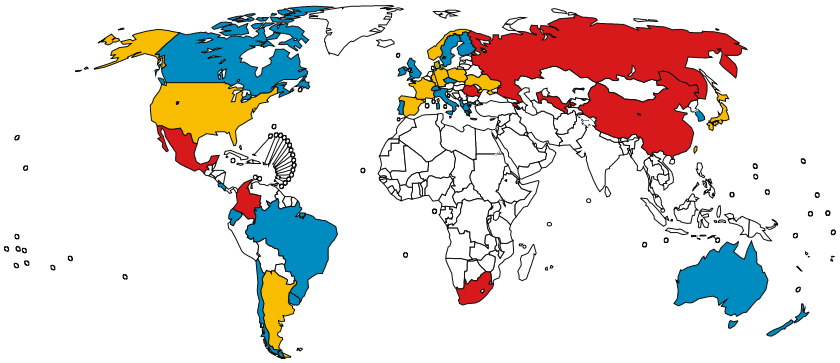
Trends in asthma prevalence vary between countries. For the past 40 years, the prevalence of asthma has increased in all countries in parallel with that of allergy. Asthma is still increasing worldwide as communities adopt modern

lifestyles and become urbanized (*13, 53, 54*). With a projected increase in the proportion of the world's population living in urban areas, there is likely to be a marked increase in the number of people with asthma worldwide over the next two decades. It is estimated that there may be an additional 100 million people with asthma by 2025 (*15*). However, the prevalence of asthma and allergy may decrease in children in some countries with a high prevalence of the disease and the increase in the asthma epidemic may come to an end in some countries (*55–57*).

Mortality

It is estimated that asthma accounts for about 250 000 annual deaths worldwide. There are large differences between countries, and the rate of asthma deaths does not parallel prevalence (Figure 5). Mortality seems to be high in countries where access to essential drugs is low.

Figure 5 World map of asthma case fatality rates: asthma deaths per 100 000 people with asthma in the 5–34 year age group



Countries shaded according to case fatality rate (per 100 000 people with asthma)

- ≥10.1
- 5.1–10.0
- 0–5.0
- No standardized data available

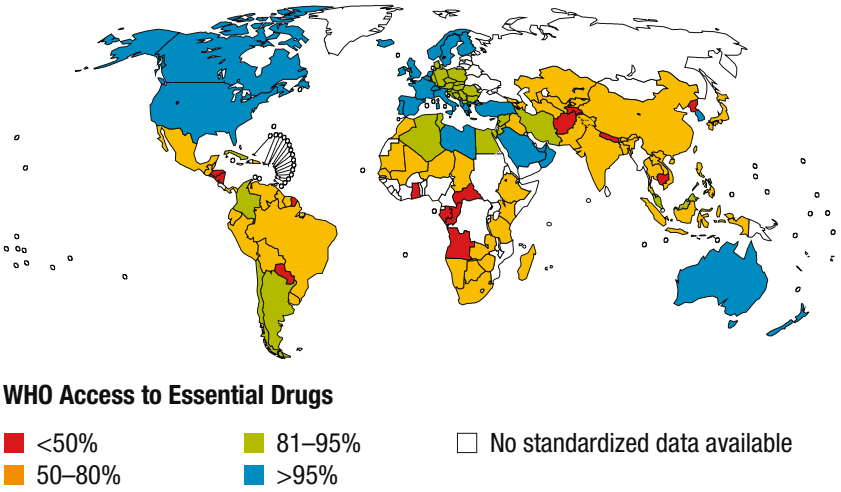
Source: reference *15*.

Many of the deaths are preventable, being a result of suboptimal long-term medical care and delay in obtaining help during the final attack. In many areas of the world, people with asthma do not have access to basic asthma medications and health care (*15*) (Figure 6). The countries with the highest death rates are those in which controller therapy is not available. In many countries, deaths due to asthma have declined recently as a result of better asthma management (*58*).

Morbidity

The hospitalization of patients with asthma is another measure of asthma severity, but data cannot be obtained in most low and middle income countries (*59*). In countries or regions where asthma management plans have been implemented, hospitalization rates have decreased (*58, 60*). Asthma is often severe in poor people and minorities (*61*).

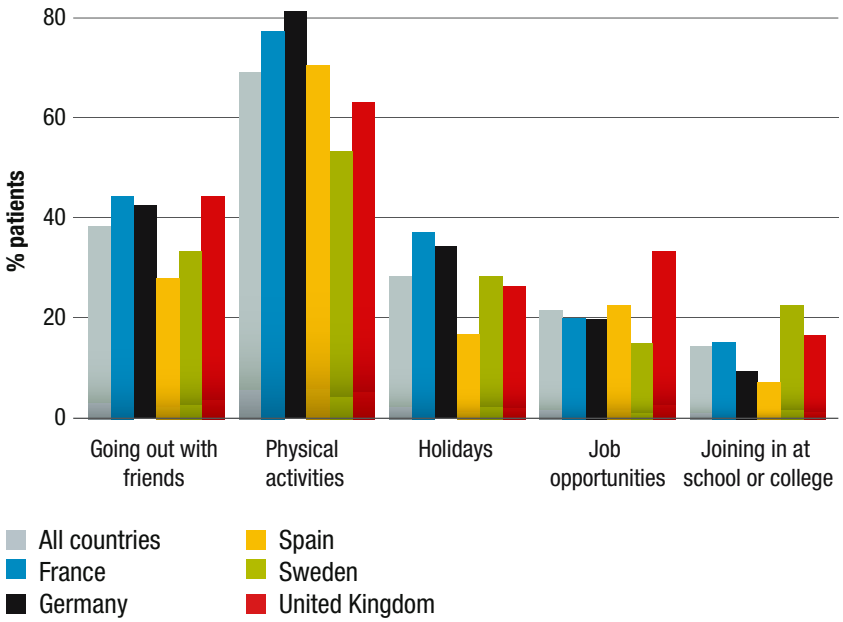
Figure 6 World map of the proportion of the population with access to essential drugs



Source: reference *15*.

Asthma impairs school and work performance and social life (*62*). Physical quality of life is impaired by bronchial symptoms, while social life is also impaired by rhinitis co-morbidity (*63*). In 2005, in some countries of the European Union, asthma still had a major effect on patients' social life and physical activities, as well as school and work (Figure 7).

Figure 7 Effects of asthma on patients, European Union, 2005



Source: reference *64*.

Childhood asthma accounts for many lost school days and may deprive the affected children of both academic achievement and social interaction, in particular in underserved populations (*65*) and minorities (*66*). Educational programmes for the self-management of asthma in children and adolescents reduce absenteeism from school and the number of days with restricted activity (*67*).

The burden of asthma assessed by disability-adjusted life years (DALYs), which ranks 22 worldwide, is similar to that of other chronic diseases such as diabetes or Alzheimer disease (Table 6).

