



# 01

## ASTHMA BURDEN

**OVERVIEW**

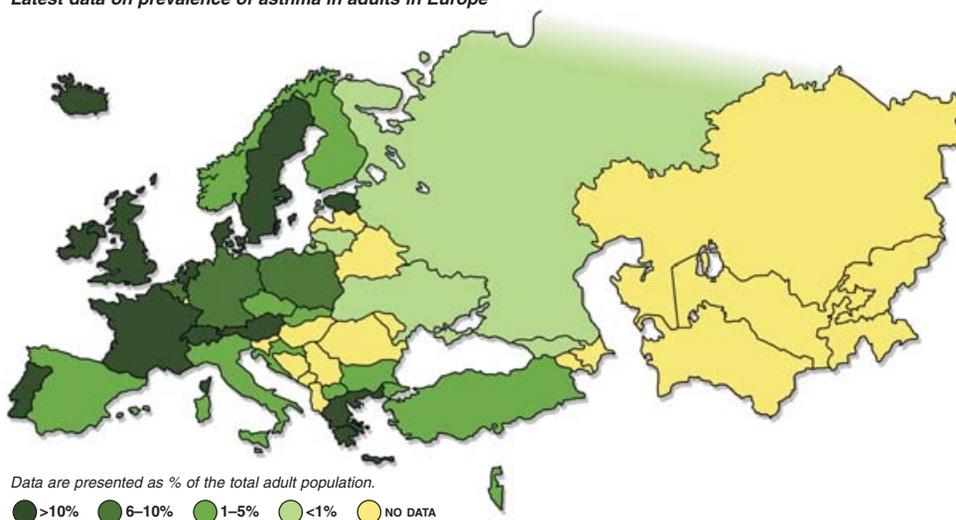
Asthma is a common life-long chronic inflammatory disorder of the airways that affects adults and children of all ages.

The most up-to-date prevalence rates of asthma in adults across Europe can be obtained from the European Community Respiratory Health Survey and local health institutions. The prevalence in adults

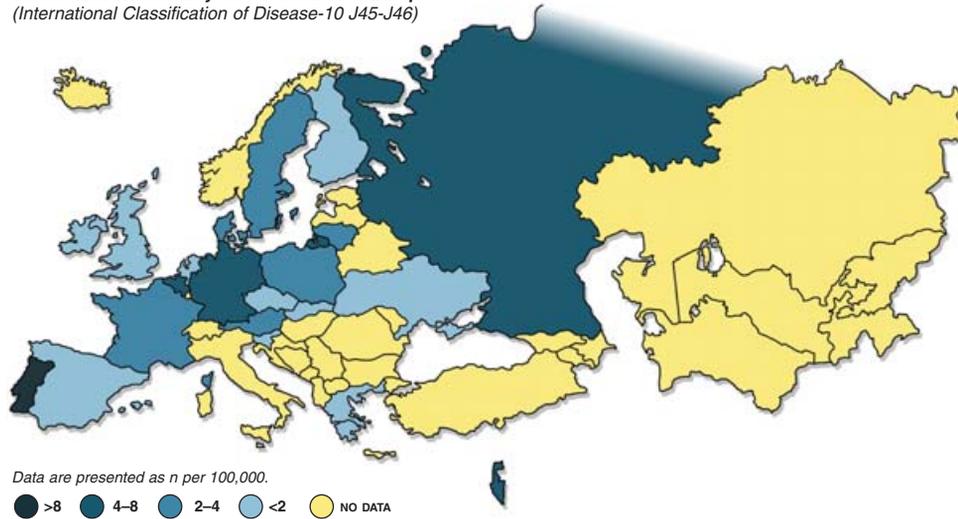
is highest in the UK (10–13%) and lowest in Georgia (0.28%). There is a paucity of prevalence data in adults in Central Europe.

Mortality rates in adults due to asthma range from 8.7 per 100,000 in Portugal to 0.54 per 100,000 in the Netherlands. Data are scarce for Central Europe.

