Global Epidemiology of Chronic Respiratory Disease 2

Asthma: epidemiology, risk factors, and opportunities for prevention and treatment

Shamanthi M Jayasooriya, Graham Devereux, Joan B Soriano, Nishtha Singh, Refiloe Masekela, Kevin Mortimer, Peter Burney

Asthma is characterised by variable airflow obstruction and is associated with symptoms of cough, wheeze, and dyspnoea, and with airway inflammation and hyperresponsiveness. There are approximately 300 million people with asthma worldwide. Despite a current plateau, the burden of this disease is likely to increase due to population growth, urbanisation, and ageing. Disease onset is associated with low birthweight, preterm birth, viral infections, in-utero passive smoke exposure, urbanisation, and occupational exposures. Obesity is associated with increased incidence and severity of asthma, whereas exposure to small allergen particles leads to severe disease. In adults and adolescents, inhaled corticosteroids in combination with formoterol (as anti-inflammatory reliever or as maintenance and anti-inflammatory reliever therapy) are widely recommended to control the symptoms of asthma. For children, low-dose inhaled corticosteroid is the preferred first-line treatment. Monotherapy with short-acting β-agonists is strongly discouraged. The WHO Global Action Plan for the Prevention and Control of Non-communicable Diseases includes availability of affordable combination inhalers for asthma. Co-ordinated national asthma policies, ensuring access to inhalers, have resulted in fewer hospitalisations and school and work absences. Future asthma prevalence could be reduced by good maternal and infant care, with reduction in premature births and reduction in infant respiratory infections, and by reduction in obesity at all ages.

Lancet Respir Med 2025; 13: 725–38

Published **Online** July 17, 2025
https://doi.org/10.1016/S2213-2600(24)00383-7

This is the second in a **Series** of four papers about the global epidemiology of chronic respiratory disease. All papers in the Series are available at www.thelancet.com/series-do/global-epidemiology-chronic-respiratory-disease

School of Medicine and Population Health, The University of Sheffield, Sheffield, UK (S M Jayasooriya PhD)**; Liverpool School of Tropical Medicine, Liverpool, UK** (G Devereux PhD)**; Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK** (G Devereux, Prof K Mortimer PhD)**; Hospital Universitario de la Princesa, Universidad Autónoma de Madrid, Madrid, Spain** (Prof J B Soriano PhD)**; Centro de Investigación en Red de Enfermedades Respiratorias, Instituto de Salud Carlos III, Madrid, Spain** (Prof J B Soriano)**; Department of Respiratory Medicine, Asthma Bhawan, Jaipur, India** (N Singh MD)**; Department of Paediatrics and Child Health, School of Clinical Medicine, University of KwaZulu-Natal, Durban, South Africa** (Prof R Masekela MD, Prof K Mortimer)**; Cambridge-Africa, Department of Pathology, University of Cambridge, Cambridge, UK** (Prof K Mortimer)**; National Heart and Lung Institute, Imperial College London, London, UK** (Prof P Burney MD)

Correspondence to: Prof Peter Burney, National Heart and Lung Institute, Imperial College London, London SW3 6LY, UK
p.burney@imperial.ac.uk

Introduction

Asthma is the second most common chronic respiratory disease globally after chronic obstructive pulmonary disease (COPD), and the most common chronic disease in children. The condition affects individuals of all ages, with a highly variable geographical distribution worldwide.[1] The population and individual burden of asthma is substantial, in terms of both morbidity and mortality. There is no gold standard for the diagnosis of asthma, and this is ultimately a clinical decision. Several physiological measurements and biomarkers are associated with asthma, but none is pathognomonic of the condition.[2] Underdiagnosis and misdiagnosis are common, leading to undertreatment of the disease.[3]

The population burden of asthma has been determined by landmark studies that have used standardised protocols to explore the distribution of asthma and related conditions by sex, age, and other determinants. Three macro-studies on asthma and allergic disorders (eczema and rhinitis) have shaped our understanding of these conditions: the International Study of Asthma and Allergies in Childhood (ISAAC) in children,[4] the European Community Respiratory Health Survey (ECRHS) in adults,[5] and the Global Asthma Network (GAN) in children and adults.[6] These studies are summarised in panel 1.

Global burden of disease

ISAAC, ECRHS, and GAN have contributed to our understanding of asthma epidemiology, risk factors, and management practices on both regional and global levels.[14–16] European adults born between 1946 and 1970 have, over the last 20 years, experienced less wheeze, largely due to reduced smoking, but have been more likely to report asthma attacks, use of asthma medication, and hay fever.[17]

Globally, approximately one in ten children and one in 20 adults have asthma. Between one in eight and one in ten adults and children have rhinoconjunctivitis or eczema. Approximately 300 million people worldwide have asthma—a burden that is expected to increase in the 21st century due to population growth, increased urbanisation, and ageing of the population.