Table 6 Disability-adjusted life years (DALYs) attributable to disorders causing the greatest burden worldwide

Rank	Disorder	Number of DALYs ($x10^3$)
1	Lower respiratory infections	91.3
2	HIV/AIDS	84.4
3	Unipolar depressive disorders	67.2
4	Diarrhoeal diseases	61.9
5	Ischaemic heart diseases	58.6
6	Cerebrovascular disease	49.2
7	Malaria	46.5
8	Road traffic accidents	38.7
9	Tuberculosis	34.7
10	**Chronic obstructive pulmonary disease**	**27.7**
11	Congenital abnormalities	27.3
12	Hearing loss – adult onset	26.0
13	Cataracts	25.2
14	Measles	22.4
15	Violence	21.4
16	Self-inflicted injuries	20.7
17	Alcohol use disorders	20.3
18	Protein energy malnutrition	16.9
19	Falls	16.2
20	Diabetes mellitus	15.4
21	Schizophrenia	16.1
22	**Asthma**	**15.3**
23	Osteoarthritis	14.8
24	Vision loss, age-related and other	14.1
25	Cirrhosis of the liver	13.9

Source: reference *68*.

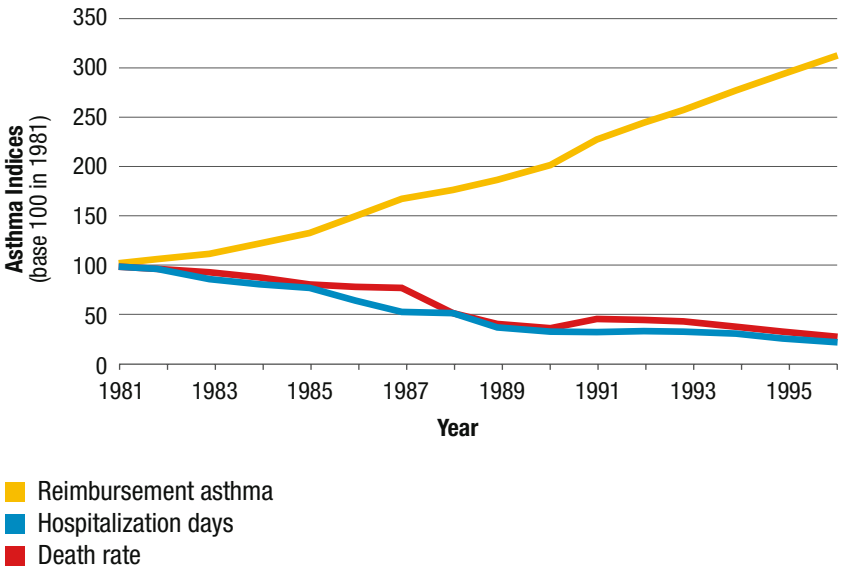
Economic costs

The economic cost of asthma is considerable both in terms of direct medical costs (such as hospital admissions and the cost of pharmaceuticals) and indirect medical costs (such as time lost from work and premature death) (*15,*

69, 70). The costs of asthma are high in severe or uncontrolled asthma (*71*). Many children with undiagnosed asthma miss school and require emergency department visits, albeit that those with a current diagnosis of asthma report more resource use (*72*). Children of low socioeconomic status are more likely to require resources because of their asthma (*73*). In low and middle income countries, childhood asthma has significant adverse effects on the child's daily activities, schooling, family life and finances (*74*).

Health-care benefits from asthma intervention programmes are clearly leading to a marked decrease in death rates and hospitalizations in high income countries (Figure 8), low and middle income countries, and deprived areas (*60, 75, 76*). In a study of 3748 low income, minority group children living in the United States, an education programme resulted in a 35% decrease in overall hospitalization rates, a 27% decrease in asthma-related visits to an emergency department and a 19% decrease in outpatient visits (*76*). However, in Finland, the asthma programme had no effect on the prevalence of the disease, which is still increasing. The number of people with asthma increased, although mortality and morbidity decreased considerably.

Figure 8 Health–care benefits of the asthma programme in Finland, 1981–1995



Source: reference *58*.

Co-morbidities

The links between rhinitis and asthma are of importance. Epidemiological studies have consistently shown that asthma and rhinitis often co-exist in the same patients. In epidemiological studies, over 70 % of people with asthma have concomitant rhinitis (*77–79*). However, only 15 to 40% of rhinitis patients have clinically demonstrable asthma. Patients with severe persistent rhinitis have asthma more often than those with intermittent disease (*80*). Allergic and non-allergic rhinitis are associated with asthma. Although differences exist between rhinitis and asthma, upper and lower airways may be considered as a unique entity influenced by a common and probably evolving inflammatory process, which may be sustained and amplified by intertwined mechanisms (*51*).

The prevalence of rhinitis has been studied in some large epidemiological studies. According to the European Community Respiratory Health Survey (ECRHS), the prevalence of rhinitis is around 35% in Europe and Australasia (*34*). According to the International Study of Asthma and Allergy in Childhood (ISAAC), the prevalence of allergic rhinitis ranges from very low to 50% of adolescents (*81*), with an average of over 30% (*13*). The ISAAC study was carried out in the 1990s. According to more recent studies, the prevalence of allergic rhinitis has increased, in particular in countries with a low prevalence (*82–90*). In a recent study in the general population in Europe, the prevalence of allergic rhinitis was around 25% (*35, 36*). The prevalence of allergic rhinitis is increasing in developing countries. The prevalence of an IgE sensitization to aeroallergens measured by allergen specific IgE in serum or skin tests is over 40% of the population in Australia, Europe, New Zealand and the United States of America (*57, 91–93*). Most but not all of the sensitized subjects are suffering from allergic rhinitis or asthma or both.

The sequential development of allergic disease manifestations during early childhood is often referred to as the "allergy march" (*94*). Various epidemiological and birth-cohort studies have begun to elucidate the evolution of allergic disease manifestations and to identify populations at risk for disease (*95, 96*). These studies emphasize the effects of environmental factors and genetic predisposition on the allergy march. In many patients, food allergy precedes inhalant allergen allergy. In the allergy march, atopic dermatitis and asthma are linked, but atopic dermatitis does not necessarily precede asthma, whereas allergic rhinitis is a risk factor for asthma and can precede asthma (*97–99*).

In most low and middle income countries, the prevalence of active smoking in adults with asthma is about 25%. Compared to nonsmokers with asthma, active smokers have more severe asthma symptoms (*100*), an accelerated decline in lung function (*101*) and a reduced response to corticosteroid therapy (*102*). Every effort should be made to encourage individuals with asthma who smoke to stop (*103*).

