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The burden of lung disease

Introduction: the global perspective

Key points

- Four respiratory disease categories appear in the global top 10 causes of mortality, together accounting for one in six deaths as well as one in 10 disability-adjusted life-years lost.
- In the 28 countries of the European Union, these diseases account for one in eight deaths.
- In European countries where detailed data are available, 7% of hospital admissions result from respiratory causes.
- Smoking and respiratory infections are major causes of the burden of lung disease in Europe, and are potentially preventable.
- In the next two decades, the proportion of deaths caused by respiratory disease in Europe is likely to remain stable, with a decrease in deaths from lung infections balanced by a rise in lung cancer and COPD mortality.

Respiratory diseases are among the leading causes of death worldwide (table 1). Lung infections (mostly pneumonia and tuberculosis), lung cancer and chronic obstructive pulmonary disease (COPD) together accounted for 9.5 million deaths worldwide during 2008, one-sixth of the global total. The World Health Organization estimates that the same four diseases accounted for one-tenth of the disability-adjusted life-years (DALYs) lost worldwide in 2008 (table 2).

The Global Burden of Disease (GBD) Study recently compared the contribution of major diseases to deaths and disability worldwide for 1990 and 2010. Among the leading causes of death, lower respiratory infections were ranked 3rd in 1990 and 4th in 2010, whereas COPD was ranked 4th in 1990 and 3rd in 2010. Lung cancer rose from 8th- to 5th-commonest cause of death, while tuberculosis fell from 6th to 10th position in the ranking.

The GBD Study also presented rankings for years lived with disability, among which asthma ranked 13th worldwide in 1990 and 14th in 2010, while COPD ranked 6th in 1990 and 5th in 2010. When premature deaths and disability were combined as DALYs lost, lower respiratory infections were ranked the leading cause worldwide in 1990, and the 2nd most important cause of DALYs lost in 2010. Also among the 25 most important causes were COPD (ranked 6th in 1990 and 9th in 2010), tuberculosis (ranked 8th in 1990 and 13th in 2010) and lung cancer (ranked 24th in 1990 and 22nd in 2010).

Each year in EU28 countries, lung diseases cause two-thirds of a million deaths, and at least 6 million hospital admissions, accounting for over 43 million in-patient bed-days

Deaths attributed to	Worldwide	WHO European Region
Ischaemic heart disease	7.3 million (12.8%)	2.40 million (24.7%)
Cerebrovascular disease	6.2 million (10.8%)	1.40 million (14.0%)
Lower respiratory infections	**3.5 million (6.1%)**	**0.23 million (2.3%)**
COPD	**3.3 million (5.8%)**	**0.25 million (2.5%)**
Diarrhoeal diseases	2.5 million (4.3%)	0.03 million (0.3%)
HIV/AIDS	1.8 million (3.1%)	0.08 million (0.8%)
Trachea/bronchus/lung cancer	**1.4 million (2.4%)**	**0.38 million (3.9%)**
Tuberculosis	**1.3 million (2.4%)**	**0.08 million (0.8%)**
Diabetes mellitus	1.3 million (2.2%)	0.17 million (1.7%)
Road traffic accidents	1.2 million (2.1%)	0.12 million (1.2%)

Table 1 – The 10 most common causes of death in 2008. Source: World Health Organization (WHO) World Health Statistics 2011.

DALYs lost to	Worldwide	WHO European Region
Lower respiratory infections	**79 million (5.4%)**	**2.2 million (1.5%)**
HIV/AIDS	65 million (4.4%)	2.6 million (1.8%)
Ischaemic heart disease	64 million (4.4%)	16.0 million (11.3%)
Diarrhoeal diseases	56 million (3.8%)	1.1 million (0.7%)
Cerebrovascular disease	48 million (3.3%)	9.3 million (6.4%)
Road traffic accidents	45 million (3.1%)	3.4 million (2.4%)
COPD	**33 million (2.3%)**	**2.9 million (2.0%)**
Tuberculosis	**29 million (2.0%)**	**1.7 million (1.2%)**
Diabetes mellitus	22 million (1.5%)	2.6 million (1.8%)
Trachea/bronchus/lung cancer	**13 million (0.9%)**	**3.2 million (2.2%)**

Table 2 – The 10 most common causes of disability-adjusted life-years (DALYs) lost worldwide in 2008.Source: World Health Organization World Health Statistics 2011.

These figures confirm that lung diseases have remained globally important causes of death and disability during the past two decades.

Where does the information come from?
This White Book includes all countries of the World Health Organization (WHO) European Region, which extends from the Atlantic coast to central Asia. The 28 countries of the European Union (EU28) have been distinguished for some presentational purposes. Within the EU28, 14 countries have reported data for both mortality and hospital admissions for recent years in a form that allows a detailed breakdown by respiratory condition. These 14 countries were selected for illustrative comparisons of disease burden in figures 3, 4, 8 and 9.

There are two main sources of Europe-wide data on hospital admissions: the WHO-Europe Hospital Morbidity Database (HMDB) and data from the European commission statistical agency, Eurostat. This publication uses information from HMDB where available, supplemented with Eurostat data. Data are available from the WHO database on hospital admissions (discharges and deaths), day-cases, and bed-days for 27 European countries. Eurostat supplies discharge data for 30 countries of which nine supplement the HMDB data. These are available for a limited set of conditions on the International Short Hospital Morbidity Tabulation (HMT). The non-HMT respiratory conditions, which comprise a small proportion of the total admissions for lung disease, are shown separately in figure 5, for countries where they are available.

Respiratory deaths in Europe

In the WHO European Region, the four most commonly fatal lung diseases accounted for one-tenth of all deaths and 7% of the DALYs lost in 2008 (tables 1 and 2). The proportion of deaths due to respiratory disease was higher among the 28 countries of the European Union (EU28) – 12.5% (661 000 deaths annually) – than among the remainder of the WHO European countries, where it was 7.5% (292 000 deaths annually).

The proportion of all deaths due to lung diseases is influenced by the age of the population, and the age-specific death rates from respiratory and nonrespiratory causes. If we concentrate solely on respiratory deaths (including lung cancer and pulmonary vascular disease) and adjust each country's mortality rates to the European Standard Population, then the age-standardised death rates are similar for EU28 and non-EU28 countries. However, within each of these groups of countries there is considerable international variation (figures 1 and 2).

Figure 1 maps the age-standardised death rates for respiratory causes in each European country in recent years. The same information is shown as a bar chart in figure 2. The highest rates tend to occur in parts of north-western Europe (Belgium, Denmark, Ireland, and the UK), central Europe (Hungary, Romania and Moldova) and some central Asian republics (Kazakhstan and Kyrgyzstan).

The specific respiratory conditions contributing to the toll of respiratory mortality in selected EU28 countries are illustrated in figure 3. The pattern is similar in the remaining EU28 countries. Over half of the respiratory deaths are due to lung

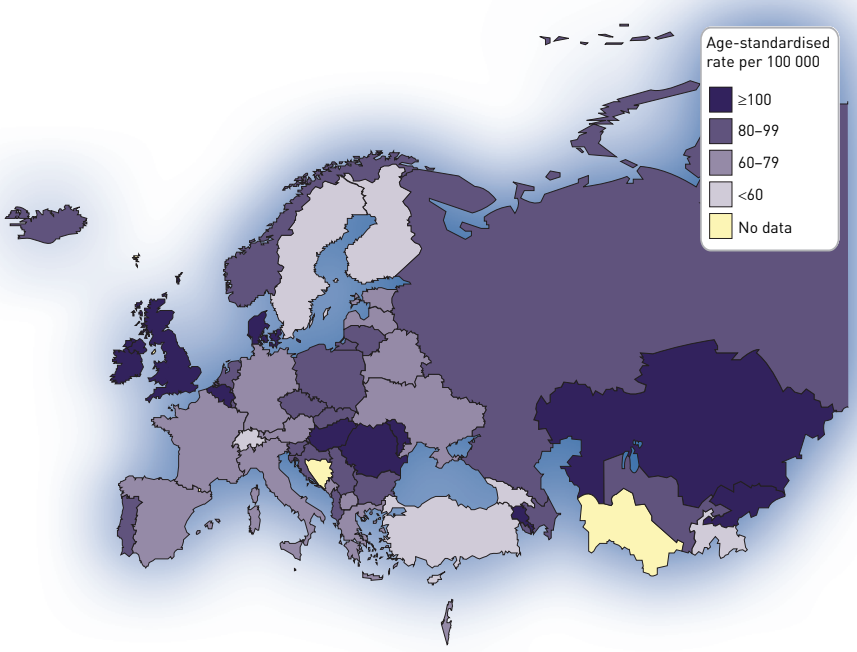

Figure 1 – Map of age-standardised mortality rates for all respiratory conditions. Source: World Health Organization World and Europe Detailed Mortality Databases, November 2011 update.

cancer or COPD, conditions that are mainly caused by tobacco smoking. Smoking is also a risk factor for pneumonia and pulmonary vascular disease, conditions which also contributed substantial fatalities.