Asthma prevalence (unadjusted for age) varies by country, ranging from 1% to 18%, with particularly high rates in the USA, the UK, and Portugal (figure 1). In contrast, mortality rates from asthma are the highest in Nepal, India, Bangladesh, Myanmar, and Indonesia

Key messages

- Asthma is a common condition, with an estimated 300 million cases worldwide, for which underdiagnosis and misdiagnosis is a global problem
- Asthma is associated with urbanisation
- Asthma is partly preventable with good mother and child health services, prevention of early-life respiratory tract infections, control of tobacco smoking, reduction in obesity, reduction in traffic-related and other outdoor and indoor air pollution, and control of occupational and home exposure to asthmagens
- Most asthma is manageable at relatively low cost, but treatment is often still unaffordable for families with low incomes; sociocultural factors play a role in accessing treatment

For more on the **ISAAC** see https://isaac.auckland.ac.nz

For more on the **ECRHS** see https://www.ecrhs.org

For more on the **GAN** see https://www.globalasthmanetwork.org

***Panel 1:* International epidemiological studies on asthma and allergic disorders**

The International Study of Asthma and Allergies in Childhood (ISAAC)

- ISAAC determined the prevalence of asthma, allergies, and eczema in school-aged children. The study used written and video questionnaires; exercise-induced asthma was measured by means of peak flow.[4] Standardised questionnaires gathered data from children and adolescents on asthma symptoms and associated risk factors.
- ISAAC involved more than 100 countries and nearly 2 million children. The standardised methodology enabled between-country comparisons and estimates of changes over time in some regions.
- The first ISAAC results, in 1992–93, showed 20-times to 60-times differences between centres in the prevalence of asthma symptoms, allergic rhinoconjunctivitis, and atopic eczema. The highest rates of asthma were observed in centres in the UK, Australia, New Zealand, and Ireland; the lowest rates were in centres in eastern European countries, Indonesia, Greece, China, Taiwan, Uzbekistan, India, and Ethiopia, with an 8-times variation seen between the 10th and 90th percentiles (3·9–30·6%).[5] The geographical distribution showed weak to moderate consistency in the prevalence rates of asthma, allergic rhinoconjunctivitis, and atopic eczema.
- Limitations included reliance on self-reported symptoms, sampling that excluded individuals not in school, and the potential for variability in interpretation of questions across different cultural contexts and languages.

The European Community Respiratory Health Survey (ECRHS)

- ECRHS determined the prevalence and distribution of asthma in young adults aged 20-44 years.[7] The survey was conducted in multiple European countries, plus other selected international centres. ECRHS employed a multi-stage stratified random sampling approach to select participants from the general population.
- The ECRHS collected detailed information through questionnaires, lung function tests including methacholine challenge, and skin prick tests to assess allergic sensitisation. Some centres also followed up participants over time to track changes in respiratory health.
- The first ECRHS results, 1990–92, showed that the prevalence of asthma symptoms varied widely, being generally lower in northern, central, and southern Europe and higher in the British Isles, New Zealand, Australia, and the USA; wide variations were observed even within some countries.[8] The prevalence of nasal allergy, bronchial responsiveness, and atopy showed a similar distribution to asthma. Strengths of ECRHS included its large scale, rigorous population-based sampling methods, inclusion of objective measures such as lung function tests and bronchial responsiveness, and longitudinal design providing insights into the natural history of asthma and the development of persistent airflow limitation due to remodelling (a process distinct from the development of chronic obstructive pulmonary disease).[9,10]
- Limitations were the survey's focus on European populations, with limited generalisability of results to other regions.

The Global Asthma Network (GAN)

- GAN,[11] formed as a collaboration between ISAAC and the International Union Against Tuberculosis and Lung Disease (The Union), collected data from a range of countries worldwide, by collaborating with national and regional centres to conduct surveys with the use of a standardised protocol.
- GAN gathered data on asthma prevalence, severity, and management in children, adolescents, and adults in schools and households.[12,13] The network promotes capacity building in asthma surveillance in low-income and middle-income countries, and its standardised methodology facilitates comparisons across regions. GAN relies on collaboration with local centres and there are potential variations in data collection methods and quality across different countries.

(figure 2). Although mortality rates in sub-Saharan Africa are lower than in south and southeast Asia, they remain high relative to the region's low prevalence rates. Differences in the within-country asthma prevalence distribution are even greater than the differences between countries.

