03 CHRONIC OBSTRUCTIVE PULMONARY DISEASE

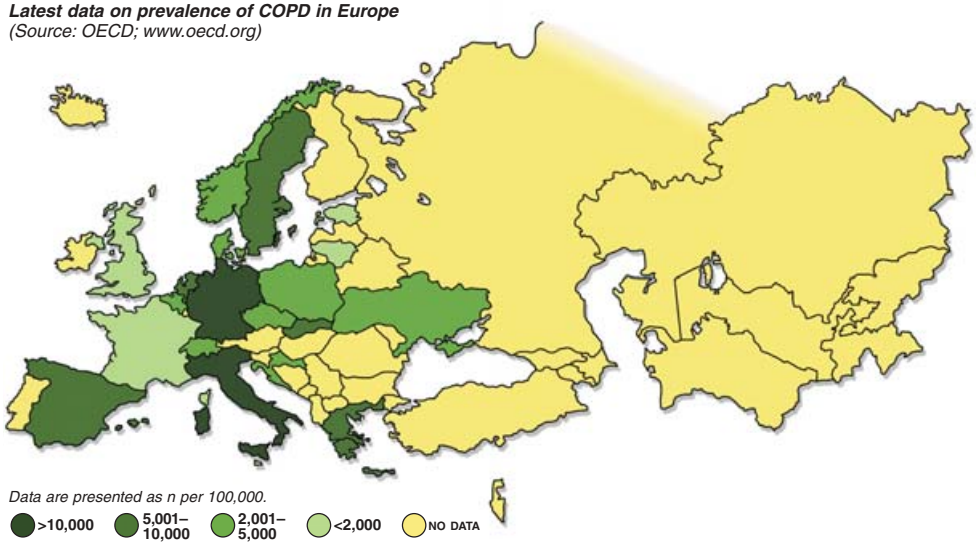
OVERVIEW

Chronic obstructive pulmonary disease (COPD) is a common, costly and preventable disease that has substantial implications for the health of Europeans. The term COPD is used in a variety of ways when it is judged to be contributing to, but not the main cause of, death leading to misclassification and omissions from medical records and vital statistics. This leads to problems of interpreting measurements of prevalence of disease and mortality in COPD, particularly with intercountry comparisons. Thus, data from COPD patients should always be interpreted with caution.

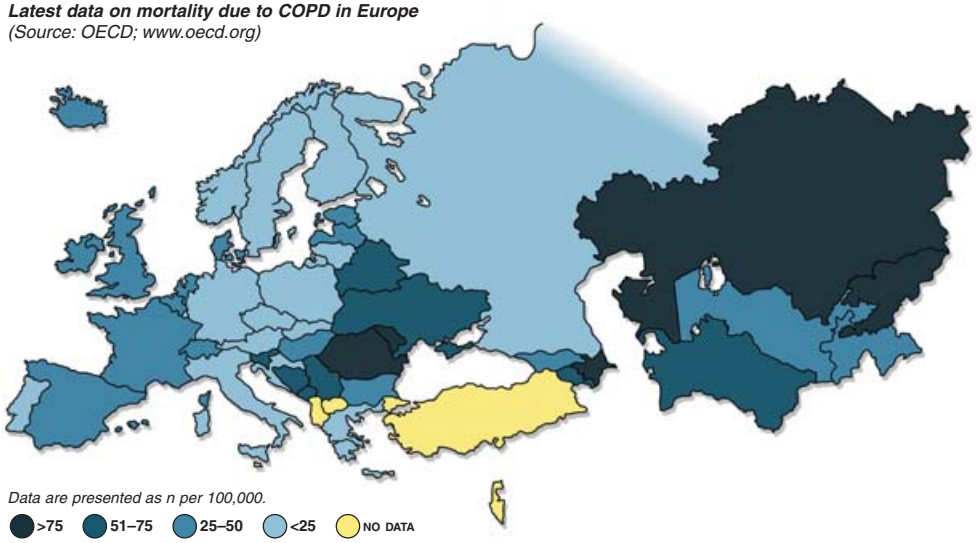
The prevalence of clinically relevant COPD varies in European countries from 4–10% of the adult population. There is a paucity of prevalence data from Central and Eastern Europe.

Mortality rates range from 95 per 100,000 in Kyrgyzstan to six per 100,000 in Greece. There is considerable variation in mortality rates between the principal data sources (national health institutions, Organisation for Economic Cooperation and Development (OECD) and published literature).