*Latest data on prevalence of asthma in adults in Europe*



Latest data on mortality due to asthma in Europe  
(International Classification of Disease-10 J45-J46)



## INTRODUCTION i

Asthma is a common life-long chronic inflammatory disorder of the airways that affects children and adults of all ages. Its cause is not completely understood. It is assumed that, as a result of this chronic inflammation, the airways become hyperresponsive to many bronchoconstrictor stimuli, and they narrow easily and excessively to these stimuli. With episodes of airway narrowing and blockage by airway wall secretions and oedema, symptoms of cough, chest tightness, wheezing and shortness of breath occur. These symptoms may improve with inhaler therapy or may worsen into a more severe episode of asthma. In a very severe attack, the patient may die of asphyxia, and pathological features of the airways include the presence of inflammatory cells in the airways, mucus plugging of the airways, shedding of the airway epithelium, airway oedema and airway smooth muscle hypertrophy. Even in the patient with stable mild symptoms, an inflammatory cell infiltrate with eosinophils and other cells can be observed in the airway wall submucosa. In many asthmatic patients, the narrowing can be intermittent and often disappear completely, but there may be irreversible narrowing in some patients, which is likely to be due to increases in airway smooth muscle mass and in airway wall fibrosis, which are features of airway wall remodelling.

Although the understanding of many aspects of asthma has improved over the past two decades, the fundamental causes of asthma are still not known. In trying to understand the problem, asthma should be divided into stages; its initiation and its perpetuation. Various genes have been associated with an increased risk of developing asthma and increased susceptibility to asthma. Such genes, for example, may include those related to allergy and to certain cytokines or inflammatory mediators involved in asthma, but many more genes may be associated. Environmental influences are also likely to play a part in the initiation of asthma by interacting with the genetic predisposing factors. These may be changing patterns of microbial exposure and of diet, exposure to allergens and to environmental pollutants. Once the state of asthma is established, often with the presence of atopy and bronchial hyperresponsiveness, various

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triggers will serve to provoke asthmatic episodes or attacks, such as exercise, cold air, allergen exposure and upper respiratory tract infections.

More detailed exposition of the causes, mechanisms and treatment of asthma can be obtained from a multi-authored monograph on the subject by asthma specialists.

## THE INCREASED BURDEN OF ASTHMA



Data regarding the epidemiology of asthma are collected in all EU member states, but are not necessarily comparable since different collection methods may have been used. More recent results from international collaborative studies provide a better idea of the problem of asthma across Europe, using an agreed definition of what is being measured. To assess the increased burden of asthma across Europe, the prevalence of asthma, mortality rates, hospital admissions, drug use and financial costs will be considered. In particular, analysis of data in the UK will be provided, because data are available for most of these aspects, and because the UK is one of the industrialised countries in Europe that has a particularly significant burden of asthma.

### Prevalence of asthma

The most up-to-date prevalence rates of asthma across Europe can be obtained from the International Study of Asthma and Allergies in Childhood (ISAAC) and European Community Respiratory Health Survey (ECRHS) studies, and the rates obtained across Europe between the two studies are generally in accordance. Prevalence studies have been performed using patients' history of intermittent wheeze. Standardised and validated methods to document the prevalence of asthma have shown large degrees of variation throughout the world. The UK had the highest current prevalence of self-reported asthma symptoms among children aged 13–14 years (fig. 1), higher than other comparable European countries, such as Germany (ranked 19th) and France (ranked 20th). In Europe, the lowest prevalence of wheeze