6. Chronic Obstructive Pulmonary Disease

KEY MESSAGES

- **Chronic obstructive pulmonary disease (COPD) affects 210 million people.**
- **Chronic obstructive pulmonary disease was the fifth cause of death in 2002 and it is projected to be the fourth cause of mortality by 2030 (*104*).**
- **Tobacco smoking is the major risk factor, but the use indoors of solid fuels for cooking and heating also presents major risks.**
- **Strategies to reduce exposure to major risk factors are likely to have an impact on morbidity and mortality.**

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease with various clinical presentations. The basic abnormality in all patients with COPD is airflow limitation. Therefore, experts from the Global Initiative for Obstructive Lung Diseases (GOLD) have defined the disease based on spirometric criteria by using the post-bronchodilator forced expiratory volume in one second (FEV_1) and its ratio to the forced vital capacity (FVC) (*105*). The main criterion for COPD is a FEV_1/FVC ratio <70%. The terms chronic bronchitis and emphysema are no longer part of the COPD definition (Table 5) (*106, 107*).

Table 7 Definitions of chronic bronchitis, emphysema and chronic obstructive pulmonary disease

Disease	Reference	Definition	
Chronic bronchitis	108	Clinical definition	Chronic productive cough for 3 months in each of 2 consecutive years in a patient in whom other causes of productive chronic cough have been excluded.
Emphysema	108	Anatomic definition	Permanent enlargement of the airspaces distal to the terminal bronchioles, accompanied by destruction of their walls without obvious fibrosis.
Chronic obstructive pulmonary disease (COPD)	107, 109	Functional definition	Preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs in response to noxious agents including cigarette smoke, biomass fuels and occupational agents. The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema). COPD is a multicomponent disease with extra-pulmonary effects.

Source: reference *110*.

Sub-classification into mild, moderate, severe and very severe disease is achieved by including various levels of FEV_1 as percentage of predicted value (Table 8) (*111*). This classification was found to correlate with pathologic findings (*112*) and the prediction for mortality (*113*).

Up to 2001, only 32 prevalence studies had been reported for COPD whereas there were hundreds for asthma and thousands for cancer or cardiovascular

Table 8 Classification of the severity of chronic obstructive pulmonary disease, based on post-bronchodilator FEV_1

Stage	Characteristics
I: Mild	$FEV_1/FVC < 70\%$ $FEV_1 \geq 80\%$ predicted
II: Moderate	$FEV_1/FVC < 70\%$ $50\% \leq FEV_1 < 80\%$ predicted
III: Severe	$FEV_1/FVC < 70\%$ $30\% \leq FEV_1 < 50\%$ predicted
IV: Very severe	$FEV_1/FVC < 70\%$ $FEV_1 < 30\%$ predicted Or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

FEV_1, forced expiratory volume in one second; FVC, forced vital capacity.

Respiratory failure is defined as arterial partial pressure of oxygen (PaO_2) less than 8.0 kPa (60 mmHg) with or without arterial partial pressure of CO_2 ($PaCO_2$) greater than 6.7 kPa (50 mmHg) while breathing air at sea level.

Source: reference *107*.

diseases (*114*). Fortunately, a number of initiatives are currently under way to produce new data. Some of these initiatives are presented in this report.

COPD is a major public health problem in subjects over 40 years of age and will remain a challenge for the future. It is a major cause of chronic morbidity and mortality worldwide (*107*) and is projected to rank seventh in 2030 as a worldwide burden of disease (*104*). The rise in morbidity and mortality from COPD will be most dramatic in Asian and African countries over the next two decades, mostly as a result of a progressive increase in the prevalence of smoking (*115*). Even if risk factors were avoided today, the toll of COPD would continue for several decades because of the slow development of the disease. However, a recent critical analysis of methods to estimate projections of the burden of diseases, by using extrapolation or by using risk factors, has called attention to the difficulties in having a precise definition of global trends on COPD burden (*116*).

Prevalence

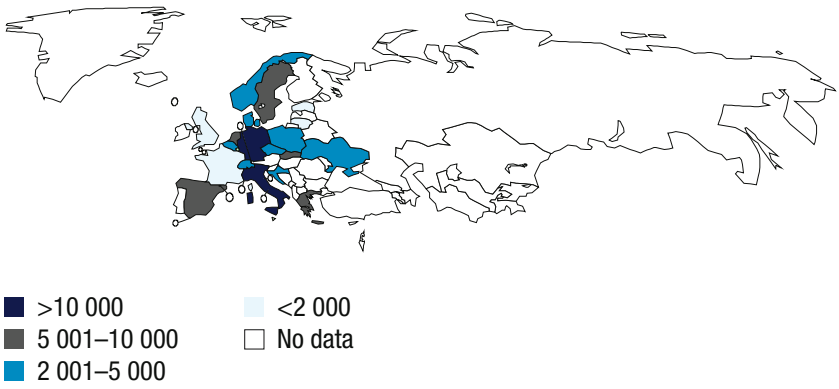
Until recently, most of the information available on COPD prevalence came from high income countries. Even in these countries, data greatly underestimate the total burden of COPD because the disease is usually not diagnosed until it is clinically apparent and moderately advanced (*117*) and the definition of COPD varies between studies. An approach using the single term COPD (rather than individual coding for chronic bronchitis, emphysema and chronic airway obstruction) is favoured (*114*), although differences in prevalence rates are reported when different definitions of COPD are used (*118*).

As calculated using appropriate epidemiological methods, the prevalence of COPD is generally higher than is recognized by health authorities or administrative databases (*119*). It has been estimated to range from 4% to up to 20% in adults over 40 years of age (*120–125*), with a considerable increase

by age, particularly among smokers. COPD nevertheless occurs in people aged 20–44 years (*126*) (Table 9, Figure 9). Large differences exist between countries. These are attributable to many factors, including differences in diagnostic methods, year of study, age of the population, and prevalence of main risk factors such as tobacco smoking. Overall, the prevalence estimates shown in Figure 9 and Table 9 are higher than those recorded by national registries, but they may nevertheless underestimate the real prevalence of COPD.

In the United States, in 2002, an estimated 24 million adults had COPD (*127*).

Figure 9 Prevalence rate (/100 000) of chronic obstructive pulmonary disease (COPD) in Europe



Source: reference *125*.

A COPD prevalence model was used to estimate the prevalence of COPD in 12 Asian countries. The total number of moderate to severe COPD cases in the 12 countries of this region, as projected by the model, is 56.6 million with an overall prevalence rate of 6.3%. The COPD prevalence rates for the individual countries range from 3.5% (China, Hong Kong Special Administrative Region, and Singapore) to 6.7% (Viet Nam) (*158*).

In China, chronic respiratory diseases are the second leading cause of death (*32*). It is estimated that over 50% of Chinese men smoke, whereas smoking rates among women are lower in this country (*159*). The prevalence of COPD in men and women in China is not very different (*160*), which points to the importance of risk factors other than smoking in causing COPD in Chinese women. A recent study found a prevalence of physician-diagnosed COPD of 5.9% in the adult population (*160*).

In India, a study collecting data without spirometry assessment suggested that 12 million people were affected by COPD (*161*). Recent studies from the same authors (*162, 163*) show a prevalence of respiratory symptoms in 6%–7% of non-smokers and up to 14% of smokers. In a recent study in southern India, the prevalence rate of COPD in adults was around 7%.