Africa

The burden of asthma in Africa is substantially under-reported due to scarce epidemiological data and local diagnostic challenges due to limited resources.[18–21] Available studies indicate prevalence rates ranging from 4% to 20%, with higher rates in urban areas. Access to health care and asthma medications is often constrained, leading to increased morbidity and mortality rates.[21,22] Demographic changes including natural population growth, ageing, and urbanisation will lead to more asthma cases in the coming decades.[23]

America

The US Centers for Disease Control and Prevention reports that more than 27 million people in the USA have asthma.[24] Although this figure has remained stable over the last decade, great statal and county disparities exist among different ethnic groups. African Americans and Hispanic populations have higher rates of asthma and asthma-related mortality compared with non-Hispanic white Americans. In Latin America, both in adults and

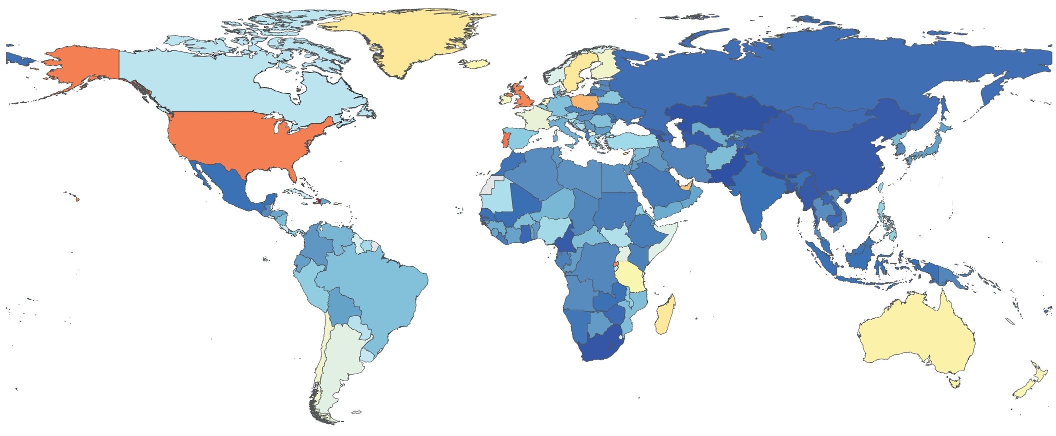

***Figure 1:* Estimates of asthma prevalence for all ages and both sexes, according to GBD 2021**

Figure adapted from: Institute for Health Metrics and Evaluation. GBD Compare data visualization. Seattle, WA: IHME, University of Washington, 2024 (accessed Nov 7, 2024). GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

For more on **GBD Compare data visualization** see http://vizhub.healthdata.org/gbd-compare

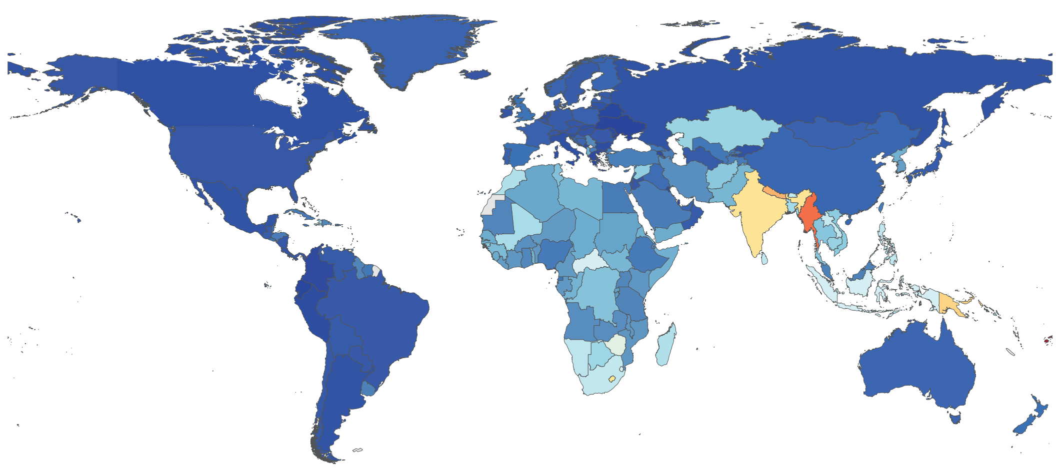

***Figure 2:* WHO estimates of annual asthma deaths per 100 000 population. All ages and both sexes.**

Figure adapted from: Institute for Health Metrics and Evaluation. GBD Compare data visualization. Seattle, WA: IHME, University of Washington, 2024 (accessed Nov 7, 2024). GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

For more on **GBD Compare data visualization** see http://vizhub.healthdata.org/gbd-compare

children, a high burden of symptoms and use of health services have been identified by GAN and ISAAC, with prevalences of asthma ranging from 5% to 15% in different countries; Chile, Argentina, Cuba, and Costa Rica report some of the highest prevalence rates of the condition in the region. Socioeconomic disparities, urbanisation, and environmental pollution contribute to the high burden of asthma from Mexico to the tip of South America. Additionally, less than ideal access to health care and medications exacerbates the effect of asthma on quality of life and increases health-care costs.