Latest data on prevalence of COPD in Europe
(Source: OECD; www.oecd.org)



Latest data on mortality due to COPD in Europe
(Source: OECD; www.oecd.org)



INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterised by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with abnormal inflammatory response of the lungs to noxious particles or gases. Symptoms, functional abnormalities and complications of COPD can partly be explained on the basis of this underlying inflammation and the resulting pathology. These changes may also have systemic consequences.

COPD is a common, costly and preventable disease that has substantial implications for the health of Europeans. However, the interpretation of measurements of the prevalence of disease and mortality in COPD in the population, particularly intercountry comparisons, is extremely problematic. The term COPD is used in a variety of ways when it is judged to be a contributing factor to, but not the main cause of, death, leading to misclassification and omissions from medical records and vital statistics. Therefore, mortality data from COPD patients should always be interpreted with caution. In contrast to asthma, the diagnostic term COPD has not been widely used by physicians or other health professionals and is generally not recognised by the public. When questioned about their condition, most patients will say that they have asthma, chronic bronchitis, emphysema or that the disease is unrecognised. A prerequisite for diagnosis is the measurement of airflow limitation by spirometry but, in many areas, primary care physicians rarely use this to detect COPD in smokers or patients with respiratory symptoms. Greater public awareness of COPD is therefore one of the main aims of the Global Initiative for Chronic Obstructive Lung Disease (GOLD; www.goldcopd.com).

"... mortality data from COPD patients should always be interpreted with caution."

Europe has a population of approximately 750 million and the World Health Organization (WHO) includes 51 countries in this region. Within Europe, there are large differences in population structure and great heterogeneity of the environment. Europe should therefore be an ideal region in which to explore the environmental influences on the incidence, prevalence and mortality of COPD. However, accurate estimates of mortality, prevalence and incidence are lacking from many countries.

EPIDEMIOLOGY

Mortality

In 1990, the WHO estimated the standardised mortality rate of COPD to be 50 per 100,000 in males (fig. 1) and 20 per 100,000 in females in European countries. Thus, approximately 200,000–300,000 people die each year in Europe because of COPD. According to the WHO, in 1997, COPD was the cause of death in 4.1% of males and 2.4% of females in Europe. A recent analysis of mortality trends in the USA from 1979–1993 showed that among 31 million death certificates, 8% had a diagnosis of obstructive lung disease (OLD). However, only 43% of the death certificates listing OLD had defined it as the primary underlying disease. The WHO previously published mortality rates for the combined category of ''bronchitis, emphysema and asthma'', International Classification of Diseases (ICD) codes 490–493, which omits the largest category of COPD mortality, ICD code 519.3 in the eighth revision and ICD code 496 in the ninth revision. This results in a considerable underestimation of COPD deaths in France, Germany, Ireland and the UK.

The mortality rates due to COPD in European countries are two to three times higher in males than in females (fig. 2) with no country greatly below or above those ratios. The countries with the highest rates (more than 80 per 100,000) for males are the Ukraine, Kazakhstan, Ireland and Romania while the highest rates for females (more than 30 per 100,000) are in Romania, Ireland, Kazakhstan and Denmark. The lowest rates (less than 20 per 100,000) for males are observed in Greece, Sweden, Iceland and Norway and for females (less than 10 per 100,000) in Greece, Finland, Switzerland and Sweden. When codes other than ICD 490–496 are used for COPD, the distribution of mortality rates for COPD changes considerably in these countries.

There were considerable differences in mortality trends from 1980–1990 among European countries. There has been an increase in mortality among females in northern European countries, such as Denmark and the UK, whereas there has been a decrease in the countries of Central and Eastern Europe, such as Bulgaria, Hungary and Romania. The upward trend in mortality is seen in females over 55 years of age and in males over 75 years. It is remarkable that over a short period of time there has been a substantial decline in death rates for the major causes of death in most countries, but not for COPD. In contrast to cardiovascular mortality rates, COPD rates are relatively insensitive to intermittent or short-term smoking cessation.

