

## Introduction



### Key points

- In Europe, about 30 million children and adults less than 45 years old have asthma.
- In western Europe, the prevalence of asthma increased in the latter part of the 20th century, but it now appears to be levelling off in many countries; the UK and Ireland have some of the highest rates of asthma in the world.
- Adults with asthma include those who have had asthma since childhood, those in whom it apparently resolved but has subsequently recurred and those who have developed asthma *de novo* in adult life.
- Asthma can develop in the elderly but, because of similar clinical features, it may be difficult to distinguish asthma from COPD in older individuals.
- Most patients with asthma can be managed successfully in primary care according to widely accepted guidelines, but a significant proportion require specialist referral and supervision.

Asthma is a chronic inflammatory disease of the airways that causes recurring episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. Three terms are used to describe the course of asthma: asthma control, asthma severity and asthma exacerbations. Asthma control is assessed by symptoms, activities of daily living and quality of life. It also includes the likelihood of loss of control, exacerbations, decline in respiratory function, and the side-effects of treatment. Asthma severity describes the difficulty in controlling asthma with treatment, reflecting the level of treatment required and the activity of disease during treatment. Asthma exacerbations are episodes of worsening of symptoms that necessitate additional treatment: asthma is severe if systemic corticosteroid treatment is needed and it requires treatment in hospital or in an emergency room.

Asthma is a common disease that affects people of all ages in all countries of Europe. Most commonly it arises in childhood and may persist into adulthood (see chapter 11). In perhaps two-thirds of children with asthma, the disease remits in the early teenage years, only to relapse, in about a third of these cases, in adulthood. Less commonly, the disease begins for the first time in adulthood. Thus, adult asthma may represent persistent or relapsed childhood disease or true incident 'new' adult disease. Adult asthma is frequently associated with allergies and/or accompanied by other allergic conditions such as hayfever.

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## Epidemiology



There is no widely applicable diagnostic test for asthma, and assessment of its frequency and determinants is based on responses to questionnaires, simple tests with imperfect sensitivity and specificity, and the outcome of medical care such as hospital attendances and drug prescriptions. Because asthma tends to remit and may relapse, it can be difficult to distinguish prevalent (or recurrent) disease from that which is truly incident. Most measures of frequency probably reflect prevalent asthma, *i.e.* that which is present at, or over, a particular time. Because the symptoms of asthma are not specific to the disease, they can be confused with those of other respiratory diseases, particularly, in later life, chronic obstructive pulmonary disease (COPD).

In the whole of Europe, about 30 million children and adults under 45 years of age have asthma. In most European countries, the prevalence and perhaps incidence of asthma increased substantially at some time between 1950 and 2000 but, at least in western Europe, the increase has levelled off in the past decade. Figure 1 shows the estimated

### Asthma data available online

[ec.europa.eu/health/major\\_chronic\\_diseases/diseases/asthma/index\\_en.htm](http://ec.europa.eu/health/major_chronic_diseases/diseases/asthma/index_en.htm)

A public health summary of asthma provided by the European Commission with links to statistical data.

[www.laia.ac.uk/pubs/sevasth.pdf](http://www.laia.ac.uk/pubs/sevasth.pdf)

A summary of the epidemiology of severe asthma in Europe.

[www.ginasthma.org/](http://www.ginasthma.org/)

Website of the Global Initiative for Asthma (GINA).

[www.bohrf.org.uk/downloads/OccupationalAsthmaEvidenceReview-Mar2010.pdf](http://www.bohrf.org.uk/downloads/OccupationalAsthmaEvidenceReview-Mar2010.pdf)

An evidence-based review of the recognition, management and prevention of occupational asthma.

[www.efanet.org/wp-content/documents/SASSevereAsthmaBackgrounder050307.pdf](http://www.efanet.org/wp-content/documents/SASSevereAsthmaBackgrounder050307.pdf)

Briefing document on asthma from the European Federation of Allergy and Airways Diseases Patients Associations.



current prevalence of asthma in European countries among adults aged between 18 and 44 years. The rates of disease tend to be higher in northern and western countries where the prevalence may be higher than 10%. Unlike childhood disease, adult asthma tends to be more common in females.