Asia

Asia presents a diverse picture of asthma prevalence. In countries such as Japan and South Korea, asthma prevalence is relatively low, at about 2–5%. In contrast, urban areas of China and India report very high prevalence rates, particularly among children. In India, between ISAAC phase 3 and GAN phase 1, there was a substantial decrease in the prevalence of current wheeze among both children and adolescents between 2009 and 2022. Of people with current wheeze, 75–82% remained clinically undiagnosed. Among individuals with current wheeze who had no diagnosis, less than 1% took a daily inhaled corticosteroid. In people with current wheeze who were clinically diagnosed with asthma, use of daily inhaled corticosteroid increased to 2–8% in different age groups.[25] In South-East Asia, mortality rates have been consistently high at about 13 in 100 000 per year; this high rate might reflect low access to inhaled corticosteroids in some areas.

Europe

Asthma prevalence in Europe shows considerable variation, with rates[25] ranging from 1% to 16% across different countries (as shown by ISAAC and ECRHS). Northern and western European countries, such as the UK, Sweden, and Finland, report higher prevalence rates, whereas eastern and southern European countries have lower prevalence rates. Portugal, Greenland, and Poland also have high prevalences of the condition. Despite the high figures, asthma prevalence continues to decrease.

Middle East

Asthma prevalence in the Middle East varies widely, with rates between 5% and 15%. The region faces unique challenges, including high levels of air pollution, sandstorms, growing obesity rates, and rapidly changing lifestyles.[26] In countries such as Saudi Arabia, Kuwait, and the United Arab Emirates, the prevalence of asthma has been increasing, particularly among children and adolescents. Asthma management strategies and public health interventions in the Middle East region must be improved.[27] Mortality rates have been falling steadily.

Oceania

The first available studies, done in Oceania in the 1960s,[28] identified Australia and New Zealand as having among the highest rates of asthma worldwide. More than 10% of the general population of all ages and 20–30% (or more) of children were determined to be affected. Additionally, socioeconomic disparities, particularly among Indigenous populations, such as the Māori and Pacific Islanders in New Zealand, were associated with poorer asthma management and outcomes due to poor access to health-care resources and education. Factors including high rates of smoking, cannabis use, and obesity further compounded the problem, making asthma control challenging and leading to increased hospitalisations and health-care costs among Maori and Pacific Islanders. In Melanesia (Fiji, Papua New Guinea, Solomon Islands, and Vanuatu) and Micronesia (Federated States of Micronesia and Kiribati), available information on the burden of asthma is more limited.[29]

Recent trends

Crude asthma prevalence rates have been decreasing in most WHO regions, although rates have plateaued since 2000 (figure 3). Asthma prevalence was consistently the highest in the Americas and Europe. The rate plateaued in the Americas from the early 2000s at 6%. In Europe, a steady decrease was observed until 2015, but the rate also plateaued for the last decade at about 4·5%. Africa has had a steady decrease from 5·4% in 1990, to 3·8% in 2021, which was parallelled by a decrease from 4·1% to 2·7% in the eastern Mediterranean region; Western Pacific and South-East Asia regions have similar low prevalences of asthma aand have also plateaued, at about 2·2% since 2015.

Crude mortality rates from asthma have also been decreasing steadily in most regions except for South-East Asia, where mortality rates have been consistently high at about 13 per 100 000 (figure 4). Mortality rates in both the Eastern Mediterranean and African regions have consistently decreased from more than eight deaths per 100 000 in 1990, to 4·6 in 2021. Asthma mortality in Europe decreased sharply from 1995 to 2005, and has plateaued since 2010 at 1·7 deaths per 100 000. 2·8 deaths per 100 000 are reported in the Western Pacific, whereas the lowest mortality of 1·2 deaths per 100 000 is reported in the Americas.

Aetiology

Genetics and atopy

Asthma is known to be heritable. A child has about a 25% chance of having asthma if one parent has the condition and 50% if both have the ilness.[30] A meta-analysis of worldwide genome association studies of asthma has identified 14 genes associated with the condition, implicating disordered immunological or airway epithelium-mediated inflammatory processes in asthma pathogenesis.[31] Atopy is the genetic predisposition to form immunoglobulin E (IgE) antibodies on exposure to allergens. A personal or family history of atopy is a strong risk factor for asthma. In the UK, for instance, approximately 30% of the population are atopic,[32] of whom about 20% will develop asthma;[33] 70–90% of children with asthma and 50% of adults with asthma are atopic.