The WHO has made worldwide estimates of mortality rates for COPD. They estimated that age-specific mortality rates for COPD were considerably higher in China than in countries with established market

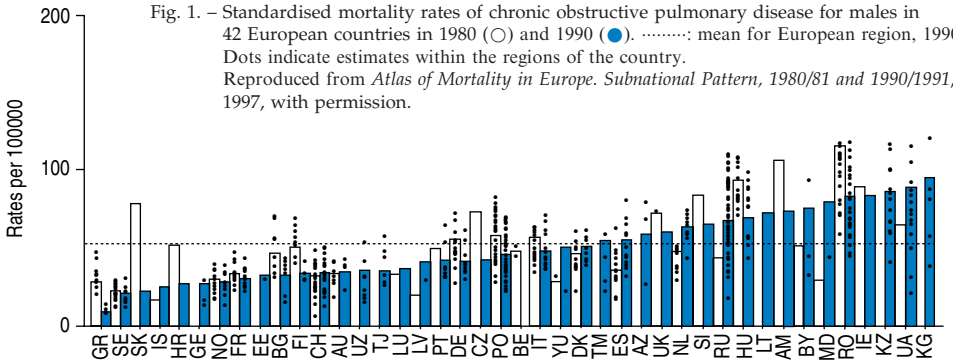


Fig. 1. – Standardised mortality rates of chronic obstructive pulmonary disease for males in 42 European countries in 1980 (○) and 1990 (●). ·····: mean for European region, 1990. Dots indicate estimates within the regions of the country.
Reproduced from *Atlas of Mortality in Europe. Subnational Pattern, 1980/81 and 1990/1991*, 1997, with permission.

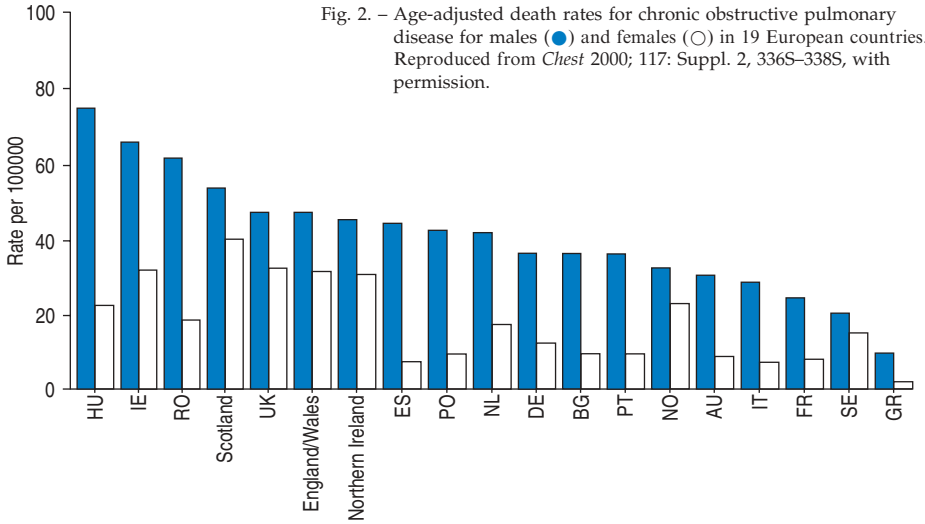


Fig. 2. – Age-adjusted death rates for chronic obstructive pulmonary disease for males (●) and females (○) in 19 European countries. Reproduced from *Chest* 2000; 117: Suppl. 2, 336S–338S, with permission.

economies. The death rates for COPD in China were also higher than in six other global health regions, being countries with formerly socialist economies: sub-Saharan Africa, India, Latin America and the Caribbean, the Middle East, and other Asian countries. The Global Burden of Disease Study has projected COPD mortality rates from 1990–2020 and estimates that COPD will account for over 6 million deaths per year in 2020, which will move COPD from the sixth- to the third-leading cause of death worldwide over this period. The overall mortality from COPD will probably also increase in Europe due to the increased proportion of females who smoke, as well as the increased age of the population.

Prevalence

The frequency of COPD has been distorted by the use of different diagnostic terms and lung function criteria. The Italian general population study showed very large differences in prevalence estimates of COPD when using the 1986 American Thoracic Society criteria, the 1995 European Respiratory Society criteria or ''clinical'' criteria. The adoption of a simple spirometric definition (forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) <70% and FEV_1 <80% of predicted) with standardised measurements may make it easier in the future to compare COPD estimates with different studies and countries. However, a meaningful evaluation of the estimates demands knowledge of age distribution and smoking habits in examined populations.

"... 4–6% of the adult population suffer from clinically relevant COPD."