## *Causes/pathogenesis*



Most adult asthma has its origins – and causes – in childhood; the sharp rise in the prevalence of childhood disease in most European countries in recent decades indicates important environmental determinants acting on a genetically susceptible population, a process commonly referred to as gene–environment interaction. The nature of the relevant drivers remains unclear, but the distribution of the disease suggests that they are associated with a ‘Western’ environment, possibly reflective of urbanisation and less exposure to microorganisms that are protective against asthma and allergy (the ‘hygiene hypothesis’). Genome-wide association studies have identified a handful of asthma genes that account for only a small fraction of the heritability of asthma, but epigenetic silencing and activation of genes involved in asthma are likely to be other important mechanisms that determine susceptibility to asthma and that underlie gene–environment interactions [see chapter 3].

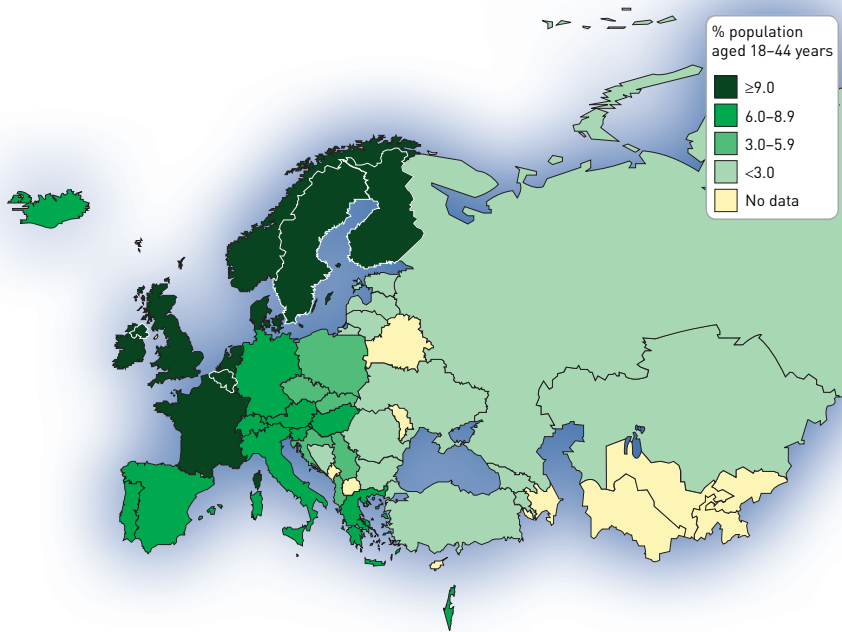
Immunopathological studies of the airways in asthma have pointed to the presence of a T-helper type 2 (Th2)-associated inflammatory process involving cytokines such as interleukin (IL)-4, IL-5 and IL-13 with a predominant eosinophilic inflammation, associated with features of airway remodelling (airway fibrosis, increased smooth muscle mass and epithelial fragility). Better understanding of the inflammatory processes has paved the way for novel, specifically targeted therapies.

## *Clinical manifestations*



Adults with asthma present with a spectrum of signs and symptoms that vary in severity from patient to patient, and within the same patient over time. Some patients complain of very few mild symptoms while others present with more severe symptoms despite having only mild airflow obstruction. Airway function should be measured routinely by tests such as forced expiratory volume in 1 second (FEV<sub>1</sub>) or peak expiratory flow (PEF).

The clinical manifestations of asthma include recurrent episodes of wheezing, chest tightness, cough and shortness