Urbanisation

The world is becoming increasingly urbanised. In 1950, 30% of the world's population lived in urban areas. By 2018, this ratio had risen to 55% and by 2050 an estimated 68% of the world's population will live in urban environments.[34] From the 1970s onwards, consistent differences were noted between the prevalence of asthma in poor rural communities and the prevalence among migrants in slightly more affluent urban areas.[35–39] Although this difference in environment was was not paralleled by differences in allergen-specific IgE,[40] it was linked to differences in skin tests to specific allergens.[41,42] These differences between positive sensitisation defined by specific IgE and negative skin tests were related to differences in BMI,[43] and to qualitative differences in diet between urban and rural populations.[44] At an ecological level, the prevalence of wheeze with a positive skin test is weaker in countries with a very low per capita gross national income, whereas wheeze with no atopic features is equally distributed between high-income and low-income countries.[45] The same is true for eczema[46] and bronchial response to exercise (figure 5).[47] In Germany before unification, there was lower prevalence in the east;[48] this difference reduced after the country's unification.

In Europe and North America, there are also urban–rural differences, with asthma and atopy being far less common in individuals brought up on farms and in rural areas.[49–52] In 1989, Strachan noted that children with more siblings were less likely to complain of allergic rhinitis;[52] research suggested that increasing hygiene was leading to high rates of allergic sensitisation—the so-called hygiene hypothesis. This hypothesis was extended to explain the reduced levels of sensitisation in individuals brought up on farms and in the countryside. Also, a case has been made for greater microbial (bacterial and fungal) diversity being the common protective component.[53] In addition to farm life and the presence of siblings, going to school at a young age if there are no siblings,[54] bedroom sharing, and pet ownership in childhood also reduce the chance of having specific IgE to common allergens in adulthood.[55]

There are two important caveats in relation to the hygiene hypothesis. First, as noted by Strachan,[52] this hypothesis relates to rhinitis and sensitisation to allergen but not to asthma or wheeze.[56] This paradoxical finding is confirmed by a randomised controlled trial[57] in which infants were randomly assigned to a thorough cleaning of the house to reduce allergen exposure as far as possible. Contrary to the expectation of the trialists, but as predicted by the hygiene hypothesis, house cleaning was associated with an increase in sensitisation, but also, paradoxically, improved lung function at the age of 3 years. Second, exposure to the countryside in childhood appears to suppress the development of allergen specific IgE in Europe,[55] but not in Africa.[40,41,58]

Allergen exposure alone does not determine the prevalence of allergy as sufficient allergen to induce allergy in some susceptible individuals exists in most environments. However, some evidence suggests that low exposures to individual allergens in early life can be associated with lower rates of sensitisation in later life. Paradoxically, evidence is also mounting for the fact that heavy exposure to peanut allergen in early life might prevent sensitisation to it.[59–61]

Early life

The origins of asthma start very early in life; in high-income countries, associations have been reported

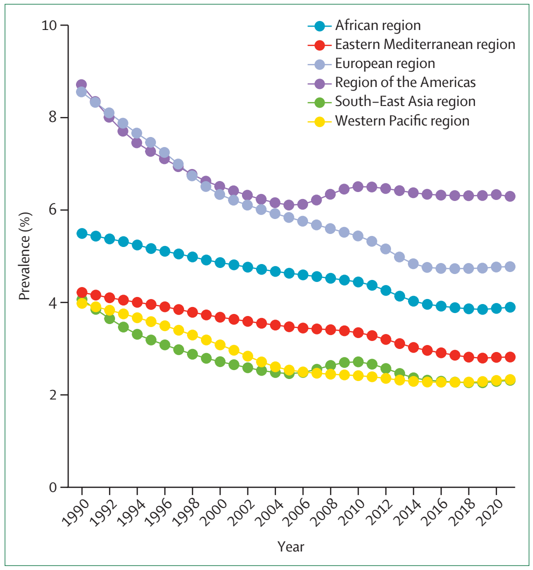

Figure 3: **Asthma prevalence for all ages and both sexes by WHO region and year**
Figure adapted from: Institute for Health Metrics and Evaluation. GBD compare data visualization. Seattle, WA: IHME, University of Washington, 2024. GBD Compare data visualization (accessed Nov 7, 2024). GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

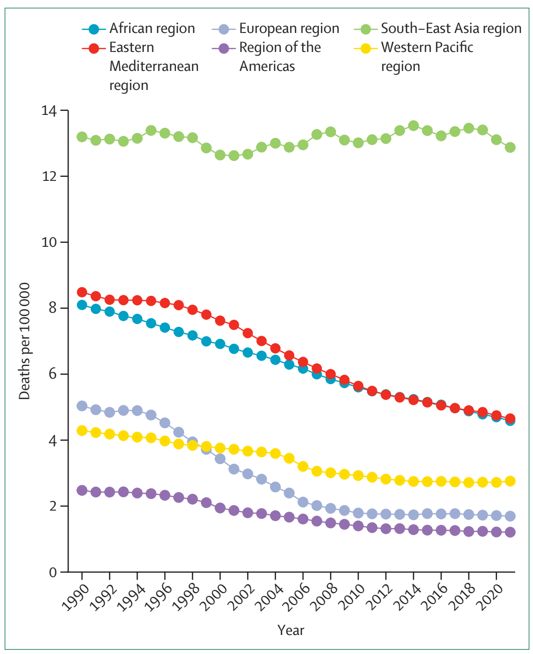

Figure 4: **Asthma deaths for all ages and both sexes by WHO region and year**
Figure adapted from: Institute for Health Metrics and Evaluation. GBD compare data visualization. Seattle, WA: IHME, University of Washington, 2024.GBD Compare data visualization (accessed Nov 7, 2024). GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.