The Burden of Obstructive Lung Disease (BOLD) study is currently being carried out in different parts of the world including low and middle income countries (*164*). This very important study compares the prevalence and burden of COPD across the world using the same protocol, including the BOLD questionnaire and spirometry. Some results are already available and show

Table 9 Prevalence estimates of chronic obstructive pulmonary disease (COPD) by diagnostic approach

Country	Reference	Year	Diagnostic criteria	Age (years)	COPD prevalence (%)		
					Overall	Males	Females
Spirometry–based diagnosis							
Denmark	*(128)*	1989	$FEV_1/FVC<70\%$, $FEV_1<60\%$ predicted	20–90	3.7		
England	*(129)*	1999	$FEV_1<5^{th}$ percentile + reversibility	60–75	9.9		
Finland	*(130)*	1994	Clinical examination + spirometry	≥ 65		12.5	3.0
	(131)	2000	Clinical examination + spirometry $FEV_1/FVC<70\%$, $FEV_1<60\%$ predicted	≥ 30		22.1 11.0	7.2 5.2
Italy	*(120)*	2000	ERS spirometric criteria	≥ 25	11.0	12.5	11.8
Norway	*(132)*	1979	Clinical examination + spirometry	16–69	4.1	3.7	4.6
	(133)	1991	Symptoms + spirometry $FEV_1/FVC<70\%$, $FEV_1<80\%$ predicted	18–70	5.4 4.5	5.6 4.8	5.2 4.2
Spain	*(134)*	1998	$FEV_1/FVC<70\%$, $FEV_1<80\%$ predicted	40–60		6.8	
	(135)	2000	ERS spirometric criteria + reversibility	40–69	9.1	14.3	3.9
USA	*(136)*	1971	$FEV_1/FVC<60\%$	20–69		13.0	2.0
	(137)	2000	$FEV_1/FVC<70\%$, $FEV_1<80\%$ predicted	≥ 17	6.8		
Symptom-based diagnosis (chronic bronchitis)							
Australia	*(138)*	1968	MRC criteria	≥ 21		9.0	3.0
Brazil	*(139, 140)*	1994-1995	MRC criteria	≥ 40	12.7	17.9	9.1
Denmark	*(128)*	1989	Daily phlegm ≥ 3 months for ≥ 1 year	20–90	10.1	12.5	8.2
England	*(141)*	1989	MRC criteria	40–74		16.7	7.1
Iceland	*(142)*	1999	ATS criteria	50–80		7.1	16.7
India	*(143)*	1994	MRC criteria	≥ 15	7.7	7.6	7.8
Nepal	*(144)*	1984	MRC criteria	≥ 20	18.3	17.6	18.9
Area comprising the state of Zimbabwe	*(145)*	1978	MRC criteria	>20	1.1	1.2	1.5
Spain	*(134)*	1998	ECSC criteria	40–60		9.2	
USA	*(135)*	1971	MRC criteria	20–69		17.0	10.0
	(146)	1977	Cough and phlegm ≥ 3 months	20–74		17	6

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TABLE 9 (CONTINUED)

Country	Reference	Year	Diagnostic criteria	Age (years)	COPD prevalence (%)		
					Overall	Males	Females
Multiple	*(147)*	1997	3 criteria based on symptoms and history	50–69		1.2-12.9	
Multiple	*(148)*	2001	MRC criteria	20–44	3.2	3.7	2.8
Patient-reported disease							
Canada	*(149)*	2000	Physician diagnosed	35–44 45–54 55–64		1.8 1.5 5.0	3.5 3.6 4.5
	(150)	1999	Physician diagnosed	≥ 55	5.7	6.3	5.2
England	*(141)*		Patient report (chronic bronchitis)	40–74		3.9	2.1
Estonia	*(151)*	2001	Physician diagnosed (chronic bronchitis)	54–64	10.7	9.3	11.5
Finland	*(152)*	1999	Physician diagnosed	20–69	3.7		
Hong Kong SAR	*(153)*	1995	Patient report of disease	≥ 70	8.0	10.7	5.5
Sweden	*(154)*	1991	Physician diagnosed	35–66	4.1	4.7	4.0
	(155)	1998	Physician diagnosed	20–59	3.7		
USA	*(156)*	1975	Patient report (chronic bronchitis)	All ages	6.6		
	(157)	1996	Patient report (chronic bronchitis)	All ages	5.4		

[a] MRC, Medical Research Council ; ATS, American Thoracic Society ; ECSC, European Commission for Steel and Coal.
Source: reference *121*.

that the prevalence of COPD is far higher than is recorded. In Guangdong, China (*165*), the prevalence of COPD is 9.4% and it is higher in the rural area than in the urban area suggesting a synergic effect of smoking and biomass burning. In Latin America (*166*), the *Proyecto Latinoamericano de Investigacion en Obstruccion Pulmonar* (the PLATINO Project) (*167, 168*) showed that COPD prevalence was over 10% in subjects older than 40 years of age (Table 10). The results shown in Table 10 were obtained using the BOLD method (*164*). These results indicate that the prevalence of COPD is higher than previously reported, and that women who do not smoke can be affected by COPD. Most patients have mild COPD. However, the concomitant diagnosis of asthma, chronic bronchitis or emphysema is common among COPD patients from the general population, particularly in adults aged over 50 years (*123, 169*). It is important to make the distinction between asthma and COPD, even in older patients because their optimal management must be based on distinctively different approaches (*27, 50, 106*).

Smoking is a major risk factor in men (*170*). In non-smoking women, unexpectedly, the prevalence of COPD is also high in high income countries, as well as in low and middle income countries. In low and middle income countries, COPD in women may be associated with biomass burning.

Table 10 Prevalence of chronic obstructive pulmonary disease (COPD) in Latin America: results of the PLATINO study