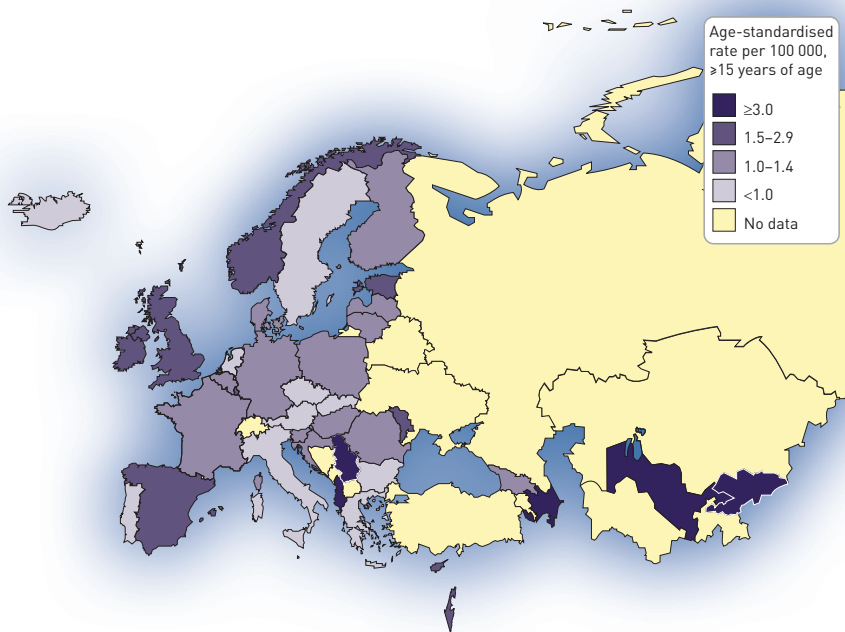


**Figure 1** – Prevalence of asthma ever in adults aged 18–44 years. Data from World Health Organization World Health Survey, 2002–2004. SIGURKARLSSON *et al.*, 2011; Polish Multicentre Study of Epidemiology of Allergic Diseases; European Federation of Allergy and Airways Diseases Patients Associations; Serbian Health Insurance Fund; the Swiss Study on Air Pollution and Lung Disease in Adults; PRIFTANJI *et al.*, 1999; Organisation for Economic Co-operation and Development.

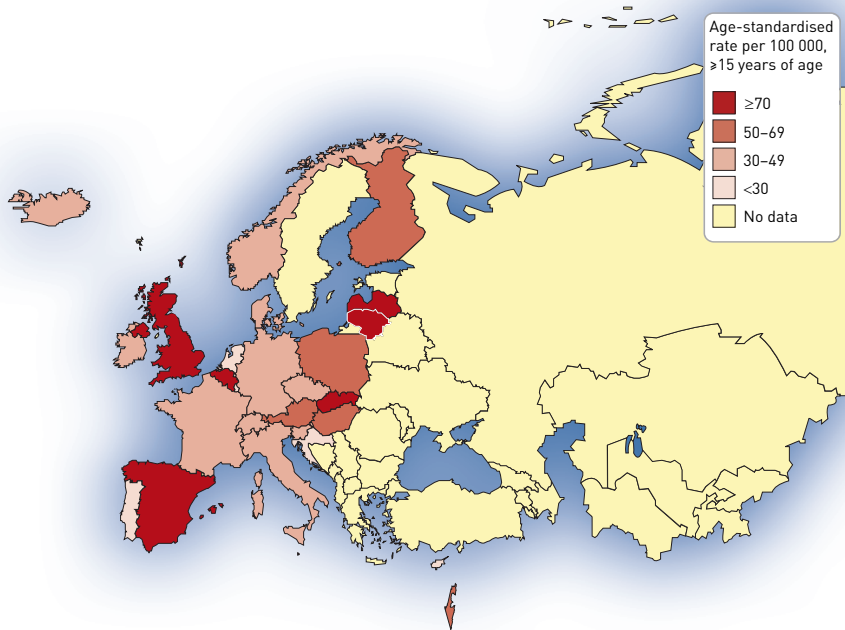
of breath. The symptoms are often worse at night or on waking from sleep. Usually, they resolve spontaneously or with the inhalation of a reliever medication. In other cases, they may worsen over hours or minutes, leading to more severe airflow obstruction and an ‘attack’ or exacerbation of asthma that is relieved only by extra medication. Some very severe episodes are life-threatening, although death from asthma in adulthood is uncommon (figure 2) and in most European countries mortality rates are falling.

Exacerbations of asthma are mostly provoked by respiratory infections – usually viral in origin – and are especially common in winter and shortly after the return of children to school after the summer holiday. In adults with allergic asthma (as indicated by the co-presence of rhinitis and conjunctivitis), symptoms are provoked by exposure to the relevant allergen(s), commonly those in house dust or from pets, or encountered at work. Other common triggers include physical exertion (particularly in cold, dry air) and traffic pollution. Certain drugs such as  $\beta$ -adrenergic blockers and nonsteroidal anti-inflammatory agents can provoke asthma. A rare, but characteristic form of adult-onset asthma presents with nasal polyps and symptoms provoked by taking aspirin or similar nonsteroidal anti-inflammatory agents; its mechanism is unclear. Asthma exacerbations remain the main reason for admission of people with asthma to hospital. While rates of hospital admission have gradually fallen in recent years, they remain high, particularly in the UK, Spain and Belgium (figure 3).