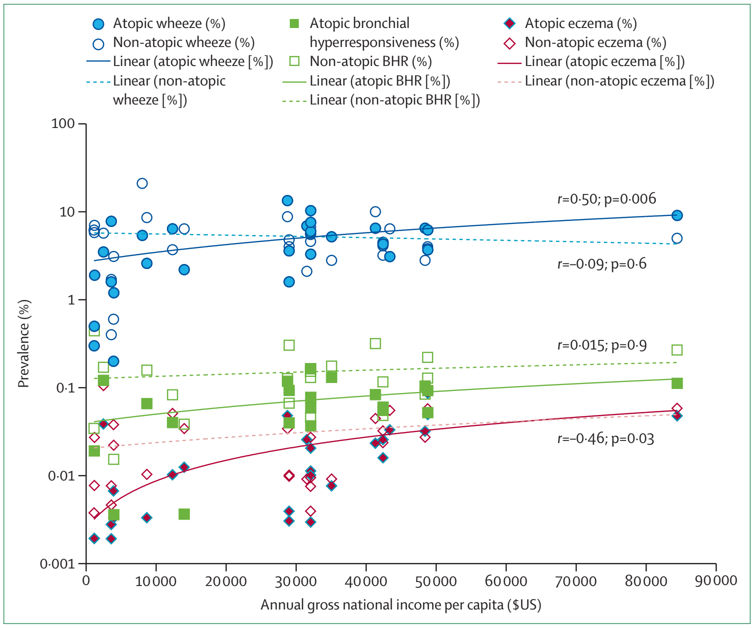

Figure 5: **Prevalence of wheeze, rhinitis, and eczema by ISAAC site, by atopy and by gross national income**[45–47]
Prevalence (percentage of population) in children at ISAAC sites, presented by atopy and by gross national income ($US). The prevalence is plotted on a logarithmic scale. Data from Weinmayr and colleagues,[45] Flohr and colleagues,[46] and Büchele and colleagues.[47] ISAAC=International Study of Asthma and Allergies in Childhood.

between childhood wheezing and asthma and fetal ultrasound measurements, low birthweight, premature birth, perinatal lung function, and infant weight gain.[62–70] Similar findings have been reported in LMICs[71] and might be pertinent to asthma aetiology in these countries given that about 70% of low birthweight births and 65% of premature births are in southern Asia and sub-Saharan Africa, with minimal improvement in birthweight in recent decades. The WHO antenatal care recommendations provide guidance on how to reduce the two underlying causes of low birthweight—preterm birth and intrauterine growth restriction.[72] Self-care recommendations for pregnant women include a healthy balanced diet, keeping physically active, and avoidance of nicotine, caffeine, alcohol, and substance use. The recommendations include guidance on the organisation and delivery of antenatal care (eg, a minimum of eight contacts with health professionals throughout pregnancy; screening for anaemia, bacteriuria, HIV, and pre-eclampsia; and fetal monitoring). The increased risk of asthma and low gestational age at birth is detectable in infants born 1 or 2 weeks early, suggesting that this is unlikely to be due to bronchopulmonary dysplasia associated with preterm birth.[68]

Late-onset asthma
Due to increasing multimorbidity and people often developing multiple age-related conditions, the differential for breathlessness often broadens in later life.[73] In addition, there are varying levels of symptom tolerance based on, sometimes erroneous, assumptions that symptoms are due to normal ageing. This increased difficulty in making a differential diagnosis of asthma is also further affected by age-related cognitive changes. All of these factors increase the likelihood of misdiagnosis and underdiagnosis of asthma.[74] Asthma mortality increases with age.[75] The needs of older adults diagnosed with asthma are variable as, in addition to increased multimorbidity, these individuals are more likely to be isolated and suffer from age-related physical impairments. Personalised care recognising the aforementioned factors should be adopted. Consideration should be given to the use of integrated respiratory care alongside virtual ward-based care outside the hospital, with robust support from primary care to address the additional needs of this patient group.