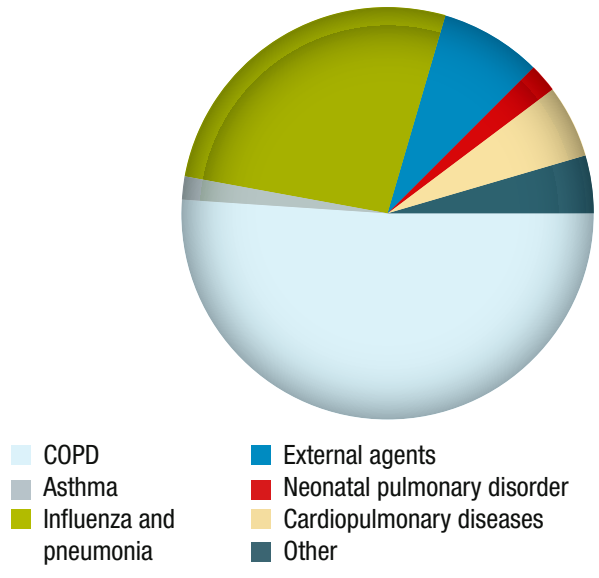
		Sao Paulo Brazil	Santiago Chile	Mexico city Mexico	Montevideo Uruguay	Caracas Venezuela
Sex	Men	18.0%	23.3%	11.0%	27.1%	15.7%
	Women	14.0%	12.8%	5.6%	14.5%	10.2%
Age	40–49 years	8.4%	7.1%	2.2%	5.1%	5.4%
	50–51 years	16.2%	13.0%	4.5%	12.7%	9.8%
	≥ 60 years	25.7%	30.3%	18.4%	21.2%	23.4%
COPD[a] stage	Stage 0	25.3%	33.6%	23.2%	19.1%	23.1%
	Stage I	10.1%	11.0%	5.2%	12.5%	6.4%
	Stage II	4.6%	4.9%	1.9%	6.4%	4.9%
	Stage III	0.9%	0.7%	0.5%	0.6%	0.7%
	Stage IV	0.2%	0.3%	0.2%	0.1%	0.1%
Education (years)	0–2	22.1%	33.3%	11.3%	29.4%	16.2%
	3–4	16.3%	21.4%	12.1%	23.5%	13.7%
	5–8	14.4%	17.7%	6.1%	21.4%	12.0%
	≥ 9	10.4%	13.6%	6.0%	15.2%	10.6%
Smoking	Never	12.5%	15.9%	6.2%	15.3%	6.6%
	0–9.9 pack–years	12.8%	13.9%	6.3%	14.3%	8.1%
	10–19.9 pack–years	15.3%	15.5%	15.7%	14.7%	15.3%
	≥ 20 pack–years	24.6%	30.8%	15.4%	32.0%	24.8%

[a] COPD was defined as post-bronchodilator $FEV_1/FVC<70\%$.
Source: reference *168*.

Mortality

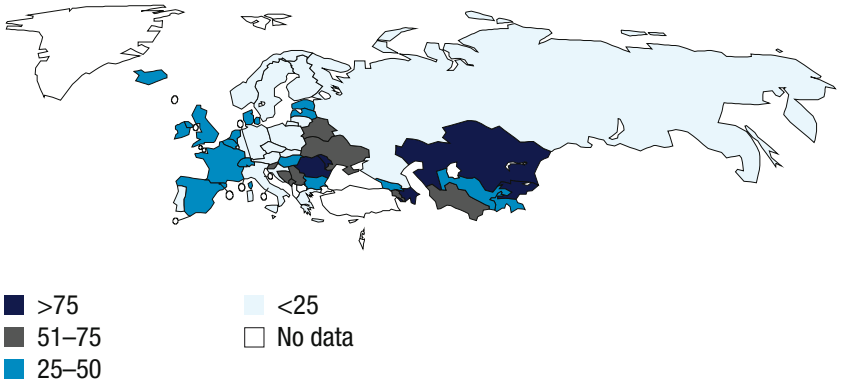
Mortality data are rarely available. When available, they usually underestimate COPD as a cause of death by around 50% (*171, 172*). Moreover, there may be misuses of mortality data such as attributing death to cor pulmonale when this condition was caused by COPD (*173*). The proportion of deaths from various diseases, as reported in the United States, is shown in Figure 10 (*174*). In Europe, large differences exist and they are likely to be attributable to variations in reporting and risk factors (Figure 11).

Figure 10 Deaths from lung diseases in the United States in 2001



Source: reference *174*.

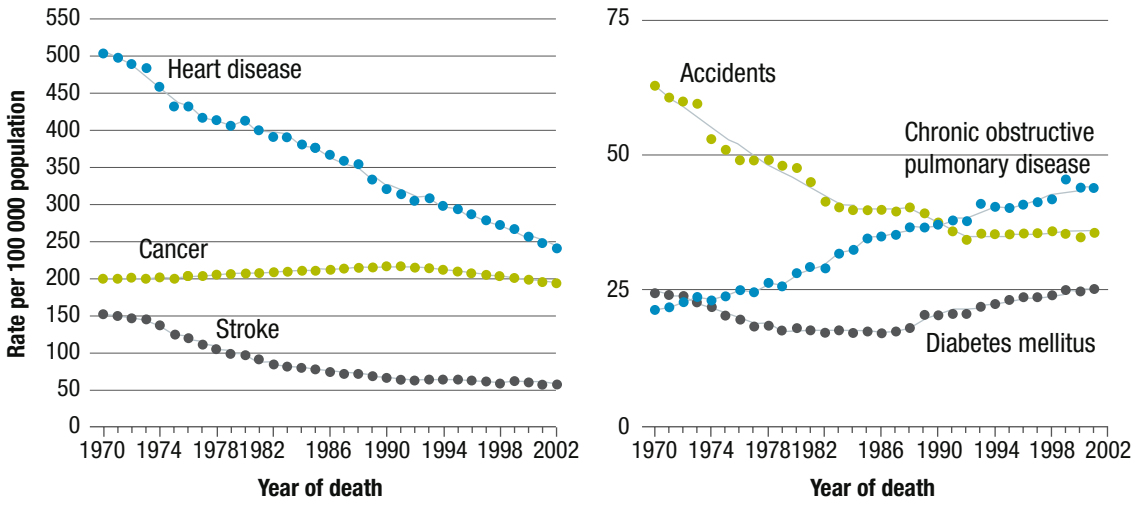
Figure 11 Mortality rate (/100 000) attributable to chronic obstructive pulmonary disease (COPD) in Europe



Source: reference *125*.

Deaths attributable to COPD have increased sharply in countries where data are available. According to WHO, COPD will move from fifth leading cause of death in 2002, to fourth place in the rank projected to 2030 worldwide (*104*). In high income countries, COPD is the major chronic disease for which deaths are increasing. In the USA, death rates for COPD have doubled between 1970 and 2002 (*175*) (Figure 12). There is a perception that COPD affects more males than females; however, 50.3% of the deaths attributable to COPD in 2000 in the USA were among women (*176*). In Latin America, COPD deaths have increased by 65.0% in the last decade (*166*). Treatment interventions were found to reduce COPD mortality (*177*).

Figure 12 Trends in age–standardized death rates for the six leading causes in the United States, 1970 to 2020



Source: reference *175*.

Morbidity

COPD is a major cause of chronic morbidity worldwide (*107, 178*). It is projected that it will rank seventh in 2030 as a worldwide burden of disease (*104*) (Table 11).

Table 11 Changes in rankings for 15 leading causes of DALYs, 2002 and 2030

Category	Disease or injury	2002 Rank	2030 Ranks	Change in Ranks
Within top 15	Perinatal conditions	1	5	-4
	Lower respiratory infections	2	8	-6
	HIV/AIDS	3	1	+2
	Unipolar depressive disorders	4	2	+2
	Diarrhoeal diseases	5	12	-7
	Ischaemic heart disease	6	3	+3
	Cerebrovascular disease	7	6	+1
	Road traffic accidents	8	4	+4
	Malaria	9	15	-6
	Tuberculosis	10	25	-15
	COPD	11	7	+4
	Congenital anomalies	12	20	-8
	Hearing loss, adult onset	13	9	+4
	Cataracts	14	10	+4
	Violence	15	13	+2
Outside top 15	Self-inflicted injuries	17	14	+3
	Diabetes mellitus	20	11	+9

Source: reference *104*.