The impact on health services

Information on hospital use for respiratory diseases is available for all EU28 countries except Greece, and for a few of the non-EU28 countries. However, some countries contribute information only on the most common conditions. Among European countries that report in greater detail, about 7% of all hospital admissions are due to lung disease.

The proportion of all hospital admissions contributed by specific lung diseases is illustrated in figure 4, for the same countries as selected for the equivalent presentation of deaths in figure 3. Almost half of respiratory admissions are attributable to acute infections (including pneumonia), and episodes of infection are often a cause of exacerbations of asthma and COPD. More than one quarter of respiratory admissions are due to lung cancer and COPD, diseases which are strongly related to smoking.

Age-standardised admission rates for lung diseases vary substantially within western and central Europe (figures 5 and 6), showing some similarity of geographical pattern to that for mortality, but also important differences. Thus, while some high-mortality countries (such as Belgium, Hungary, Ireland and Romania) also have relatively high respiratory admission rates, there are countries with high mortality but below-average admission rates (such as the UK), and others with low or average mortality rates but high admission rates (for example, Austria and Lithuania).

The burden of lung disease in Europe remains as large today as it was at the turn of the millennium, and is likely to remain so for several decades

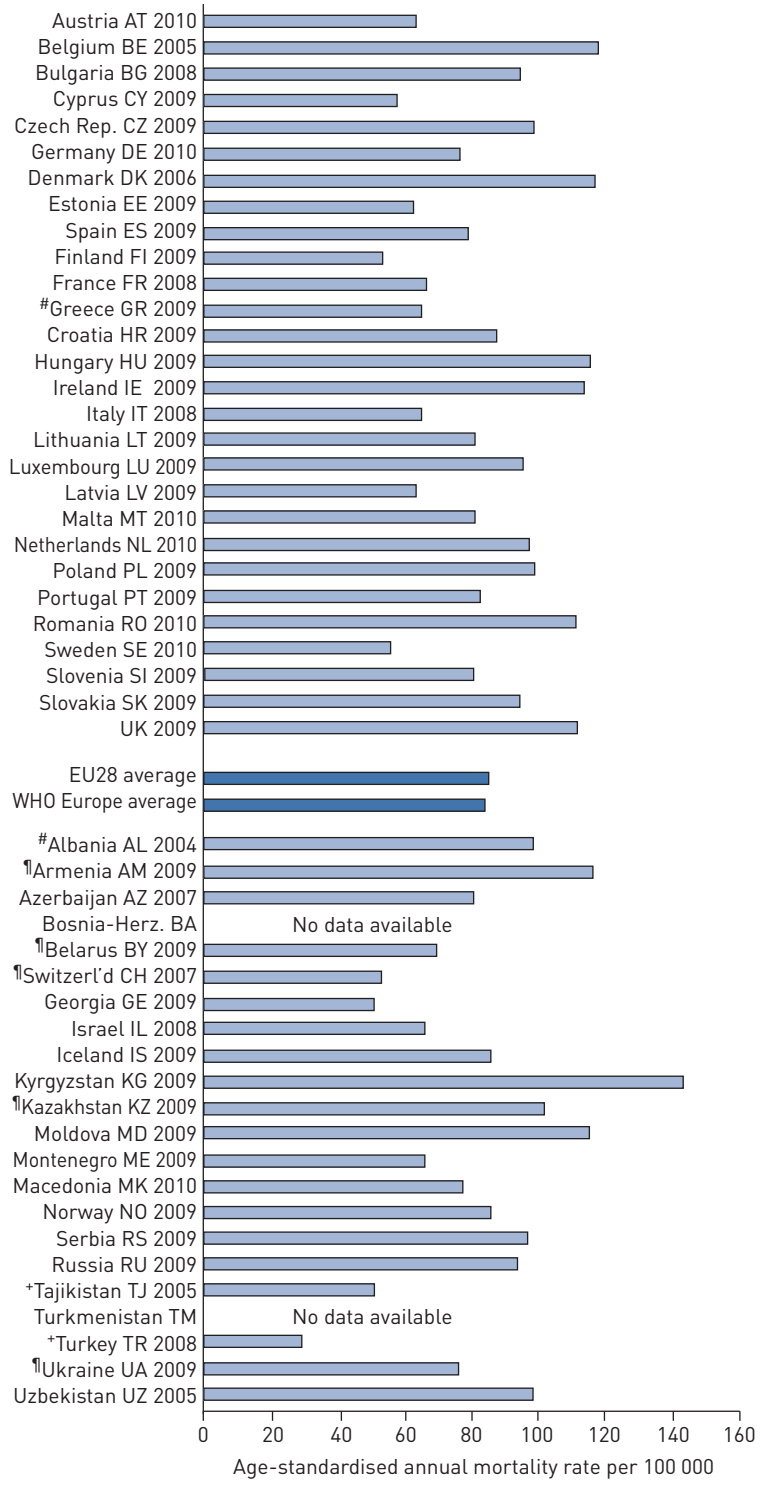

Figure 2 – Age-standardised mortality rates for all respiratory conditions, by country. #: International Classification of Diseases (ICD)-9 diagnoses; ¶: ICD-10 condensed list of diagnoses; +: ICD-9 condensed diagnoses or ICD-8 diagnoses. All other countries used full ICD-10 codes. Source: World Health Organization World and Europe Detailed Mortality Databases.

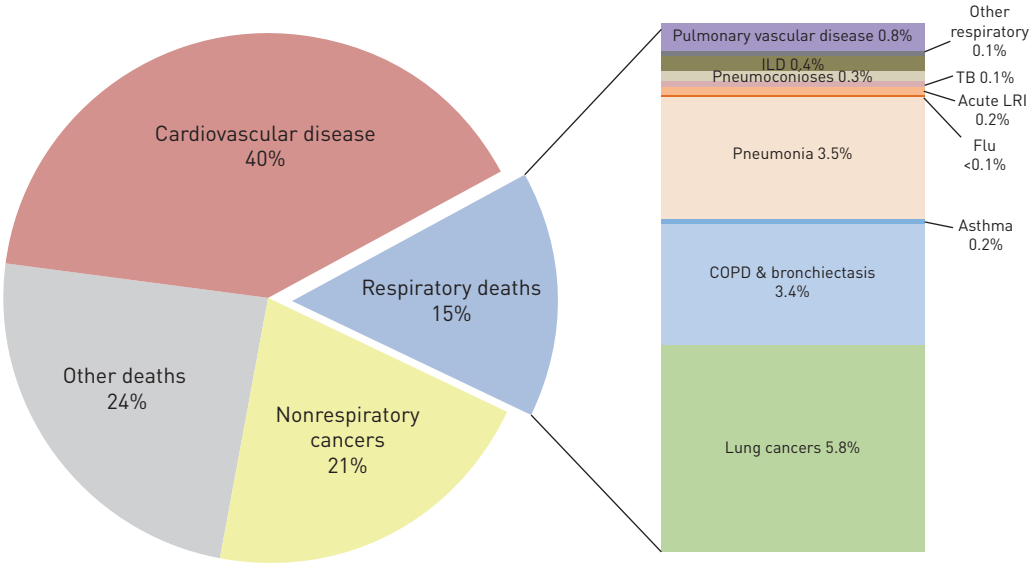

Figure 3 – Percentage of deaths in selected European Union countries, by respiratory condition. ILD: interstitial lung disease; TB: tuberculosis; LRI: lower respiratory infections; COPD: chronic obstructive pulmonary disease. The countries represented are those for which full ICD-10 coding of diagnoses was available for both hospital admissions and deaths (Austria, Croatia, Cyprus, Czech Republic, Denmark, Finland, Latvia, Lithuania, Luxembourg, Malta, Poland, Slovenia, Slovakia, UK). Source: World Health Organization World and Europe Detailed Mortality Databases.