Infections
Evidence suggests that lower respiratory tract infections, particularly if repeated, severe, and occurring in early life, reduce childhood lung function.[76–79] Viral respiratory tract infections are common in young children. Early-life viral respiratory tract infections with human rhinovirus and respiratory syncytial virus (RSV), especially when accompanied by wheezing, are associated with subsequent recurrent wheeze, diagnosis of asthma, and reduced lung function.[76–78,80,81] These associations are particularly strong for wheezing episodes occurring in the first year of life, more frequent episodes, severe infections requiring hospitalisation, and concurrent atopy. The interactions between these viruses and the innate and adaptive immune systems are the most likely mechanisms underlying these associations.[82] However, whether early-life viral respiratory tract infections manifesting as wheezing episodes cause asthma or identify children who are predisposed to develop asthma remains unknown. The advent of RSV monoclonal antibody prophylaxis and RSV vaccination provides an opportunity to investigate this important issue. A systematic review and meta-analysis[83] of monoclonal antibody prophylaxis against RSV bronchiolitis published in 2020 did not identify an overall statistically significant reduction in recurrent wheeze or asthma; however, a subgroup analysis excluding studies at high risk of bias did identify a statistically significant benefit.[83]

Tobacco smoking
Tobacco use is on the decrease in all regions of the world. Currently, about 22% of the world's population uses tobacco products. This rate has decreased from 33% in 2000 and is predicted to decrease to 18% in 2030.[84] Passive exposure to tobacco smoking either in utero or during childhood is associated with a 20–70% increased risk of developing childhood asthma.[85] Children are also more likely to develop asthma if their maternal grandmother smoked during pregnancy, independent of the mother's asthma and smoking status.[86,87] Maternal

smoking during pregnancy has been associated with altered cord blood immunology and reduced early-life lung function.[88,89] The adverse effects of maternal smoking on fetal airway development appear to be predominantly caused by nicotine, in part by inducing epigenetic modifications to DNA.[90] The recognition that nicotine is a causative factor for asthma has obvious implications for the safety of nicotine-containing e-cigarette vaping products, the use of which has substantially increased among young adults in England[91] and the USA[92] in the last 10 years. Use of these products has also been linked to new-onset asthma in adolescents.[93]

Air pollution

Evidence suggests that long-term exposure to air pollution, most notably nitrogen dioxide and particulate matter from traffic air pollution, is associated with the development of asthma. This evidence is restricted to children.[94,95] Potential mechanisms include effects on airway and alveolar development and promotion of immunological and airway epithelial cell inflammatory pathways.[94] Changes in particulate matter and nitrogen dioxide exposures are complex. Over the last two decades, global exposures appear to have decreased due to improvements in air quality in North America, Europe, China, and Japan, but exposures have been increasing (in line with increasing economic activity) in the Middle East, south Asia, and sub-Saharan Africa.[96,97]

Occupation

Specific occupations with distinctive inhalational exposures are well documented but often under-recognised causes of asthma. In high-income countries, an estimated 15–20% of new-onset asthma in working-age adults is likely to be occupational in origin;[98] much less is known about the incidence of occupational asthma in LMICs because occupational asthma surveillance programmes are less well developed in those countries.[99,100] More than 400 causes of occupational asthma have been described and categorised into high-molecular-weight (eg, animal urine or proteins, cereal grains or flour, and enzymes) and low-molecular-weight sensitisers (eg, acid anhydrides, biocides, colophony, and di-isocyanates).[101] The main risk factor for occupational asthma is exposure to the asthmagen (allergens and other chemicals that can induce asthma), as well as the level and duration of exposure. Atopic status, smoking, and genetic susceptibility might modify risk.[98] The prevention of occupational asthma can be achieved by controlling workplace exposure to occupational asthmagens by, for example, replacement of the hazardous substance with less harmful materials, use of engineering controls preventing exposure, and provision of personal protective equipment for workers.

Obesity

The prevalence of obesity is increasing globally and, by 2035, more than half the world's population is predicted become overweight.[102] The reasons for the increase in obesity prevalence are complex, but probably reflect interactions between genetic susceptibility, environmental factors, and psychosocial factors resulting in energy intake (diet) chronically exceeding energy expenditure (physical activity), with ultra-processed convenience foods contributing to the problem.[102] Once considered a problem of high-income countries, obesity is now increasing in LMICs.[102] Evidence confirms that overweight and obese children and adults are at an increased risk of developing asthma.[103,104] Obesity also appears to be associated with increased severity of asthma.[105,106] Evidence also suggests that children and adults with asthma are more likely to become obese, possibly because of inactivity, corticosteroid exposure, or factors that influence both asthma and weight.[107,108] The mechanisms underlying the association between obesity and increased asthma risk are incompletely understood, but altered pulmonary mechanics, systemic inflammation, altered microbiome, and increased susceptibility to air pollution have been implicated.[109]

Insufficient exercise

Physical inactivity (not meeting the WHO global recommendations on physical activity) and sedentary behaviour (sitting or lying down for long periods) are lifestyle factors[110] that have been implicated in asthma aetiology. Addressing these factors is recommended in Global Initiative for Asthma (GINA) treatment guidelines to improve the general health, exercise capacity, and quality of life of people with asthma.[111] Globally, about 31% of adults were physically inactive in 2022—an increase of nearly 8% from 2000.[112] Physical inactivity appears to be even higher in adolescents, with 81% of the world's adolescents (aged 11–17 years) fulfilling the criteria for physical inactivity.[113]