COPD severely impairs quality of life (*179, 180*). There are multiple generic and disease-specific instruments that can be used to measure health-related quality of life (HRQOL), each incorporating various aspects of physical, psychological and social function (*181*). The association between HRQOL and lung function is usually weak, whereas it is greater with COPD co-morbidities (*182*). Exacerbations lead to substantial reductions in HRQOL, both in physical as well as other domains (*183*). HRQOL usually improves on resolution of the exacerbation (*181*).

Acute exacerbations of COPD are a common cause of morbidity and mortality. There is no universally accepted definition of an exacerbation of COPD (*184*). Most definitions use an increase in symptoms requiring increased treatment. The common etiological factors are bacterial or viral infections and air pollutants. There are no data on the frequency, severity and duration of exacerbations in COPD. Exacerbations of COPD adversely affect the natural history of COPD (*185*). Hospitalizations attributable to COPD are common and their frequency is recognized as a prognostic marker (*186*). The European Respiratory Society (ERS) white book states that the number of hospitalizations for COPD in 1993 in Germany was 125 000, in Italy 40 000, and in the United Kingdom 73 000 (*125*). Hospitalizations attributable to COPD are sharply increasing in most countries.

Economic costs

The economic burden of COPD is considerable and will continue to grow as the number of elderly people continues to increase (*187*). Data are, however, limited and available only for high income countries (Table 12). BOLD is developing a health economic model to estimate the future burden of COPD and to assess the cost–effectiveness of an intervention.

Table 12 Comparison of the costs associated with chronic obstructive pulmonary disease (COPD) in different countries

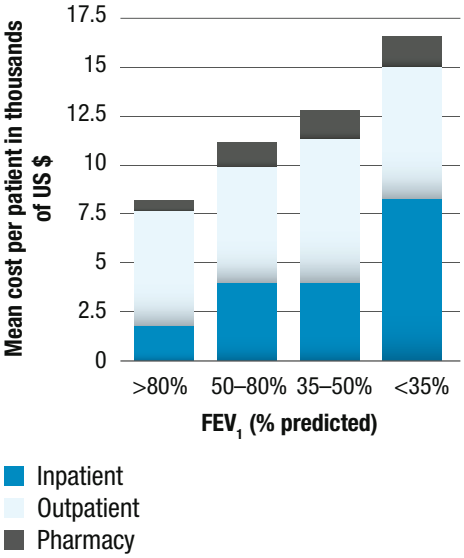
Country	Reference	Year of publication	Costs	Cost per patient per year	Global costs per year (in millions)
Spain	*(188)*	1992		€ 959	Direct: € 319 Indirect: € 451
USA	*(189)*	2000	Direct	Stage I: US$ 1681 Stage II: US$ 5037 Stage III: US$ 10 812	
Sweden	*(190)*	2000	Direct and indirect		Direct: € 109 Indirect: € 541
USA	*(191)*	2000	Direct	emphysema: US$ 1341 chronic bronchitis: US$ 816	US$ 14 500
Netherlands	*(192)*	1999	Direct	US$ 876	
Italy	*(193)*	2002	Direct	Stage I: € 151 Stage II: € 3001 Stage III: € 3912	
Sweden	*(194)*	2002	Direct and indirect	US$ 12 984	
Spain	*(195)*	2003	Direct	Stage I: € 1185 Stage II: € 1640 Stage III: € 2333	€ 427
Spain	*(196)*	2004	Direct	€ 909	€ 239
USA	*(197)*	2005	Direct and indirect		US$ 32 000

Source: reference *114*.

In the United States, in 2000, total annual costs were in excess of US$ 32 billion (*197*). The majority of patients using health-care resources are those with moderate to severe disease, with this group responsible for up to 70% of the total medical expenditure in the United States (*176*). Hospitalizations for acute exacerbation of COPD are the major contributor to the annual cost. COPD is the most expensive of the chronic diseases found in elderly patients. COPD is the fourth most common diagnosis cited on discharge for all hospitalized elderly people and the most common diagnosis for those aged 65 to 74 years (*197*). Direct costs increase with COPD severity, as assessed by FEV_1 values (*198*) (Figure 13).

In the European Union, among respiratory diseases, COPD is the leading cause of work days lost (*125*).

Figure 13 Costs for chronic obstructive pulmonary disease (COPD) in the United States, by severity as assessed using FEV_1 values



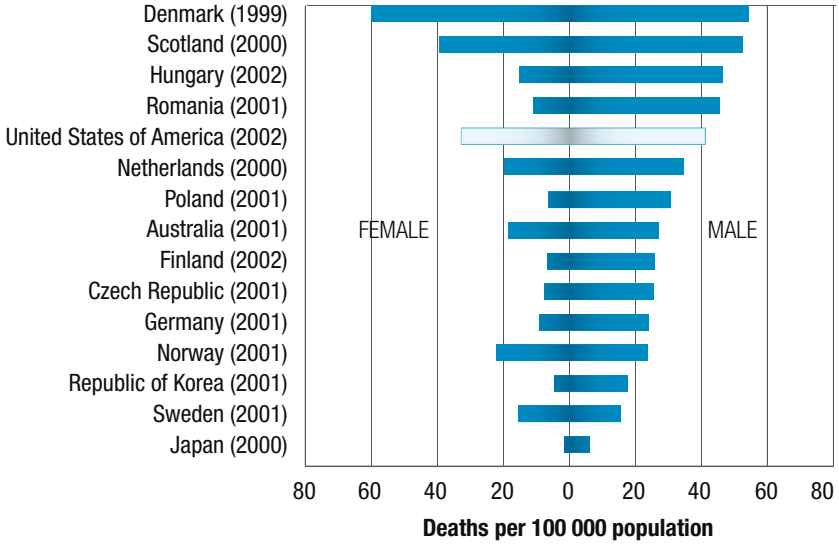
Source: reference *198*.

COPD in women

The effect of COPD on women is not sufficiently studied, but there appear to be sex differences in the prevalence, severity, risk factors (*199, 200*) and death rates (Figure 14).

In the NAHNES III study carried out among 13 995 non-smokers, 4.7 ± 0.3% had mild COPD (age, 60.9 ± 1.3 years) and were mostly female (82.5%), while 1.9 ± 0.3% had moderate-to-severe COPD (age 39.3 ± 1.3 years) and were mostly male (88.1%). Few non-smokers with COPD (12.1 ± 2.4%) had

Figure 14 Age–adjusted death rates for chronic obstructive pulmonary disease (COPD) in males and females aged 35–74 years



Source: reference *202*.

a previous diagnosis of chronic bronchitis or emphysema. Similar data have been found in Japan (*124*).

It is possible that the level of FEV_1 in smokers has a different effect in men and women since, in the Euroscop study, reduced baseline FEV_1 was associated with respiratory symptoms in men but not in women (*201*).