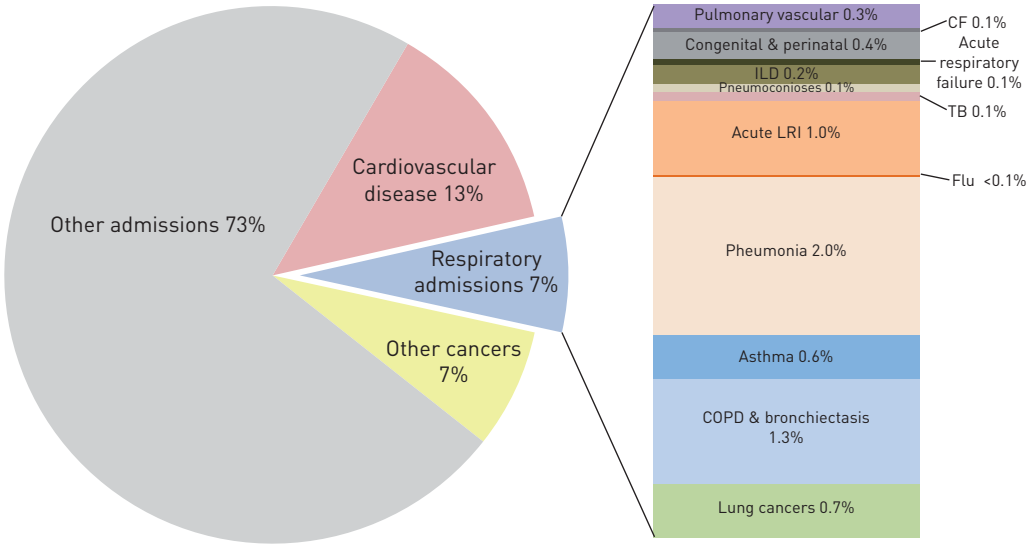

Figure 4 – Percentage of hospital admissions in selected European Union countries, by respiratory condition. CF: cystic fibrosis; ILD: interstitial lung disease; TB: tuberculosis; LRI: lower respiratory infections; COPD: chronic obstructive pulmonary disease. The countries represented are those for which full ICD-10 coding of diagnoses was available for both hospital admissions and deaths (Austria, Croatia, Cyprus, Czech Republic, Denmark, Finland, Latvia, Lithuania, Luxembourg, Malta, Poland, Slovenia, Slovakia, UK). Source: World Health Organization Hospital Morbidity Database and Eurostat.

The "iceberg of disease"

National mortality and hospital utilisation statistics present an incomplete picture of the burden of lung disease. Variations in disease coding and death certification may lead to spurious international differences, and for many diseases, hospital admissions and deaths are only the "tip of the iceberg".

More than half of all the deaths from lung disease in Europe, and at least one-quarter of all respiratory hospital admissions, are due to diseases caused by smoking

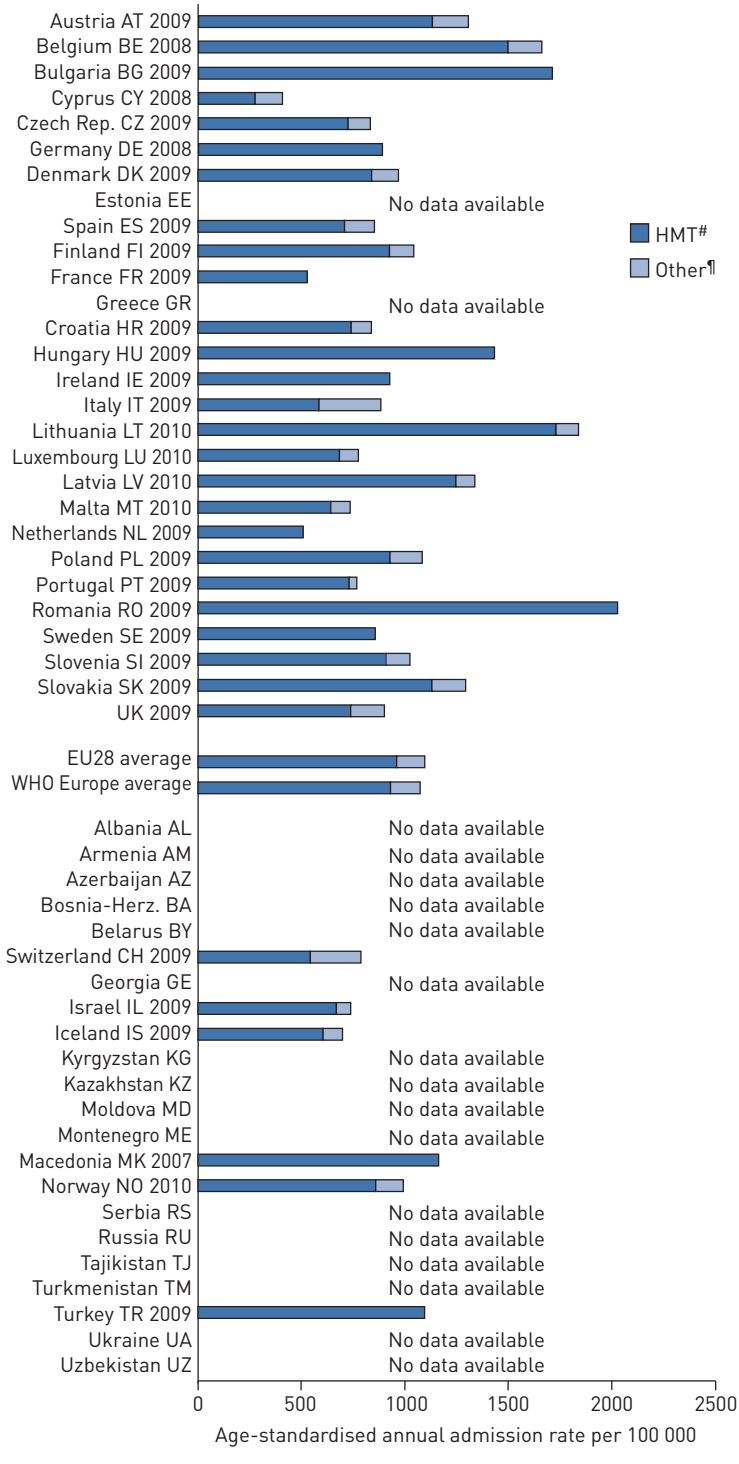

Figure 5 – Age-standardised admission rates for all respiratory conditions, by country. HMT: International Short Hospital Morbidity Tabulation. #: Asthma, COPD, bronchiectasis, acute lower respiratory infections, pneumonia, lung cancer, tuberculosis, pulmonary vascular disease; ¶: influenza, interstitial lung disease, cystic fibrosis, congenital respiratory disease, pneumoconioses, mesothelioma. Source: World Health Organization Hospital Morbidity Database and Eurostat.

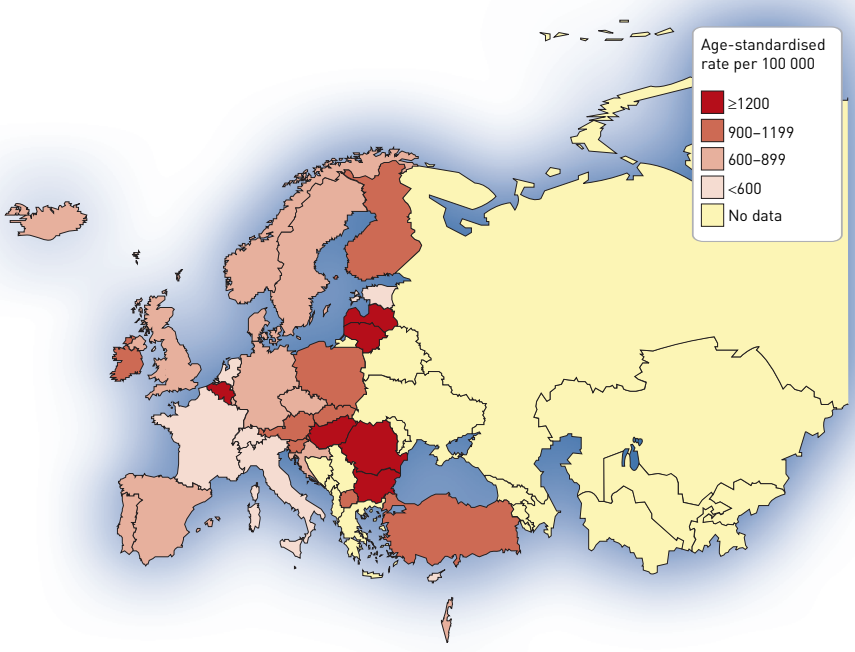

Figure 6 – Age-standardised admission rates for all respiratory conditions. The figure shows International Short Hospital Mortality Tabulation (HMT) categories only (as these are covered by both data sources, giving a wider comparable set of countries). Combined rates are shown for asthma, COPD, bronchiectasis, acute lower respiratory infections, pneumonia, lung cancer, tuberculosis and pulmonary vascular disease. Source: World Health Organization Hospital Morbidity Database (October 2011 update) and Eurostat (March 2012 update).