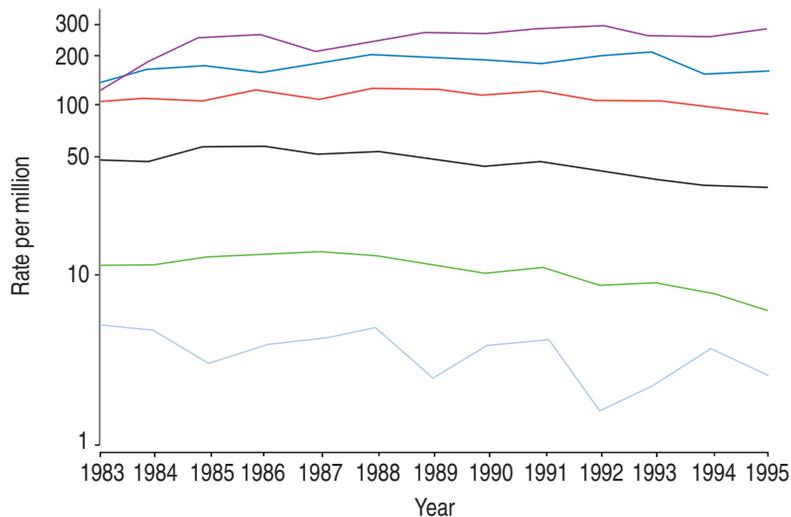


Fig. 1. – Asthma deaths per million population subdivided into various age groups in England and Wales. — 5–14 years; — 14–44 years; — 45–64 years; — 65–74 years; — 75–84 years; — ≥ 85 years. Data presented with permission from *BMJ* 1997; 314: 1439–1441.

or asthma was reported in what was previously East Germany, and in Eastern block countries such as Albania, indicating the possibility that the Western lifestyle may be involved. In the ISAAC study of children aged 12–14 years in a large sample of mixed secondary schools across the UK, almost one in five children had used asthma treatment in the past year, and 21% reported having had a diagnosis of asthma. One estimate is that 3.4 million people in the UK, with one of every seven children aged 2–15 years (1.5 million) and one of every 25 adults (1.9 million), have asthma symptoms requiring treatment. The number of asthmatics in Germany is estimated at 4 million. The prevalence of asthma has doubled in the UK over recent years. Two epidemiological studies performed 20 years apart (the Midspan Family Study Surveys) compared the prevalence of asthma in 1,708 parents and 1,124 offspring in the Renfrew and Paisley area of Scotland. At the time of assessment (1972–1976 and 1996), both populations were aged 45–54 years. The prevalence of adult asthma was 3% in 1972–1976 compared with 8.2% in 1996 and, as with childhood asthma, had more than doubled in the 20 years. Similarly, 25-years-ago the incidence of asthma was 2% in the Swiss population, which has increased and is currently 8%. At least a doubling of the prevalence of asthma has also been reported in centres in Nordic countries, such as Finland and Sweden. A study undertaken by the UCB Institute of Allergy in Belgium concluded that the prevalence of asthma in Western Europe has doubled in the last 10 years.

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### Prevalence of asthma symptoms

In the ECRHS study, age-/sex-standardised prevalence of asthma symptoms in the last year showed that UK centres along with centres in Ireland and the Netherlands had the highest values in terms of wheeze and shortness of breath prevalence, shortness of breath at night and asthma attack. These were also associated with a large amount of asthma medication. The centres in France showed a lower reporting of asthma symptoms and less use of medication. In primary care in the UK, the prevalence of treated asthma was highest in children, affecting 12% of males and 10% of females aged 5–14 years. Throughout most of adult life, the prevalence was higher in females than in males.

In a telephone survey of the household prevalence of diagnosed asthma in seven European countries, 8.6% of 73,880 households reported asthma. The household prevalence was highest in the UK with 15.2% compared with Germany with 2.5%. These prevalence rates paralleled those for rhinoconjunctivitis.

### Consultations for asthma

Another way of examining prevalence of asthma, and of assessing the burden of asthma in general practice, is to examine the consultations for asthma in general practice, particularly in the UK where such information is readily available. In 1981, the patient consultation rates for asthma were 1.8% rising to 4.3% in 1991. Although increases were seen in all age groups, it was most marked in the youngest children (aged 0–4 years), in whom the rate increased seven-fold between 1971–1991. These changes may reflect increasing prevalence and severity of asthma, changes in the balance between primary and secondary care, changes in therapy and management practice, and increased concern about asthma. Over the same time period, consultations for hay fever/allergic rhinitis increased in all age groups, but those for upper respiratory tract infections remained constant. A more recent report indicated that there has been a gradual decrease in the incidence of asthma episodes presenting to general practitioners in the UK since 1993.