Sex differences in hyper-responsiveness were first noted in the Lung Health Study (*203*). Women are more predisposed to suffer the adverse respiratory consequences of tobacco smoking, with the development of COPD at an earlier age and with a greater degree of lung function impairment for a given amount of tobacco exposure (*204–206*). Women may benefit most from smoking cessation (*206, 207*). Conversely, reduction in smoking behaviour has been more pronounced in men than women.

Co-morbidities

COPD is a multi-component and systemic disease (*208, 209*). The components affect both the lungs and organs outside the lungs – the so-called systemic effects of COPD (*210–212*) – and can be of either a structural (including airway remodelling, emphysema, skeletal muscle wasting or osteoporosis) or functional nature (inflammation, apoptosis, senescence). Furthermore, these components are interdependent in a closely linked vicious cycle.

Even allowing for common etiological factors, a link has been identified between COPD and other systemic diseases (*213*), such as cardiovascular disease (*214*), diabetes (*215*), osteoporosis (*216*) and possibly peptic ulcer.

COPD and other disorders associated with reduced lung function are strong risk factors for cardiovascular hospitalizations and deaths, independent of smoking (*214, 217, 218*). Studies suggest that cardiovascular risk should be monitored and treated with particular care in any adult with COPD (219) and that COPD and other co-morbidities should be carefully considered in patients with chronic heart failure (*220*).

COPD and lung cancer are common in the same patients (*221*). Although other risk factors for lung cancer exist, smoking is the major risk factor. The presence of moderate or severe obstructive lung disease is a significant predictor of lung cancer in the long term (*222*). The screening for lung cancer in patients at risk is, however, still a matter of debate (*223*).

7. Obstructive Sleep Apnea Syndrome

KEY MESSAGES

- **Obstructive sleep apnea syndrome is the most common organic sleep disorder.**
- **It may affect children and adults, and result in excessive daytime somnolence and poor performance.**
- **It has been associated with increased frequency of accidents and arterial hypertension.**

Snoring and sleep apnea are common disorders that affect both men and women. The prevalence of snoring and obstructive sleep apnea syndrome increases with age, with a peak between the ages of 55 to 60 years (45–48). Women start to snore later in life, with an increased prevalence after menopause.

Obstructive sleep apnea syndrome is a clinical disorder marked by recurring episodes of upper airway obstruction that lead to markedly reduced (hypopnea) or absent (apnea) airflow at the nose or mouth. These episodes are usually accompanied by loud snoring and hypoxemia, and are typically terminated by brief micro-arousals, which result in sleep fragmentation (*224*). Patients with obstructive sleep apnea syndrome are typically unaware of such arousals, but the resulting deterioration in sleep quality contributes greatly to excessive daytime sleepiness. Most obstructive sleep apnea syndrome patients have no detectable respiratory abnormality while awake.

Prevalence

The prevalence of obstructive sleep apnea syndrome has been extensively studied in recent decades and has been variously estimated at between 1% and over 6% of the adult population (*225–229*). The Wisconsin cohort study, which studied 1069 employed men and women between 30 and 60 years of age by means of full polysomnography (*225*) found that 9% of women and 24% of men had an apnea index greater than 5 per hour but this estimate of prevalence fell to 2% of women and 4% of men when an apnea index >5 was combined with symptomatic daytime sleepiness. These findings underline the importance of not viewing obstructive sleep apnea syndrome in terms of sleep-related breathing disturbances alone. In a Spanish community study, 6.5% of males met the minimal diagnostic criteria for obstructive sleep apnea syndrome with an apnea-hypopnea index > 5 combined with daytime sleepiness (*226*). In Hong Kong Special Administrative Region, China, the prevalence of symptomatic obstructive sleep apnea syndrome is over 4% of men and over 2% of women ranging in age from 30 to 60 years (*230, 231*). A summary of prevalence from other major epidemiological studies is provided in Table 13.

The male to female ratio of obstructive sleep apnea syndrome is about two to one. This greater prevalence in males is still poorly understood. However, sex-specific hormones may play a role, with androgens promoting upper airway collapsibility (*232*), while progesterone, in contrast, seems to lead to an augmented ventilatory response. It has long been recognized that sleep apnea is very common in elderly people but the clinical significance of this

Table 13 Prevalence of obstructive sleep apnea syndrome

Country and reference	Population subjects	Age (years)	Criteria	Prevalence (%)
USA *(225)*	352 men 250 women	30–60 30–60	Hypersomnia and RDI>5	4.0 (M) 2.0 (F)
Spain *(226)*	2148 1050 men 1098 women	30–70	AHI >5 plus symptoms	6.5 (M) 3 (F)
USA *(227)*	4364 men Subsample: 741	20–100	AHI>10 plus daytime symptoms	3.3 45–64 years: 4.7
United Kingdom *(228)*	893 men	35–65	ODI_4 >20, symptomatic ODI_4>10 ODI_4>5	0.3 1.0 4.6
Australia *(229)*	294 men	40–65	RDI>10 Subjective EDS and RDI>5	10.0 3.0

RDI, respiratory disturbance index; AHI, apnea/hypopnea index; ODI_4, oxygen desaturation > 4%; EDS, excessive daytime sleepiness; M, males; F, females.

finding remains unclear (*233, 234*). While many of these subjects are otherwise asymptomatic for obstructive sleep apnea syndrome, there is evidence that sleep apnea in elderly people has an adverse prognosis (*234*).

Children may develop a sleep apnea syndrome similar to that seen in adults, and various epidemiological reports suggest a relatively high prevalence, although somewhat less than in adults (*235, 236*). The etiology of obstructive sleep apnea syndrome in children differs from the etiology in adults in that adenotonsillar hypertrophy is the most common cause of the disorder, although the increasing prevalence of obesity among children in recent years represents an important contributing factor in many cases. Many children with obstructive sleep apnea syndrome can be helped by tonsillectomy.

Morbidity and mortality

The principal physical morbidity and mortality of obstructive sleep apnea syndrome relates to the cardiovascular system. However, there is a high prevalence of other cardiovascular risk factors in patients with obstructive sleep apnea syndrome, which makes the identification of an independent contribution from obstructive sleep apnea syndrome to cardiovascular disease more difficult (*237*). The Sleep Heart Health Study, which includes over 6000 volunteer subjects undergoing in-home polysomnography, identified a modest independent association with hypertension (odds ratio 1.37), increasing with greater severity of the disease (*238*). The Wisconsin Sleep Cohort study identified an even stronger correlation with an odds ratio of 3.1 (*239*). There is also growing evidence of an independent link between obstructive sleep apnea syndrome to other cardiovascular diseases. In the Sleep Heart Health Study cohort, obstructive sleep apnea syndrome emerged as an independent risk factor for congestive cardiac failure (odds ratio 2.2), cerebrovascular disease (odds ratio 1.58) and coronary artery disease (odds ratio 1.27) (*240*). Furthermore, effective continuous positive airway pressure therapy decreases cardiovascular morbidity and mortality, as demonstrated in long-term cardiovascular outcome studies (*241–243*).