For the last 40 years, the prevalence of COPD has been estimated in community surveys within several Nordic countries. Studies from the last two decades indicate that 4–6% of the adult population suffer from clinically relevant COPD. The prevalence increases greatly with age and recent surveys show only small differences between sex. Prevalence studies in the UK have been reviewed and it was found that only one national study of ventilatory function had been conducted. This study of 5,547 males and females aged 16–65 years of age showed that an FEV_1 of two or more standard deviations below the age- and height-predicted value was present in 10% of males and 11% of females. A Norwegian spirometry survey of the general population aged 18–73 years gave a prevalence of 6% for airflow limitations defined as an FEV_1/FVC ratio below 0.70, while 4.5% had this ratio in addition to an FEV_1 of less than 80% of predicted. Using the stages advocated by the British Thoracic Society (BTS) and Norwegian reference values, only 0.2% of the adult population could be defined as having severe COPD

with an FEV_1 less than 40% of predicted (fig. 3). Below the age of 45 years severe COPD is a rare disease. A spirometric survey in a random sample of people, aged 25 to 73 years in the Po community in northern Italy, yielded spirometric prevalence estimates similar to those obtained in Nordic countries. Approximately 0.5% of the population could be considered to have severe COPD defined as an FEV_1 less than 50% of predicted. A comparison of community surveys in Sweden, Italy and Norway, using standardised methods showed similar prevalence estimates for bronchitic symptoms and airflow limitation. In a study carried out in random population samples aged 40–69 years in seven different regions of Spain, COPD was defined as an FEV_1/FVC ratio less than 88% of predicted in males and less than 89% of predicted in females with a negative (less than 12% increase in FEV_1) bronchodilator test. This study observed an overall prevalence rate of 10.6% for COPD. In a 1988–1994 population survey of 16,695 inhabitants of the USA, aged 17–89 years, airflow limitation was defined (as in the Norwegian study) as a combination of FEV_1/FVC less than 0.7 and FEV_1 less than 80% of predicted. The overall prevalence of airflow limitation was 5.2%, while 8.2% reported a previous and/or current diagnosis of OLD. A model has been developed from this Third National Health and Examination Survey to estimate prevalence of COPD from the known smoking status of the population. With this model, it was estimated that 1.8 million people suffer from COPD in Spain, 3.0 million in the UK, 2.7 million in Germany, 2.6 million in Italy and 2.6 million in France.

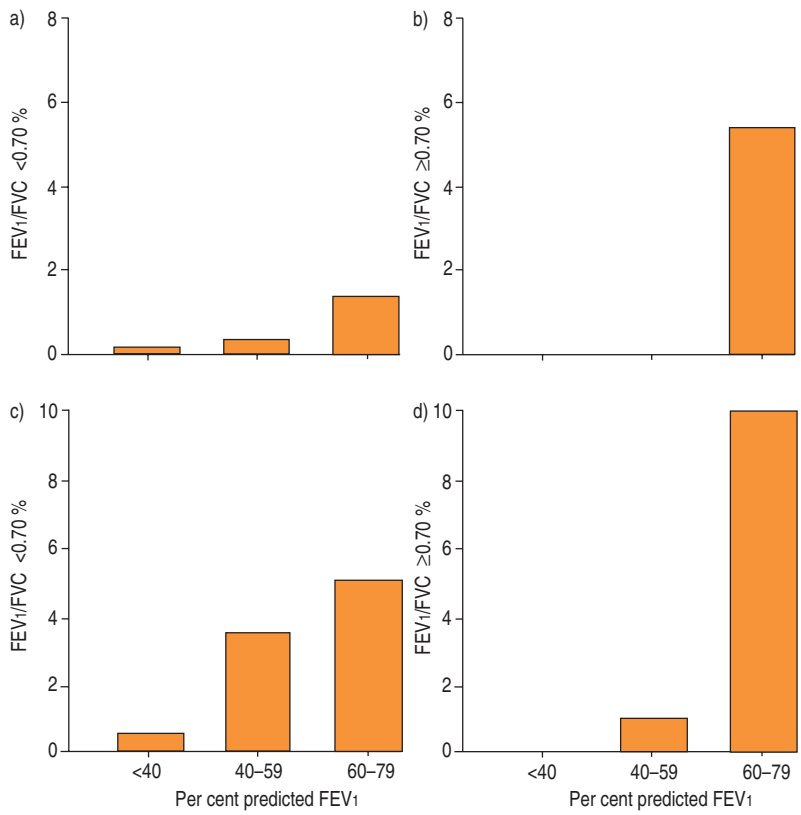


Fig. 3. – Percentage distribution of prevalence of chronic obstructive pulmonary disease and restrictive spirometric pattern in a general population aged 18–44 (a and b) and 45–73 years (c and d) in Bergen, Norway. FEV_1: forced expiratory volume in one second; FVC forced vital capacity.