Sources of routinely collected data do not extend beyond deaths and hospital admissions for all respiratory conditions, but for some diseases it is possible to place the routine data into context against the frequency of the condition in the general population. Figure 7 summarises the burden of asthma, COPD, lung cancer and tuberculosis in EU28 countries, taking data from a range of sources for recent years.

These estimates highlight the widespread nature of obstructive lung disorders (asthma and COPD), for which a substantial proportion of patients are managed in the community and never reach hospital. In contrast, most new (incident) cases of lung cancer and tuberculosis come to the attention of hospital services. For tuberculosis, deaths represent only the tip of the iceberg, but for lung cancer, which is often rapidly fatal once diagnosed, the incidence and death rates are similar.

Recent trends

Over the first decade of the 21st century, age-standardised rates of mortality from lung diseases have declined across the EU, as illustrated for selected countries in figure 8. Similar trends have occurred for mortality in other EU countries. In contrast, there has been little change in the crude, unstandardised respiratory mortality rates for the same countries over this 10-year period, due to the ageing of the European population, and the tendency for mortality rates to be higher in the elderly. In non-EU countries, both crude and age-standardised mortality rates have changed little over the past decade.

Age-standardised rates of hospital admission have been stable in most countries (figure 9), and this pattern is similar for crude admission rates. The impact of lung diseases

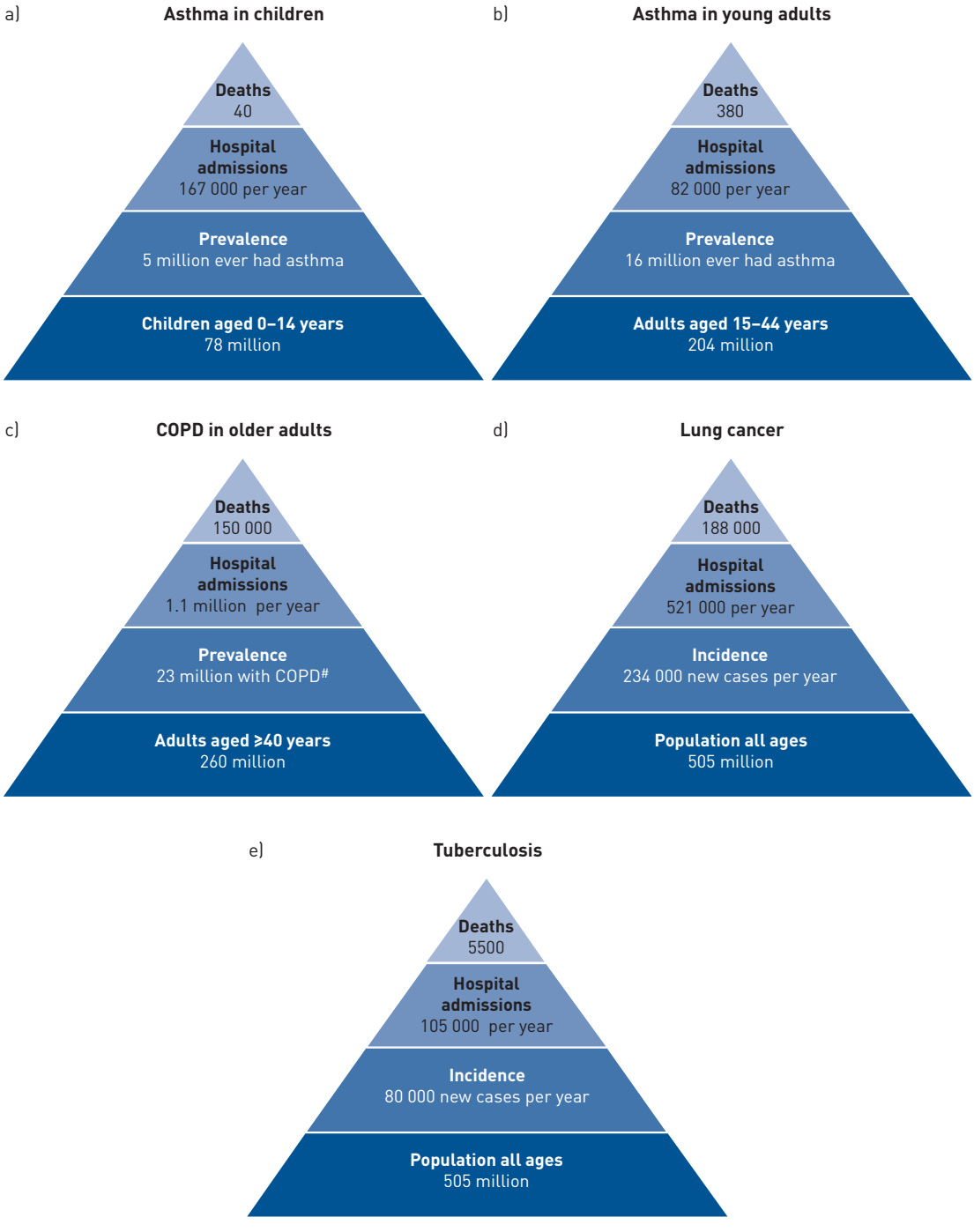

Figure 7 – The burden of various respiratory diseases, around 2010, in the 28 countries of the European Union. #: Global Initiative for Chronic Obstructive Lung Disease stages II–IV. An additional 17 million adults aged ≥40 years had stage I chronic obstructive pulmonary disease (COPD). Sources: BOLD study; EPISCAN study; European Cancer Observatory; ISAAC studies; World Health Organization (WHO) Detailed Mortality Database; WHO Hospital Morbidity Database; WHO Europe Surveillance Report; WHO World Health Survey.

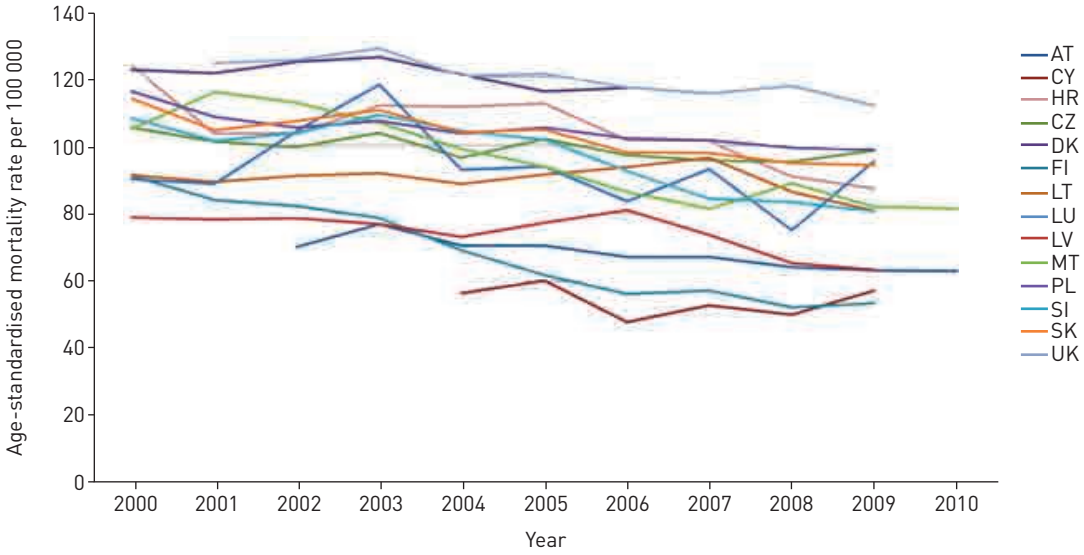

Figure 8 – Trends in age-standardised respiratory mortality rates in selected countries, 2000–2010. The countries represented are those for which full ICD-10 coding of diagnoses was available for both hospital admissions and deaths. Source: World Health Organization Detailed Mortality Database.