Economic costs

There is evidence that, prior to diagnosis, patients with obstructive sleep apnea syndrome incur higher health-care costs than matched control subjects (*244–247*). One study reported that obstructive sleep apnea syndrome patients used more than twice as many healthcare services in the 10-year period prior to diagnosis compared to controls (*244*), and the excess cost compared to control subjects was in the region of 4265 Canadian dollars per patient. Furthermore, the same group reported a significant reduction in health-care costs in the two-year period after introduction of continuous positive airway pressure therapy, compared to the 5-year period before diagnosis and also compared to matched controls during the same 7-year period of follow-up (*246*). Another study (*247*) reported an annual health-care use cost of US$ 2720 for obstructive sleep apnea syndrome patients prior to diagnosis, compared to US$ 1384 among matched control subjects.

The economic costs of obstructive sleep apnea syndrome should also be placed in the context of the potential impact of untreated disease on society. There is now clear evidence of an increased risk of road traffic accidents in untreated patients with obstructive sleep apnea syndrome. Various studies have demonstrated an increase in accident rate to between 3 and 7 times that of the general population among untreated obstructive sleep apnea syndrome patients; these rates fall to normal levels after successful therapy with continuous positive airway pressure (*248–250*).

A further aspect of the economic cost of obstructive sleep apnea syndrome relates to diagnosis and treatment. The traditional approach to diagnosis has been the demonstration of the disorder through overnight sleep studies in a dedicated sleep laboratory (*251*). These studies are, however, resource intensive. Increasing emphasis is thus being placed on limited diagnostic techniques that focus on cardio-respiratory variables and are suitable for home-based studies (*252*). The cost of treatment with continuous positive airway pressure is relatively modest (*253*) – involving the provision of a device with a lifespan of at least 5 years – and compares favourably with the cost of treatment for other chronic respiratory disorders such as asthma and chronic obstructive pulmonary disease.

Co-morbidities

Obstructive sleep apnea syndrome is associated with many adverse sequelae, both behavioural and physical. Behavioural consequences include daytime sleepiness, impaired concentration and neuropsychological dysfunction (*254, 255*) while physical consequences include cardiovascular disorders, particularly hypertension (*238–241, 256*). However, the excessive daytime sleepiness and associated behavioural consequences of obstructive sleep apnea syndrome are reversible with effective treatment, and there is emerging evidence that cardiovascular complications also benefit from therapy (*242, 243, 257*).

8. Pulmonary Hypertension

KEY MESSAGES

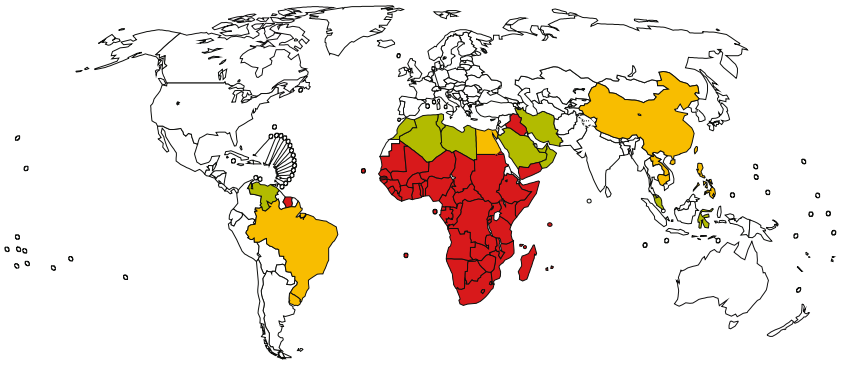
- **Pulmonary hypertension may be primary, or a consequence of various conditions, such as chronic obstructive pulmonary disease, pulmonary fibrosis, sickle cell disease and schistosomiasis.**
- **It is often associated with a poor prognosis.**
- **Interventions to control risk factors and treat pulmonary hypertension may reduce the burden of the disease.**

Pulmonary hypertension is defined as a mean pulmonary artery pressure above 25 mm Hg (*258*). If untreated, this condition has a poor prognosis.

Idiopathic pulmonary arterial hypertension, also known as primary pulmonary hypertension, is rare and has an estimated prevalence of 6 per million in France. Pulmonary arterial hypertension associated with other conditions such as systemic sclerosis, congenital heart diseases, portal hypertension and HIV infection has a cumulated prevalence of around 15 per million (*259*). Although it is not a common disease, pulmonary hypertension affects millions of patients around the world.

Several major risk factors of pulmonary hypertension have been identified (Figure15). Pulmonary hypertension and cor pulmonale may complicate many advanced pulmonary conditions including COPD (*260, 261*), bronchiectasis, cystic fibrosis, or lung fibrosis. When present, pulmonary hypertension directly contributes to disability and early mortality, causing a heavy burden worldwide.

Figure 15 Countries where schistosomiasis is prevalent



almost eliminated
ongoing large–scale control
limited or no control

Source: reference *267*.

Pulmonary hypertension may affect a substantial proportion of highlanders in many countries, causing a large burden in Bolivia and other Andean countries, as well as in Kyrgyzstan, China and other Himalayan countries (*44, 262, 263*).

Pulmonary hypertension is a major cause of disability and mortality in patients with hepatosplenic forms of schistosomiasis, causing a heavy burden in Brazil, Egypt, South-East Asia and sub-Saharan Africa (*40, 264, 265*). It is estimated that up to 20% of patients with schistosomiasis (Figure 15) may suffer from pulmonary hypertension. Many aspects of morbidity attributable to schistosomiasis are expected to change after schistosomiasis is controlled (*266*). Some aspects are expected to change quickly (worm burden, Salmonella bacteraemia, hepatosplenic schistosomiasis in children), whereas others will persist for years (pulmonary hypertension, glomerulonephritis, neuroschistosomiasis).

Pulmonary hypertension is a major cause of disability and mortality in patients with sickle cell disease and thalassaemia, causing a substantial burden in Africa and in people of African origin worldwide, as well as in people from Mediterranean countries (*268*). In adult patients with sickle cell disease, although the rise in pulmonary arterial pressure is mild, the associated morbidity and mortality are high, and pulmonary hypertension is emerging as the major independent risk factor for death (*42*).

Patients with tuberculosis, HIV infection, liver cirrhosis, autoimmune diseases, congenital heart diseases and sarcoidosis are also at risk for pulmonary hypertension (*259*).

After an acute pulmonary embolism, up to 3% of patients may develop chronic thrombo-embolic pulmonary disease. This may lead to severe chronic thrombo-embolic pulmonary hypertension, a condition that can be cured by means of surgical thrombo-endarterectomy.

Obesity has been associated with various forms of pulmonary hypertension, mainly attributable to associated risk factors such as appetite suppressant intake, hypoxemia, left heart disease and thrombo-embolic disease (*269*).