## Death rates

Data available for 1989 show that the age-standardised mortality rate per 100,000 for asthma was as low as 0.08 for Greece and as high as 1.00 for England and Wales. Other countries with high mortality rates per 100,000 were Ireland (0.97), Luxembourg (0.91), West Germany (0.80), Belgium (0.78) and France (0.65). Fewer than expected deaths were seen in Greece, Denmark, Italy, the Netherlands, Portugal and Spain. However, there may be some question regarding the comparability of such data from country to country.

Fluctuations in asthma death rates have been observed since 1958, as illustrated by the data available in the UK. Since the high peak in the 1960s, the number of deaths started to rise from the mid-1970s, peaking in 1988 at just over 2,000, an increase more noticeable in the older age groups. Since then, asthma deaths have begun to fall, but are still currently around 1,500 per year for England and Wales. The majority of asthma deaths occur in those aged over 45 years, with around 40% of deaths occurring in the 75+ age group.

## Hospital admissions

Comparative figures for hospital admissions within Europe are not easily available. Hospital discharge rates in the UK in 1993 were 213 per 100,000 with a 4.3-day stay compared with 149 per 100,000 with a 3.8-day stay in Sweden. In England and Wales, hospital discharge rates for asthma were one of the highest compared with other countries in Europe between 1990–1994, with rates of 200 discharges per 10,000 population. Only Finland showed higher rates.

In the UK, hospital admissions for asthma patients have increased in all age groups over the last 30 years, but the most dramatic increase occurred within the 0–4 years group. For example, in 1992, the number of hospital in-patient treatment rates with a main diagnosis of asthma in England was approximately 10, 3.3, 1.3 and 1.3 per 1,000 population in the 0–4, 5–14, 15–44 and 45–64 years age groups, respectively. Hospital admissions in the UK totalled 85,585 in 1996, although since then the trend has been downwards. The trend in the increase in hospital admissions for asthma in children has also been observed in data collected between 1978–1988 in Greece, between 1980–1987 in the Netherlands, between 1976–1978 and 1985–1986 in Lombardy, Italy.

## Severity of asthma

In the Asthma Insights and Reality in Europe study, the severity of asthma was graded similarly for patients from the UK, France and Sweden. In the UK, 18% of patients graded their asthma as severe persistent, 18% as moderate persistent, 18% as mild persistent and 46% as mild intermittent, according to the Global Initiative for Asthma guidelines. A higher proportion of patients reported severe persistent asthma in Germany and the Netherlands. In the UK sample, up to 27% of asthma patients had needed acute healthcare services for their asthma over the past year, including hospital and emergency room visits and urgent care visits. Thirty-eight per cent of children and 16% of adults had lost school/work days in the past year, with higher figures recorded in France, the Netherlands and Spain.

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In a World Health Organization study of air pollution in eight major Italian cities, 30,000 asthma attacks per year were recorded in children less than 15 years of age, and children living by roads with heavy traffic had a two-fold greater risk of suffering respiratory problems than those who lived by less congested roads. In France, it has been calculated that traffic-related particulate air pollution (less than 10 µm in diameter) contributes to 243,000 attacks of asthma in children alone.

Other asthma morbidity measures included incapacity for work, school absence and measures of quality of life or limitation of activity. In the UK, the data indicate that asthma is a significant cause of short-term absence from work, with 2.7 million days of sickness benefit paid in 1991/1992, equivalent to £5.4 million (€7 million). The amount of sickness benefit paid out is rising. The percentage of all certified days of incapacity attributable to asthma is 1.9%.

To appreciate the problem of asthma from the point of view of the primary care level, it is instructive to look at the presentation of asthma to a typical primary care organisation serving a population of 330,000, as estimated by the National Asthma Campaign in the UK (fig. 2).

## Drug use

Individual use of anti-asthma drugs was evaluated in a recent ECRHS study. In this questionnaire survey, where the percentage of respondents varied from 12–90%, anti-asthma medication was taken by 1.5–11.1%, with inhaled anti-inflammatory medication taken by 0.3–6.5% of respondents. There were regional variations within each European country, but the UK had the highest percentage of patients on inhaled corticosteroid therapy.