The Global Burden of Disease Study has estimated the worldwide prevalence of COPD as 834 per 100,000 people, which yields approximately 44 million cases of COPD worldwide. In countries with established market economies the prevalence rate was estimated to be as low as 535 per 100,000. This estimate covers all ages. Since most cases of COPD usually become clinically apparent after the age of 45 years, this study grossly underestimates the prevalence of the disease in adults and the elderly. For countries with a life expectancy of 80 years or longer, and with more than 20% being smokers, these estimates are much too low.

Incidence

Longitudinal studies of lung function have shown that the development of airflow limitation is heavily dependent on smoking habits and dust exposure. The decline in FEV_1 seems to occur along a slowly accelerating curvilinear path. However, the distribution of the decline in lung function has a very wide range. Some relatively small studies did not show the development of FEV_1/FVC ratios below 0.70 in nonsmoking males, followed up over 10–25 years.

"... airflow limitation is heavily dependent on smoking habits and dust exposure."

A community study in Finland in 1961, of a population aged 40–64 years, was re-examined in 1971. The average incidence of an FEV_1/FVC less than 0.6 was 0.2% per year for the whole population and almost 1% per year in continuous smokers. In Zutphen, the Netherlands, the incidence of chronic nonspecific lung disease (CNSLD) was studied from 1965–1985 in a population of males aged 40–59 years. CNSLD was defined as respiratory symptoms, such as regular cough and sputum production for longer than 3 months, or episodes of wheezing and shortness of breath reported to the survey physicians; or a diagnosis by a clinical specialist of CNSLD, including chronic bronchitis or emphysema. The average incidence was estimated to be 1.5% per year and remissions did occur. The figures may imply that asthmatics may have been included in this survey. A 13-year follow-up study between 1968–1981 was conducted in a population aged 19–70 years in Krakow, Poland. COPD was defined as an FEV_1 below 65% of predicted. The average incidence per year was 0.5%. The incidence was almost two times higher in males than in females and a considerable number of new cases of COPD were seen in nonsmokers in this community.

The experts of the Global Burden of Disease Study were encouraged to make informed estimates of incidence of COPD in the eight health regions. The estimate for countries with established market economies was calculated to be 84 per 100,000 population, which is less than one-fifth of that observed in Krakow, Poland. The observed incidence of COPD varies greatly in the available literature, partly due to the use of different indices of disease and partly due to reports of studies of small populations that were not followed for a sufficient length of time.

Precise estimates of the incidence of physician-diagnosed COPD, or spirometric airflow limitation, as defined by GOLD (FEV_1/FVC less than 0.7 and FEV_1 less than 80% of predicted) are lacking for many countries. The overall incidence of FEV_1/FVC less than 0.7 over a 9-year period was 9.8% in an adult general population aged 18–74 years in Western Norway. In those aged 60–74 years, the incidence was 23%.

Exacerbation rates, hospital admissions and consultation rates

There is no universally accepted definition of an exacerbation of COPD. Most definitions use an increase in symptoms requiring increased treatment and the severity is assessed in terms of the healthcare. There are no data on the frequency, severity and duration of exacerbations of different severity among COPD patients in a general population.

Between 1990–1996 annual hospital admissions due to physician-defined OLD varied between 360–460 per 100,000 per year among inhabitants of Nordic countries. Admission rates have been increasing in females and the elderly. In those older than 60 years of age, the rates are more than 1,000 per 100,000. Thirty per cent had re-admissions during the same year. The average length of hospital stay was 9 days for patients with COPD and 5 days for patients with asthma. In contrast, admission rates due to asthma have declined considerably over the last 15 years. Hospitalisation rates for OLD are also dependent on the organisation of emergency units as well as the availability of hospital beds. Most of the admissions are recurrent admissions in elderly COPD patients. The number of hospitalisations for COPD for 1994 in Germany was 125,508 (1993), in the UK 73,342, Spain 45,624 and Italy 40,190.

In the UK, general practice annual consultation rates in 1991–1992 for COPD per 10,000 population increased with age from 417 at age 45–64 to 886 at age 65–74 and 1,032 at age 75–84 years, values that are two to four times the equivalent consultation rates for angina pectoris. The use of outpatient services for COPD patients also increases steeply with age.