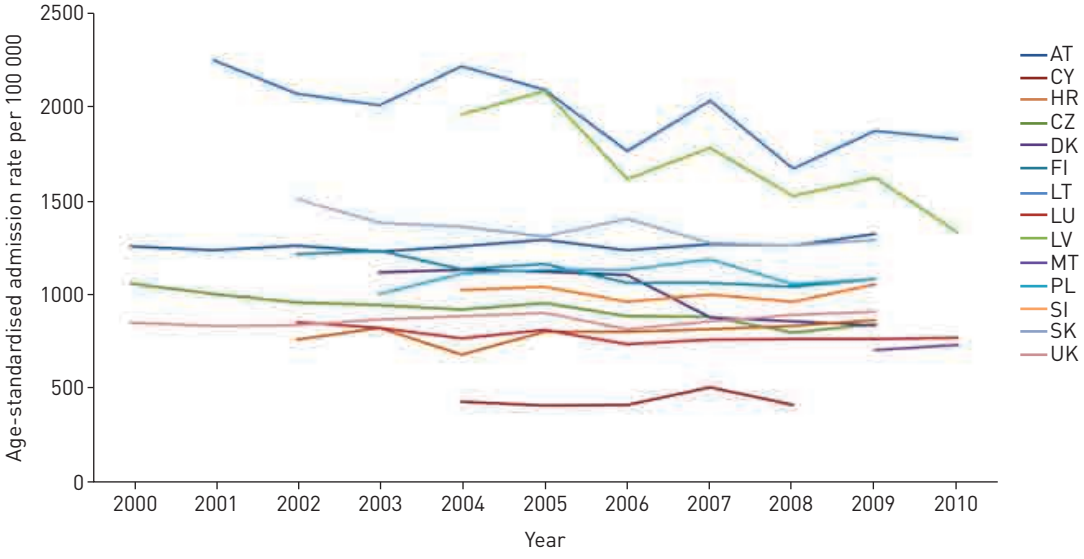

Figure 9 – Trends in age-standardised respiratory admission rates in selected countries, 2000–2010. The countries represented are those for which full ICD-10 coding of diagnoses was available for both hospital admissions and deaths. Source: World Health Organization Hospital Morbidity Database and Eurostat.

on in-patient health services has diminished substantially only in Latvia and Lithuania, countries which formerly had high rates.

One of the factors underlying the decline in age-standardised rates of mortality and hospital admissions is the generally favourable trend in smoking over the past four decades, at least in western European states (figure 10). Nevertheless, higher rates of smoking in earlier years contribute to the burden of lung disease now, and will continue to do so for several decades. There is still considerable room for improvement, both among men and women, and in several countries smoking rates in women have changed little over the past 20 years (figure 10b).

Percentage of deaths worldwide	2008	2015	2030
Lower respiratory infections	6.1	5.5	4.2
COPD	5.8	6.6	8.6
Trachea/bronchus/lung cancer	2.4	2.8	3.4
Tuberculosis	2.4	1.6	3.4
Percentage of deaths in WHO European region	**2008**	**2015**	**2030**
Lower respiratory infections	2.3	2.2	1.9
COPD	2.5	2.7	3.2
Trachea/bronchus/lung cancer	3.9	3.9	4.1
Tuberculosis	0.8	0.7	0.4

Table 3 – Projected proportion of deaths due to leading respiratory causes. COPD: chronic obstructive pulmonary disease. Source: World Health Organization World Health Statistics 2011.

Percentage of DALYs worldwide	2008	2015	2030
Lower respiratory infections	5.4	4.6	3.2
COPD	2.3	2.7	3.8
Trachea/bronchus/lung cancer	0.9	1.0	1.4
Tuberculosis	2.0	1.6	1.1
Percentage of DALYs in WHO European region	**2008**	**2015**	**2030**
Lower respiratory infections	1.5	1.3	1.0
COPD	2.0	2.0	2.2
Trachea/bronchus/lung cancer	2.2	2.2	2.6
Tuberculosis	1.2	1.1	0.6

Table 4 – Projected disability-adjusted life-years (DALYs) lost due to leading respiratory causes. COPD: chronic obstructive pulmonary disease. Source: World Health Organization World Health Statistics 2011.

Future projections

By 2030, the WHO estimates that the four major potentially fatal respiratory diseases (pneumonia, tuberculosis, lung cancer and COPD) will account for about one in five deaths worldwide, compared to one-sixth of all deaths globally in 2008. Within the WHO European Region, the proportion is expected to remain stable at about one-tenth of all deaths, with an increase in COPD and lung cancer deaths balancing a decline in deaths from lower respiratory infections and tuberculosis (tables 3 and 4).

Although asthma causes few deaths, it is an important cause of disability. There are no well-informed projections of the future burden of asthma, but in many

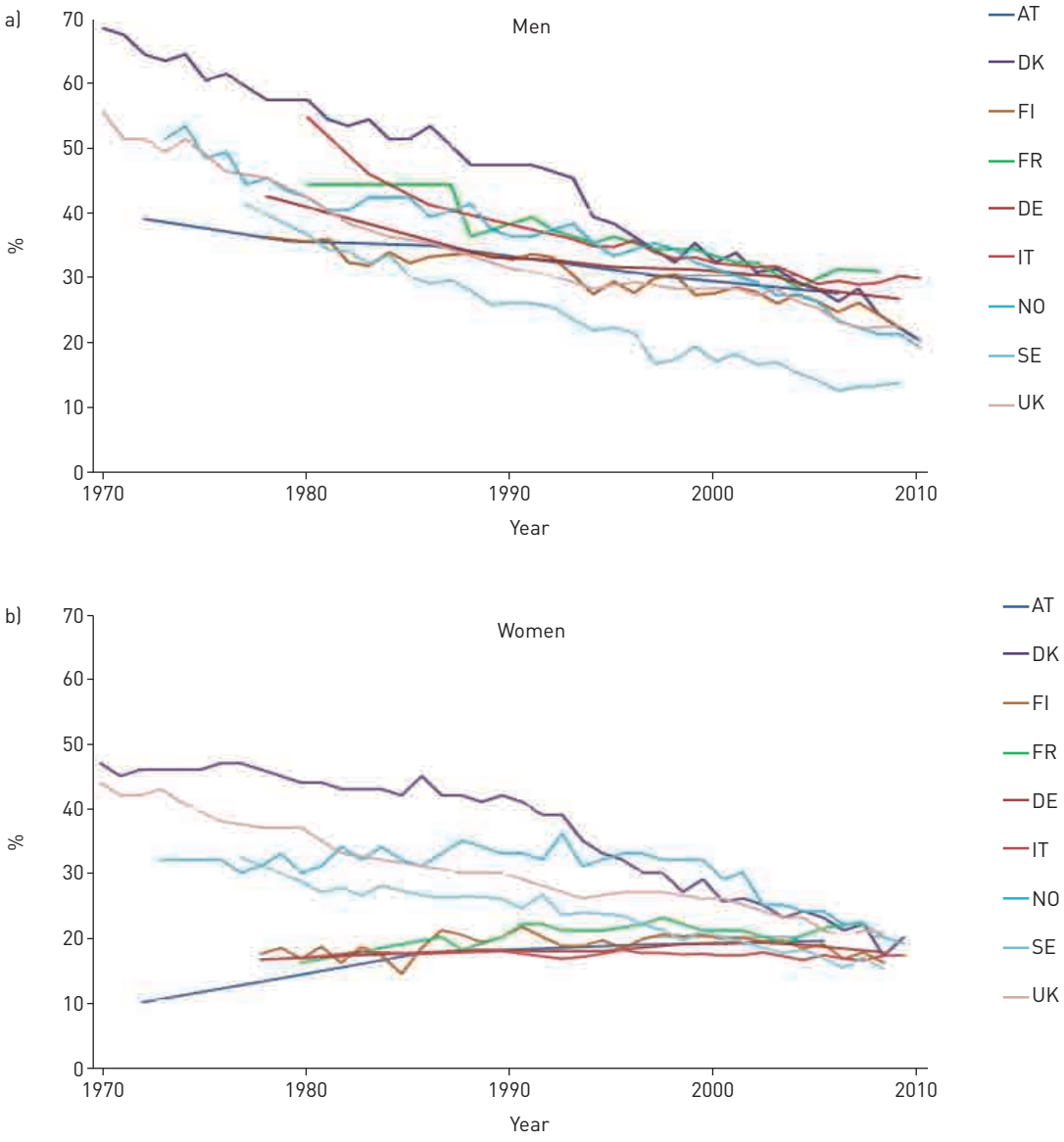

Figure 10 – Trends in daily smoking prevalence among a) men and b) women in selected countries, 1970-2010. Source: Organisation for Economic Co-operation and Development StatExtracts.