One important type of disease that arises in adulthood is occupational asthma, which is induced by airborne agents encountered in the workplace. Occupations in which there is a high risk of occupational asthma include baking, spray painting, chemical processing,



**Figure 2** – Mortality rate of asthma in adults. For some countries, data are missing due to deaths being reported for asthma and chronic obstructive pulmonary disease combined. Data from World Health Organization World and Europe Detailed Mortality Databases, November 2011 update.



**Figure 3** – Hospital admission rate for asthma in adults. Data from World Health Organization Hospital Morbidity Database, October 2011 update, and Eurostat, March 2012 update.

detergent manufacture and hairdressing. In addition, adults with asthma of unknown origin may find that irritant exposures or physical exertion at work exacerbate their disease. It is estimated that, in these ways, some 15% of all adult asthma is 'work related' (see chapter 24).

## Prevention



In most adults with asthma, the origins of the disease are unknown and therefore it is difficult to know what measures can be taken to prevent its development. One important exception is occupational asthma, which can generally be prevented effectively by careful control of relevant exposure in the workplace. In general, prevention or control of asthma symptoms and exacerbations is usually possible with current asthma medication.

## Management



There is currently no cure for most types of adult asthma, and the primary goals of management are: 1) to achieve and maintain control of symptoms; and 2) to prevent asthma exacerbations. In many cases, it is also possible to improve and/or maintain respiratory function, to retain normal activity levels, to prevent the development of irreversible airway narrowing and to prevent deaths from asthma. Clearly, it is also desirable to avoid short- and long-term adverse events from asthma medication.

Management starts with the identification of factors that trigger or worsen asthma. Avoiding passive or active smoking, exposure to high levels of airborne allergens or environmental pollution, and certain medications that may provoke asthma can each help improve control. Appropriate patient education and self-management are important aspects of care; in many countries, this is efficiently delivered and supervised by specialist asthma nurses.

Pharmacological treatment comprises 'controller' medication, exemplified by inhaled corticosteroids (ICS), with or without long-acting  $\beta_2$ -agonists (LABA), and 'reliever' medication taken as required to relieve symptoms, exemplified by short-acting  $\beta_2$ -agonists (SABA). The amount of treatment is adjusted according to the severity and frequency of asthma symptoms. Patients' needs for treatment may change over time and treatment should be adjusted accordingly.

Mild asthma is usually controlled using SABA alone and on demand, or by the addition of low doses of ICS. Asthma of moderate severity can be controlled with a combination of low- or high-dose ICS with LABA. More severe asthma may necessitate the addition of other controller medications such as leukotriene inhibitors and slow-release theophylline. Oral corticosteroids may be needed intermittently for treatment of exacerbations, or on a daily basis in those with the most severe disease. In some countries, anti-immunoglobulin (Ig)E antibody treatment is now available as an additional therapy for patients with severe allergic asthma.

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Using established treatment guidelines, most adult patients with asthma can be managed adequately in general practice, but those with more severe disease, and particularly those who present with recurrent exacerbations of asthma, are managed in hospital clinics. The rate of acute hospital admission for asthma varies widely across Europe (figure 3) but in most countries admission is less common than it used to be, probably reflecting improvements in the delivery of asthma care and the increased use of ICS therapies.

### *Medication use in Europe*

In the Asthma Insights and Reality (AIRE) study of seven western European countries, published in 2002, 2083 adults and children with asthma or their parents were surveyed about their asthma by telephone interview. In this survey, 12–18% of children and 15–28% of adults were classified as having severe persistent asthma. However, in the severe category, only 14–83% of children and 8–49% of adults were being treated with ICS therapy. The country with the highest use of ICS in both children and adults was Sweden. Because it would be expected that all patients with severe persistent asthma would be taking ICS, the survey indicated that there was severe undertreatment of asthma, the major reason perhaps being the lack of uniform application of asthma management guidelines across these countries.