Disability-adjusted life years lost

Disability-adjusted life years (DALYs) have been used by the World Bank and supported by the WHO as a measure of the burden of disease. DALYs are the sum of years lost due to premature mortality and the amount of years lived with disability, adjusted for the severity of the disability. The disability weight for untreated COPD was estimated to be 0.43, using a person trade-off method, where death is weighted as 1.0 and perfect health as 0. Estimated DALYs for the world were calculated to be 29 million in 1990 and from this 2.3 million DALYs are accounted for by countries with established market economies. In 1990, COPD was the twelfth most common cause of disability in the world. According to the projection from the Global Burden of Disease Study, COPD will rank fifth as a cause of disability in 2020 and will be responsible for 4% of the total DALYs lost. Only ischaemic heart disease, depression, traffic accidents and cerebrovascular disease will be a greater burden.

CAUSES

Tobacco smoke

The most important aetiological factor for COPD is active smoking. Cigarette smokers have a higher prevalence of respiratory symptoms, lung function abnormalities, a greater annual rate of decline in FEV_1, and higher death rates for COPD than nonsmokers. Females may have more symptoms than males given the same number of pack-years smoked. Passive exposure to cigarette smoke may also contribute to respiratory symptoms and a lower lung function in schoolchildren. Not all smokers develop clinically significant COPD, which suggests that genetic factors may modify each individual risk.

Occupational dust

When the exposure is sufficiently intense or prolonged, occupational dust, chemicals and vapours can cause COPD independently of cigarette smoking and increase the risk of the disease in the presence of concurrent smoking. Although the risk is smaller than with tobacco smoke, it does affect a large proportion of the population and its contribution to the ultimate incidence of COPD is not negligible.

Outdoor and indoor pollution

High levels of urban air pollution are harmful to individuals with COPD. The role of outdoor air pollution in causing COPD is unclear. Indoor air pollution from biomass fuel has been implicated as a risk factor for the development of COPD.

Socioeconomic status

There is evidence that the risk of developing COPD is inversely related to socioeconomic status. This may reflect factors such as nutrition, overcrowding and air pollutants, as well as genetic determinants.

Genetic factors

The only proven genetic risk factor for COPD is the hereditary deficiency of α_1-antitrypsin in which a smoker will considerably increase the risk for COPD in smokers at a young age. In most populations, the homozygotic state of α_1-antitrypsin deficiency is observed in fewer than five per 10,000 inhabitants. Abnormalities/polymorphisms in many genes may increase (or decrease) a person's risk of developing COPD.

FINANCIAL BURDEN

Among respiratory diseases COPD is the leading cause of lost work days. In the EU*, approximately 41,300 lost work days per 100,000 population are due to COPD. The number is far lower in Central and Eastern Europe, where merely 4,300 lost work days per 100,000 population are due to COPD. Productivity losses amount to a total of €28.5 billion annually. Accordingly, indirect costs represent the major financial burden in COPD.

The total of COPD-related expenses for outpatient care is €4.7 billion. The annual number of consultations per 100,000 population ranges from 40,900 in Greece to 4,100 in Turkey, with an average of 17,300 within the EU. Inpatient care generates costs of €2.9 billion, followed by expenses for pharmaceuticals at €2.7 billion.

CURRENT AND FUTURE NEEDS

The priorities of research should be the following:

- To create a stronger foundation for fighting COPD by acquiring accurate data on illness, exacerbations, natural history, deaths and cost.
- To perform scientific surveys with spirometry of forced expiratory volumes in population samples in all European countries to improve knowledge of the distribution of COPD.
- To establish higher standards of COPD care through studies on the effectiveness of current prevention, education, medication and rehabilitation.
- To develop new therapeutic modalities that inhibit the decline in lung function.
- To establish studies of the most effective smoking cessation intervention, and techniques to prevent people from starting to smoke.
- To guide caregivers and care-payers in the most efficient and effective ways to manage this disease.

*: distinguished as 15 member states plus Norway and Switzerland throughout this chapter.

THE SITUATION IN 5 YEARS' TIME

- A more complete picture will be available on the prevalence, incidence and natural history of COPD.
- More knowledge will be available on the genetic factors that may influence the development of COPD.
- New drugs for COPD will be available to improve symptoms and the natural history of the disease.

CONCLUSION

COPD is the only leading cause of death that is increasing in prevalence worldwide. Awareness of the increased burden of COPD in Europe has to reach governments, industry and the public. Europe should implement strategies for effective prevention, diagnosis and treatment of this disabling and life-threatening disease.

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