European countries the prevalence of childhood wheezing increased between the late 1990s and the early 2000s, as measured by the International Study of Asthma and Allergies in Childhood (ISAAC). Whether these trends continue, or are matched in older age-groups, is uncertain.

Respiratory diseases are therefore likely to remain a major burden on European societies for decades to come. Both the prevention and treatment of lung diseases will need to be improved if their impact on longevity and quality of life of individuals, and their economic burden on society, are to be reduced in Europe and worldwide.

Terminology and data

Prevalence

The prevalence of a disease measures the number of cases of existing disease in the population at a given time, or over a period such as the past 12 months. It is calculated as the number of people with the disease divided by the total population, and is usually expressed as a percentage. Age- and sex-specific prevalences can also be calculated. The prevalence of a disease can be difficult to measure directly as these data are usually not collected routinely. In this book, we present information for a number of countries on the prevalence of asthma and COPD derived through multi-centre cross-sectional surveys which have used the same methodology. Data on some other conditions, such as cystic fibrosis and occupational lung diseases, are available through local or national registries.

Incidence

The incidence of a disease measures the number or rate of new cases of disease occurring in the population, over a specified period such as 12 months. Annual incidence is calculated as the number of new cases of a disease occurring in 12 months divided by the population who were disease-free at the beginning of the period. Incidence can be hard to measure, as it involves knowing who was disease-free at the beginning of the period. Incidence data for lung cancer, tuberculosis and certain occupational diseases are available through routine data collection sources and are usually related to an estimate of the mid-year population. Incidence data for other diseases and conditions are sparse.

Mortality

Deaths are coded to an underlying cause using conventions established by the WHO's International Classification of Diseases (ICD). Mortality data are available for European countries coded under the ICD-10, ICD-9 and ICD-8 revisions. In the data presented here, most countries used ICD-10 coding, usually individual ICD-10 codes, although a few used one of two ICD-10 condensed lists or an ICD-9 condensed list and Turkey used an ICD-8 condensed list. A list of the required respiratory conditions with ICD-10 codes was drawn up and a mapping exercise carried out to ascertain the equivalent ICD-9 and ICD-8 codes. The World Detailed Mortality Database (World DMDB, November 2011 update) was used as the primary source and numbers of deaths and corresponding populations by year, sex and 5-year age-group for 50 European countries were extracted. For each country, the latest available year of data was used (2005–2010). No data were available for Bosnia & Herzegovina, and no recent data were available for Turkmenistan (latest available 1998). For countries not reporting by individual ICD-10 codes, data for some conditions, such as asthma and COPD, were not available. To increase coverage, the WHO Europe Detailed Mortality Database was also downloaded (Europe DMDB, last accessed February 2012) as this database contains deaths coded by individual ICD-9 codes.

Hospital admissions

Admissions are episodes of hospital in-patient care, classified by ICD coding on discharge. They are a measure of health service utilisation and reflect local medical care practices, data coding and recording patterns as well as the epidemiology of the conditions described. Since admissions are a complex outcome (measuring episodes or patients, including or excluding transfers and emergency admissions and sometimes covering multiple comorbidities), in this book we present admissions data from two large international databases – the WHO Europe Hospital Morbidity Database (HMDB) and data from the European Commission statistics agency, Eurostat – for greater comparability. This publication uses information from HMDB where available, supplemented with Eurostat data. Data are available from the WHO database on hospital admissions (discharges and deaths), day-cases, and bed-days for 27 European countries. Eurostat supplies discharge data for 30 countries of which nine supplement the HMDB data. These are available for a limited set of conditions on the International Short Hospital Morbidity Tabulation (HMT). For some countries in the Eurostat database (Bulgaria, Estonia, Romania, Sweden), data are only available for all ages combined so for these countries, admission rates for age-specific conditions (childhood and adult asthma, paediatric respiratory disease and acute lower respiratory infections in adults) are not available.

Age-standardised rates

In this book, most of the country-specific hospital admission and mortality rates presented are age-standardised to the European Standard Population. The age-standardised rate for a particular disease or condition is calculated by applying the country's age-specific rates to the standard population. This enables comparisons to be made between countries with different age-structures and time-periods. As some conditions vary with age, countries with a relatively high proportion of elderly people might have proportionately more cases. The European Standard Population is the same for males and females.

Data sources

Analyses, interpretations and conclusions are the responsibility of the authors and not the World Health Organization.

Mortality

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2

The economic burden of lung disease

Background

Key points

- The total cost of respiratory disease in the 28 countries of the EU alone amounts to more than €380 billion annually.
- This total cost includes the costs of direct primary and hospital healthcare (at least €55 billion), the costs of lost production (at least €42 billion) and the monetised value of disability-adjusted life-years (DALYs) lost (at least €280 billion).
- The annual costs of healthcare and lost productivity due to COPD are estimated as €48.4 billion and those due to asthma at €33.9 billion.
- The average direct healthcare cost per case of TB is about €7500 but for multidrug-resistant disease (MDR-TB) this increases to €33 000 and for extensively drug-resistant disease to €47 500.
- The average value of the DALYs lost by a patient with lung cancer is about €350 000.
- Approximately half of the economic burden of respiratory disease is attributable to smoking.

Respiratory disease places a huge burden on society in terms of disability and premature mortality, and also in direct health service costs, drugs prescribed and the indirect costs related to lost production. This chapter estimates these costs across the current 28 member countries of the European Union using published cost estimates and WHO and European data. Because of a lack of information related to other respiratory diseases, costs are estimated for only the more common conditions: chronic obstructive pulmonary disease (COPD), asthma, lung cancer, tuberculosis (TB), pneumonia/acute lower respiratory infections (ALRI), obstructive sleep apnoea syndrome (OSAS) and cystic fibrosis. The analysis is limited to countries of the EU because of the paucity of representative data relevant to most non EU countries.

Methods

General

A systematic literature search was carried out to identify published research on costs in Europe for each lung disease. For the most part only papers in English were included with occasional exceptions where English abstracts or translations to English were available. The literature identified for each medical condition was reviewed for data on estimates of disease-related costs per patient. Estimates were combined with prevalence or incidence rates as given

5.2 million disability-adjusted life years are lost annually to respiratory disease in the EU at a minimum value of almost €300 billion

in chapter 1 and elsewhere in this book, together with population data, to obtain costs per European Union (EU) country. There is a considerable volume of non-diagnosed respiratory disease, which is, by definition, difficult to cost and define, and so has been excluded from the calculations

For COPD, asthma, OSAS, and cystic fibrosis, cost estimates have been combined with prevalence data to estimate national costs. The costs of lung cancer were estimated using an incidence approach due to the availability of incidence rather than prevalence data, the usually short survival of patients making this approach appropriate. Likewise for TB, incidence data were used; since TB treatment and other related costs are likely to occur within a given year in most cases, estimation from incidence data is justifiable. For pneumonia, calculations were based on annual hospital bed-days and an estimate of total pneumonia cases in the EU.

We estimated the economic burden of each disease for each of the EU 28 countries, although cost estimates were available from only a small set of countries, and we used adjusted cost data from some comparable non-EU European countries (Norway and Switzerland) where necessary. The costs of labour, hospital inpatient care, outpatient care and drugs vary between countries and we therefore used World Bank data on gross domestic product (GDP) per capita to convert costs, as GDP may be considered a major indicator of costs involving labour. The estimated costs per patient for each disease were adjusted proportionally to each country's relative income level and then aggregated into total costs for each country using prevalence or incidence and national population data. No, or insufficient, data were available for sensible estimation of the costs of several diseases including bronchiectasis, pulmonary fibrosis, pulmonary vascular diseases and occupational lung diseases. Inevitably, therefore, the overall economic burden of respiratory disease is seriously underestimated.

The direct costs of healthcare relate to inpatient and outpatient costs of both hospital and primary care, together with the costs of drugs (including oxygen). Indirect costs include costs of lost production due to absence from work and early retirement and are valued according to the average daily salary including social benefit payments, using the human capital approach. All costs are calculated in year 2011 euros, expressed in sums equivalent to the purchasing power of Belgium, using purchasing power parities and national inflation rates.