However, in both France and the UK, there is evidence that the number of prescriptions for anti-asthma drugs more than doubled between 1980 and 1990, particularly for SABA and ICS. In the UK, the number of prescriptions for ICS in 1980 was approximately 1.2 million, increasing to 7 million in 1992. In a cross-sectional review of treatment carried out in five large general practices in the UK, 54% of adult patients with asthma were prescribed SABA alone, with most of the remainder using various combinations of additional drugs; 8% were using no treatment at all. Over the previous year, 14% had received 10 or more prescriptions for SABA/LABA and 13% had been prescribed at least one course of oral corticosteroids. Both of the latter occurred more frequently in patients taking more prophylactic treatment, indicating that there is a group of individuals, albeit relatively small in number, who have asthma that is refractory to the best available treatments.

### *Prognosis*



Most adults with asthma achieve good or very good control of their disease and are able to lead a normal life, punctuated

only by the need to take small amounts of regular medication and by occasional exacerbations. A small subgroup of about 10% of adults with asthma have persisting symptoms and exacerbations despite taking adequate treatment at the highest doses; the impact of this severe or 'difficult-to-control' asthma is often significant and many of these patients struggle at home and at work, and are prone to the adverse side-effects of treatment, particularly those associated with oral corticosteroids at high doses. Asthmatics of particular concern are those who smoke or are exposed to passive smoking, which can make asthma worse. The challenge of severe asthma is to find ways of controlling the frequency of exacerbations and reversing the chronic airflow obstruction that are the most frequent hallmarks of this condition, despite the use of optimal anti-asthma treatment.

The most important long-term consequence of asthma is the development of persistent airway narrowing, which is non- or poorly responsive to treatment; it is unclear whether this is preventable by regular treatment with controller therapies. Death from asthma, although very uncommon in Europe, can occur in adults with all forms of the disease, especially if treatment has been suboptimal.

## *Future developments and research needs*



Asthma is common in European adults and in many countries it is more common than it used to be. There remains a pressing need to understand its origins – in most cases in childhood – so that effective primary prevention can be devised. Where its causes are known – notably in occupationally induced disease – greater efforts need to be made in the regulation and control of causative exposures.

## *Propagation of good asthma care in Europe*

Current medications are generally very effective but require appropriate availability and means of delivery. The establishment of national and international guidelines has been instrumental in improving the care of adults with asthma, through better education of medical practitioners, involvement of asthma-trained nurses and the implementation of standardised treatment regimens. In some countries, such as Finland and France, the active participation of government health departments has led to important improvements in asthma control with consequent reductions in morbidity, mortality and costs attributable to the disease, demonstrating that focused, national programmes can work and are probably cost-effective. In any such programme, it would be important to address three particular issues that contribute to the continuing burden of asthma. 1) Are all patients who need treatment receiving and taking adequate controller medication? 2) Are patients with persistent uncontrolled asthma being adequately monitored and investigated as to the cause of the poor control? 3) Are the co-existing factors associated with asthma being treated or addressed, such as cigarette smoking or secondary smoke exposure, allergies, sino-rhinitis and obesity?

## *Difficult-to-control severe asthma*

Difficult-to-control severe asthma can be subdivided into: 1) untreated severe asthma caused by poor access to medical care and asthma therapies; 2) difficult-to-treat,



severe asthma resulting from poor management or poor patient adherence to treatment; and 3) treatment-resistant asthma for which control is not achieved despite the highest level of recommended treatment (refractory asthma and corticosteroid-resistant asthma) or for which control can be maintained only with the highest level of recommended treatment with a risk of side-effects.

New therapeutic approaches are needed for the category of patients with treatment-resistant asthma. First, we need a better understanding of its pathophysiology and its relation to the various phenotypes of adult asthma with respect to clinical presentation, functional abnormalities and features of airway inflammation and remodelling. Several distinguishable phenotypes of adult asthma have been described: for example, those with the most severe disease, requiring treatment with two or more controller medications, have a later age of onset, the greatest degree of airflow obstruction and the poorest bronchodilator response. Another characteristic of some types of severe asthma is the presence of a persistently high number of eosinophils in the sputum, despite high-intensity treatment. This type of asthma would be expected to respond to novel therapies targeting eosinophils, such as anti-IL-5 antibody treatments. Thus, the importance of defining phenotypes lies in matching them with novel, specific therapies that would benefit the individual patient.

## Further reading



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