In both France and the UK, the number of prescriptions for anti-asthma drugs has doubled from 1980 to 1990, particularly for  $\beta_2$ -receptor agonists and corticosteroids. For example, for corticosteroids the number of prescriptions in 1980 was approximately 1.2 million, increasing to 7 million in 1992. The General Practice Research Data in the UK showed that in 1996, approximately two-thirds of asthma patients were treated with both symptomatic (reliever) and prophylactic (preventer) medication, and that this proportion is tending to increase.

In a cross-sectional review of treatment carried out in five large general practices in Nottinghamshire, UK, the percentage of patients with asthma on steps 1, 2, 3, 4 and 5 of treatment was 54%, 22%, 11%, 3.6% and 1%, respectively, with a further 8% having had no treatment. During the previous year, 13.6% had been prescribed 10 or more  $\beta$ -agonist inhalers and 12.5% had received at least one course of oral steroids. Both measures occurred more frequently in patients taking more prophylactic treatment (step 3 or above). This study indicates that there is a group of asthmatics, although relatively small in number, who have more severe asthma that is refractory to the best available anti-asthma treatments. Similarly, in a National Asthma Campaign (UK) survey, symptoms were experienced every day and/or every night by 11% at step 1, 22% at step 2, 41% at steps 3 and 4, and 34% at step 5.

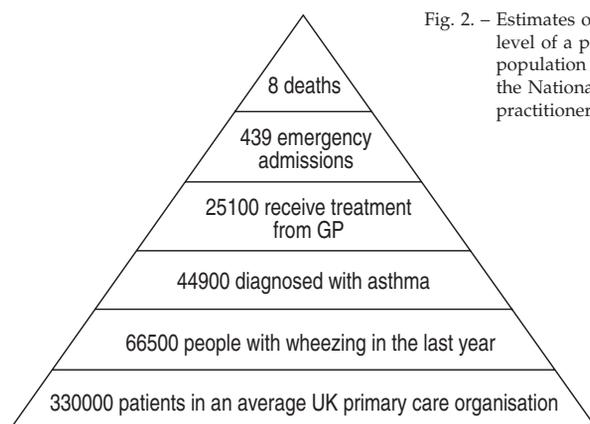


Fig. 2. – Estimates of various aspects of the asthma burden at the level of a primary care level organization serving a population of 330,000 in the UK. Estimates prepared by the National Asthma Campaign (UK), 2001. GP: general practitioner.

## FINANCIAL BURDEN



The total cost of asthma in Europe is approximately €17.7 billion per annum.

The most asthma-related consultations are observed in the UK (circa 32,800 per 100,000 population per annum), followed by Greece (19,400) and Germany (16,200); the EU average is 13,000. The least asthma consultations are recorded for Poland (7,200) and Turkey (2,400). Altogether outpatient care generates the higher cost of €3.8 billion, followed by expenses for anti-asthmatic drugs (€3.6 billion). In terms of cost of illness, inpatient care plays a relatively minor role, costing €0.5 billion.

As poor asthma control is responsible for significant work impairment, productivity losses add up to €9.8 billion per annum.

## CURRENT AND FUTURE NEEDS



### Current national programmes

In some European countries, such as Finland and France, asthma has been officially recognised by their respective health authorities as a priority area for action.

### The Finnish experience (1994–2000)

In Finland, a 10-year programme, launched in 1994, aimed to achieve the following: 1) the recovery of most patients with early asthma; 2) that asthmatics should feel well and their ability for work and functional capacity should correspond with their age; 3) a reduction in the percentage of patients with severe and moderate asthma from the current 40% to 20%; 4) a decrease in the number of bed days to 50% by the year 2000; and 5) a reduction in annual treatment costs per patient by 50% as a result of more effective prevention and treatment of symptoms. The measures taken towards achieving these goals were: 1) early diagnosis and active treatment; 2) guided self-management as the primary form of treatment; 3) decreasing respiratory irritants, such as smoking and tobacco; 4) implementation of rehabilitation on an outpatient basis combined with normal treatment planned individually and timed appropriately; 5) increasing knowledge about asthma in key groups; and 6) promotion of scientific research. Increased funding to provide structured care, training and greater expertise has led to a fall in mortality, attributed to early use of inhaled corticosteroids.