In addition to these direct and indirect costs, respiratory disease is associated with a considerable cost due to disability and loss of life-years. To put a monetised value on this disability and premature mortality, a 'willingness to pay' methodological approach has been used, based on the value of a statistical life. Society is willing to pay a considerable amount to save life, as shown, for example, by expenditure on road and other safety precautions, healthcare and rescue costs. The values of disability and life-years lost are based on surveys and observation of the trade-offs which society is prepared to make between risk and monetary gain. A European Commission research study has collated such estimates and reported a typical range of €50 000–100 000 for the value of a life-year, with a median value of €52 000 in 2009 – equivalent to €55 000 in 2011 values. This estimate is applied here to the projected disability-adjusted life-years (DALYs) lost due to respiratory causes. Data on DALYs lost are available from WHO World Health Statistics 2011 and from the Global Burden of Disease study.

Chronic obstructive pulmonary disease

It has been reported that only 21–25% of persons identified at screening as having COPD, already had a prior diagnosis of COPD. Undiagnosed individuals with COPD may have indirect costs related to morbidity, but, since the large majority of these have mild disease, we have assumed that those without a diagnosis have no treatment or indirect costs attributable specifically to COPD. The lack of data on this point may, however, again result in significant underestimation of costs.

Cost estimates for COPD from seven European countries were identified in the literature, some of which gave direct cost estimates by disease severity, which is important as disability and costs vary widely according to severity of the disease. Cost estimates were modelled using linear regression analysis, adjusting for severity and for the setting from which the patients were recruited (see online methods section). Indirect costs, by degree of severity, were obtained from two studies, and combined with prevalence by severity and population size to give costs per country. The grading systems of severity used in the studies included the Global Initiative for Chronic Obstructive Lung Disase (GOLD) definition of severity of COPD (I: forced expiratory volume in 1 second (FEV_1) ≥80% of predicted; II: 50% ≤ FEV_1 < 80%; III: 30% ≤ FEV_1 < 50%; IV: FEV_1 < 30% of predicted) and those of the French Pneumology Society (SPLF), the American Thoracic Society (ATS) and the Spanish Society of Pneumology and Chest Surgery (SEPAR). All the grading systems use the criterion FEV_1/FVC <70%. We used the GOLD grading system, and reclassified SPLF, ATS and SEPAR grades to the nearest GOLD equivalent. Studies which presented national aggregated costs were used as such with no prevalence calculation required.

Asthma

The severity of asthma was graded according to the Global Initiative for Asthma (GINA) classification. As for COPD, estimates of direct costs presented by disease severity were modelled using linear regression analysis, adjusted for severity and the setting from which the patients were recruited (see online methods section). Indirect costs by severity of disease were obtained from two studies from Sweden and Germany (JANSSON *et al.*; SCHRAMM *et al.*). The studies used fairly similar standards of severity, based on the GINA guidelines of 1995 to 2003. The direct healthcare costs of a child with asthma were determined from the costs for an adult, by adjusting for the relation of costs between age-groups, using the demographic population structure of the European Union based on Eurostat data. Children incur indirect costs if, for example, a parent needs to be absent from work in order to care for the child. Costs by severity were combined with prevalence by severity; cost estimates representative of asthma patients overall, and not presented by degree of severity, were used together with overall prevalence to determine national costs.

Lung cancer

Two studies were identified giving estimates of direct costs, including costs of surgery, inpatient and outpatient care, chemotherapy and other drugs from onset of the disease to death. These were assumed to be representative of the mean and variation in direct costs between the EU countries. Indirect costs were estimated from Organisation for Economic Co-operation and Development (OECD) Health Data for Germany, adjusted by national GDP and extrapolated to each of the 28 countries.

Tuberculosis

Estimates of costs related to TB are based on the recent review by DIEL *et al*. for 27 EU countries (excluding Croatia), quoted at 2012 values; this analysis includes estimation of the direct healthcare costs associated with multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB.

Pneumonia/ALRIs

Cost estimates for hospital admissions for pneumonia were used together with data on the number of hospital bed days to make a best estimate of inpatient costs. However, this total seriously underestimates the total costs of pneumonia/ALRI due to the lack of usable data on patients treated as outpatients (including in primary care) as well as the indirect costs of pneumonia and the costs of other acute respiratory infections.

Obstructive sleep apnoea syndrome

A registry-based study of patients diagnosed with OSAS identified direct costs for outpatient and inpatient care and drugs, and indirect costs due to absence from work.

Cystic fibrosis

Three studies presented estimates of the total direct costs of cystic fibrosis. Costs were shown to increase with age. Prevalence data were similar in the three countries, so the average cost per patient was used. Again, no estimates of indirect costs were identified. See chapter 14 for further discussion of the costs of cystic fibrosis treatment.

	Drug cost	Outpatient cost	Inpatient cost	Total direct#	Total indirect¶
COPD	7.1	8.9	7.3	23.3	25.1
Asthma	8.0	6.7	4.8	19.5	14.4

Table 1 – Aggregated annual costs of inpatient stay, drugs and outpatient care including primary care attributable to chronic obstructive pulmonary disease (COPD) and asthma in the EU (billions of euro at 2011 values). #: Total of costs for drugs, outpatient including primary care, and inpatient care; ¶: costs for absence from work and early retirement (adults).

"The average direct healthcare costs per case of COPD and asthma are about €1000 and €2000 per year, respectively, often over several decades"

The cost of respiratory disease

The estimated annual economic burden of COPD and asthma in terms of conventional direct (healthcare) and indirect (lost production) costs is presented in table 1, amounting to €82 billion in total. The direct and indirect costs of COPD and asthma are of similar magnitude (figure 1).

Fewer cost data are available for the remaining respiratory conditions. Together with those for COPD and asthma, the estimates are summarised in table 2, which also shows the monetised value of DALYs lost due to those conditions where estimation was possible. Taking the mean of the ranges, the grand total of direct costs is at least €55 billion annually. The indirect costs, even though only partially estimated, amount to at least €42 billion annually.

The inpatient costs of pneumonia are estimated as €2.5 billion per annum. Estimation of the other direct and indirect costs of pneumonia was not possible. The cost of lost DALYs (€43.5 billion) represents those due to acute lower respiratory infections, including pneumonia.

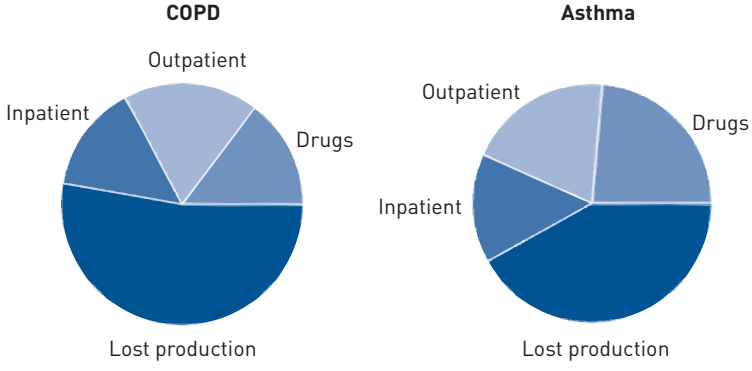

Figure 1 – Distribution of direct and indirect costs by category for chronic obstructive pulmonary disease (COPD) and asthma.

	Direct costs# € bn	Indirect costs¶ € bn	Monetised value of DALYs lost € bn	Total costs € bn
COPD	23.3	25.1	93.0	141.4
Asthma	19.5	14. 4	38.3	72.2
Lung cancer	3.35	NA	103.0	106.4
TB	0.54#	#	5.37	5.9
OSAS	5.2	1.9	NA	7.1
Cystic fibrosis	0.6	NA	NA	0.6
Pneumonia/ALRI	2.5	NA	43.5	46.0
Total	55.0	41.4	283.2	379.6

Table 2 – Aggregated annual direct and indirect costs and the value of disability-adjusted life-years (DALYs) lost for EU countries 2011 by disease (billions of euro at 2011 values). COPD: chronic obstructive pulmonary disease; TB: tuberculosis; OSAS: obstructive sleep apnoea syndrome; ALRI: acute lower respiratory infections; NA: not available. #: primary care, hospital outpatient and inpatient care, drugs and oxygen; ¶: lost production including work absence and early retirement; +: indirect costs included with direct costs.

Data on DALYs lost due to respiratory disease were obtained from WHO Health Statistics 2011 and the Global Burden of Disease study and are set out for each disease in tables 2 and 3, together with their monetised value. The major DALY losses are from lung cancer, COPD, lower respiratory tract infections and asthma. The total loss is about 5.2 million DALYs at a cost of €300 billion.

The greatest economic burden of respiratory diseases on health services and lost production in the EU is due to the chronic problems of COPD and asthma, at about €20 billion each for healthcare and €25 billion and €15 billion, respectively, for lost production. The greatest loss from disability and premature mortality is from lung cancer and COPD, followed by pneumonia/ALRI and asthma (tables 2 and 3).

The course of both lung cancer and TB tends to be short-lived, with total treatment and costs concentrated within the year of diagnosis. Although there are many more cases of COPD and asthma, the individual mortality from lung cancer is much higher, while the course of COPD and asthma extends over many years. The costs per case per year, therefore, show a very different order than for total costs (table 4), with lung cancer and TB showing the heaviest annual costs per case for healthcare, disability and premature mortality. The direct costs of cases of drug resistant TB are considerably higher than those associated with drug sensitive disease. In effect, because of the nature of the diseases, in most patients the estimates for lung cancer

Disease	DALYs lost per year (thousands)	Annual monetised value € bn
Lung cancer	1873	103.0
COPD	1691	93.0
TB	103	5.6
Pneumonia/ALRI	790	43.5
Asthma	697	38.3
Total	5154	283.4

Table 3 – Cost of disability-adjusted life-years (DALYs) lost to respiratory disease in the EU (monetised values are billions of euro at 2011 values). COPD: chronic obstructive pulmonary disease; TB: tuberculosis; ALRI: acute lower respiratory infections.

	Deaths (thousands)	Cases (thousands)	Direct costs per case €	Indirect costs €	Monetised value of DALYs lost €	Total annual cost per case €
COPD	150	23 000	1013	1091	4043	6147
Asthma	0.42	10 000	1950	1450	4043	7443
Lung cancer	257	292	11 473	NA	352 740	364 213
TB	4.9	72	7467#,¶	¶	78 750	86 217

Table 4 – Average annual cost per case for the major respiratory diseases in the EU, 2011. COPD: chronic obstructive pulmonary disease; TB: tuberculosis; NA: not available. #: fully sensitive TB €6832 per case; MDR-TB €33 320 per case; XDR-TB €47 573 per case; ¶: indirect costs included with direct costs.

and TB approach the lifetime costs, but they represent only a small proportion of lifetime costs for COPD and asthma, for which over several years the total costs per case are likely to be 20–30-fold greater than the annual cost.

Discussion

The analysis presented here is based on published estimates of the cost of respiratory diseases in European countries, and on prevalence, incidence and population data as reported in chapter 1 and from WHO and Eurostat publications. There are major gaps in cost estimates in the literature, particularly those of pneumonia/ALRI, as well as the indirect costs of several diseases and all costs of the many respiratory diseases not listed here. Consequently, our estimates are by default, considerable underestimates.

Even with diseases in which good studies are available there is inevitable uncertainty in our overall cost estimates due to the need for extrapolation of data from a small number of countries to all 28 countries of the EU. For inclusion in the present analysis, the profiles of the countries concerned had to share at least some characteristics for the costs to be relevant. This could have an impact on both direct and indirect costs. In asthma and COPD, regression analysis was used to extrapolate from the costs for a few hundred patients, or a registry study of thousands of patients, to a population of some 500 million persons, so errors may grow substantially. However the regression models of cost data give a reasonable fit and no evidence of serious bias. The DALY estimates are published by WHO by region and sub-region and therefore are less prone to error, but there were variations in estimates from different sources; the WHO estimates used here were the lowest estimates available. Even among the limited range of diseases

considered, no estimates of indirect costs were available for cystic fibrosis or OSAS. The total estimates presented here must therefore be considered minimum and very conservative.

We have aimed for simplicity of design and methodology and more sophisticated methods might have improved certain aspects. Some costs such as patients' out-of-pocket costs are missing due to an almost complete lack of data. Furthermore, some indirect costs relating to absence from work and early retirement are missing for several conditions, where there is no relevant literature. On the other hand, the method of costing sickness absence and early retirement by average earnings may somewhat overestimate indirect costs where there is high unemployment.

An alternative approach to estimation of costs is by primary research, such as a multinational study with data collection and costing of each patient using local unit costs, and taking median costs across nations to obtain the overall estimate. Accordini *et al*. recently carried out such a study of persistent asthma in eleven European countries. They estimated the direct and indirect cost of persistent asthma based on 5 million subjects aged 15–64 years at €7.9 billion. After adjusting for age, our estimated total cost was €16.3 billion; although about twice their estimate, the costs per case are comparable as our estimate was based on a total of 9.1 million cases.

Another source of uncertainty is the variation in healthcare systems between EU countries; we have taken account of this by averaging data and adjusting for relative average income levels. Taking the differences in levels of care and cost of each country's healthcare system fully into account was beyond the scope of the present exercise. We used annual costs per patient together with prevalence rates of disease across Europe, both of which are inevitably associated with uncertainty. Only a minority of those with COPD have been diagnosed and, even though the undiagnosed population generally have very mild disease, undoubtedly some incur costs for healthcare and lost production not accounted for here.

In estimating the costs of lung cancer, the incidence approach is reasonable for small cell cancer with its average short survival, but is less appropriate for nonsmall cell lung cancer. The follow-up periods (up to 18 months and 30 months respectively) of the two lung cancer cost studies used may not have covered the full costs for these patients; thus we probably underestimated their healthcare costs. The indirect costs for lung cancer rely on a single cost estimate from Germany and assume that the incidence is representative of all EU countries.

For pneumonia/ALRI, our estimate serves as only a partial illustration of the economic burden, limited to costs of inpatient care. Healthcare and lost production costs were reported to cost about €10 billion annually in the previous edition of the White Book (2003), and in 2011 values this would be close to €12 billion. Although our estimate for healthcare is about a quarter of this, it is limited to inpatient costs. The cost of DALYs lost due to pneumonia, however, is included and is considerable.

Our estimate for OSAS relies on a single study from Denmark, and furthermore, the prevalence of OSAS for our calculations, 0.36%, was derived from the same study [32].

Half of the direct healthcare cost of respiratory disease in Europe is due to smoking

Extrapolation to the other 27 countries is inevitably associated with considerable uncertainty. Other studies generally report higher prevalence, albeit with considerable variation, related partly to varying definitions. A further important aspect of OSAS is its considerable socioeconomic impact beyond the usual direct and indirect costs, in particular related to road traffic accidents caused by the associated sleepiness. A review of obstructive sleep apnoea in the USA reported costs of some $16 billion (€17 billion at 2000 exchange rates) for road accidents in 2000.

The costs of cystic fibrosis are dependent on access to treatment and survival into adulthood, both of which may vary across Europe. We have no data on indirect costs, which are likely to be substantial due to premature death, disability and inability to work (including of parents), so once more our estimate is inevitably conservative.

The economic burden of bronchiectasis, pulmonary fibrosis, pulmonary vascular diseases, and occupational diseases such as asbestosis or silicosis could not be estimated, and would also add to the economic burden of respiratory disease, both from healthcare and work limitation such as lost production due to reduced efficiency at work, absence from work, early retirement and premature death; in 2004, new cases of occupational asthma in the United Kingdom alone cost £70–100 million (€115–165 billion at 2004 exchange rates).

Many of the causes of respiratory disease are behaviour related or otherwise potentially preventable, particularly those due to smoking tobacco or poor air quality. For example, it is estimated that 60% of COPD in the EU is attributable to smoking, along with 85% of lung cancer and 10% of other lower respiratory disease. This would suggest that the direct healthcare costs of respiratory disease attributable to smoking are approximately €27.4 billion, which is about half of the direct healthcare costs of respiratory disease estimated here. Consequently, with similar proportional savings in indirect costs and DALYs lost, a huge amount of money could be saved by reducing the preventable causes of respiratory disease in the EU.

The total cost of respiratory disease in EU, including the value of DALYs lost to respiratory disease, is estimated at a minimum of €380 billion. Even though this figure is a gross underestimate, as it excludes many respiratory diseases for which costs were not available, it represents a massive loss to the EU every year.

Further reading

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