### The French plan (2002–2005)

In France, the asthma programme (2002–2005), has five objectives: 1) development of information on asthma for asthmatics and for the general public, together with the introduction of advisers regarding the internal environment; 2) improvement of the quality of asthma care with regard to the treatment of acute severe asthma, follow-up of chronic asthmatic patients, and detection of new cases with management of asthmatic children in the school environment; 3) development of therapeutic education; 4) improvement of the management and detection of occupational asthma; and 5) establishment of a system to collect information on all epidemiological and economic aspects of asthma, and to identify the risk factors.

## Research into asthma

In some European countries such as the UK and the Netherlands, National Asthma Societies run by non-governmental voluntary groups provide money specifically for research into asthma, ranging from applied to basic research, but the amount of research money available is limited. Some money is available from governmental research councils but the money spent on respiratory research is very limited. Despite the significant problem that asthma poses as a health issue in the UK, there has been no governmental programme to address this issue. Since this problem is transnational, affecting all European countries, the problem of asthma should be tackled at a European level. The partners in this war on asthma should include: healthcare professionals (doctors, nurses, pharmacists); national and local government bodies; policy makers; researchers into epidemiology and into causes and mechanisms, and into the treatment of asthma; patient groups; and pharmaceutical companies developing new treatments.

Research into both the basic and epidemiological aspects of asthma needs to continue. An important aim of asthma research is to discover the cause(s) of asthma, so that it can be prevented. This requires an understanding of the epidemiology of asthma because recent studies have pointed to the beginnings of asthma and allergy in the womb. At the other end of the spectrum there are patients with established asthma in whom treatments are refractory. More effective treatments are needed. Implementation of guidelines through education of patients and healthcare doctors is needed.

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The National Asthma Campaign in the UK has set up a consultation on the Basic Asthma Research Strategy and has identified the following areas for further research: genetics, early life events, environmental impact, immunology and immunotherapy, inflammation and anti-inflammation and airway remodelling. The following general aspects were raised: the definition of phenotypes in a heterogeneous disorder, putting greater emphasis on longitudinal studies rather than snapshots in time; the testing of existing hypotheses of causation of asthma, having strong translational research from bench to patient; the collections of lung tissue to maximise research opportunities; and the setting up of multidisciplinary networks with the greater use of existing databases. At a European level, a few networks have been established from EU funding, on epidemiology, on mediators and on severe asthma; the most structured approach is that aimed at studying the impact of environmental air pollution on health, including allergies and asthma. Currently, the research funding into asthma is not coordinated at EU level. What is needed is the recognition that asthma and allergy should be a priority at EU level, and also a long-term programme of focused research should be set-up, following extensive consultation with asthma researchers, asthma patients and national asthma organisations. A particular area of focus should be the need for long-term funding for long-term studies involving cohorts.

## Unmet needs

First, an understanding of the reasons behind the increasing prevalence and severity of the disease in Europe is needed in order to control it more effectively. This understanding should be based on research into the causation and the pathophysiological mechanisms of asthma, as recently elaborated by the National Asthma Campaign in the UK. Many plausible hypotheses relating to immunology, early life events, and environmental pollutants are now ready to be tested definitively. Equally, investigation is needed into the early stages that predispose and predict asthma, and into the later stages of airway remodelling. What should result from this increased understanding are better preventive and therapeutic strategies.

Secondly, improved implementation of the asthma guidelines is needed with regard to its management, in order to improve adherence to treatments. Along with improved implementation of guidelines is the need to develop therapeutic education of patients so that they can manage their own asthma more effectively. This approach has been shown to lead to better control of asthma. In addition, the long-term treatment of asthma by the physician and the management of acute severe attacks needs to be improved. More specialist asthma care is likely to be important, coupled with training and support of health professionals. Better asthma care is obtained with the specialist rather than the generalist, *e.g.* in the management of acute severe asthma. However, even management of acute severe asthma in hospital emergency rooms may be deficient.

Thirdly, it is now recognised that there is a core of patients whose asthma is severe, with persistent symptoms and exacerbations, despite taking adequate asthma therapies. Although this group constitutes a minority of asthmatics, they consume a large proportion of healthcare funding devoted to asthma. Research into this group is needed for newer, more effective treatments.

## RECOMMENDED READING



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