Cross-sectional studies of children and adults have reported that physical inactivity and a sedentary lifestyle are associated with asthma, bronchial hyperresponsiveness, and reduced lung function.[114,115] However, such studies are limited by the potential for reverse causation (ambivalence as to whether asthma restricts exercise or absence of exercise leads to asthma). Although some longitudinal studies have reported that physical inactivity and a sedentary lifestyle are associated with new-onset asthma and reduced lung function, many other longitudinal studies have reported no such association.[116–122] A systematic review of longitudinal studies in children relating physical activity measurements to subsequent new-onset asthma and lung function outcomes,concluded that the results were highly inconsistent, with insufficient evidence to suggest that physical activity influences the risk of new-onset asthma or improves lung function in children.[123] Any potential benefits of physical activity in asthma aetiology and established asthma likely reflect the modulatory effects of exercise on inflammatory and immune

Panel 2: Prevention of asthma

No evidence-based primary prevention programme for asthma exists, but several key public health and clinical interventions are considered likely to reduce asthma incidence. These interventions include:

- Comprehensive maternity and child health services that offer lifestyle recommendations for pregnant women: a healthy balanced diet; keeping physically active; and avoidance of nicotine, caffeine, alcohol, and substance use.
- Organisation and delivery of antenatal care: a minimum of eight contacts with health professionals throughout pregnancy; screening for anaemia, bacteriuria, HIV, and pre-eclampsia; and fetal monitoring.
- Probiotics and omega-3 fatty acid supplementation during pregnancy and early childhood, which might lower the incidence of asthma.
- Maternal and infant vaccination.
- Prevention of tobacco smoking, particularly among young parents and adolescents.
- Prevention and control of obesity, physical inactivity, and sedentary lifestyles.
- Control of traffic-related air pollution.
- Control of exposure to asthmagens in the workplace and at home (including moulds).

processes in asthma.[124] Although the effects of exercise on these processes are unlikely to be as potent as pharmacological interventions, further studies are needed to establish whether specific asthma endotypes respond preferentially to tailored exercise regimes. This research might be particularly useful in LMIC settings where affordability and availability issues with conventional treatments exist.

Allergen exposure

For individuals who are sensitised, ample evidence exists that exposure to an allergen is a potent trigger for allergic symptoms. Pollen grains are relatively large and settle on the mucous membranes of the conjunctiva, nose, and pharynx, causing the symptoms of hay fever. However, smaller particles of an allergen, including grass allergens released from pollen grains during thunderstorms, can enter the airways and cause asthma attacks. These particles might trigger major outbreaks of acute severe asthma.[125–127] Mould spores are also small enough to enter the lower airway and can cause clusters of asthma attacks.[128,129] Allergens might also explain some associations between asthma events and increases in air pollution, as air pollution itself does not appear to have a consistent association with such events.[130] Sensitisation to small-particle allergens, including those from moulds[131] and cockroaches,[132] is associated with severe asthma. The main strategies to reduce the incidence of asthma are summarised in panel 2.

Access to care

Most children, adolescents, and adults with asthma have a disease type that is responsive to currently available treatments. The GINA strategy sets an evidence-based standard for international best practice in asthma management. GINA recommends that in adolescents and adults with asthma, the first step of treatment should be a combination inhaler containing an inhaled corticosteroid and formoterol (a long-acting β2-agonist with a rapid onset of action) used as needed to provide anti-inflammatory reliever therapy. In case maintenance therapy is also needed, the same combination inhaler can be used for both maintenance and relief as maintenance and reliever therapy (MART). This recommendation is based on substantial evidence showing fewer exacerbations and hospitalisations when inhaled corticosteroid–formoterol is used.[111,133–135] In younger children, low-dose inhaled corticosteroid still forms the backbone of asthma therapy. A strong recommendation against the use of short-acting β2-agonist monotherapy in asthma exists.

In high-income countries, use of relatively costly monoclonal antibody biologics targeting specific proinflammatory molecules (eg, anti-IgE, anti-interleukin(IL)-4, anti-IL-5, and anti-thymic stromal lymphoprotein) is transforming asthma care for the patients whose asthma cannot be adequately controlled on inhaled corticosteroid–formoterol and other non-biological therapies. In high-income countries, biologics have been shown to improve quality of life, reduce asthma exacerbations, and reduce the need for long-term oral corticosteroids, and are well described elsewhere, including in the guidelines of the GINA strategy. However, the use of biologics in LMICs is likely to be restricted by affordability and high incidence of some parasitic worm infections, which would need to be excluded or treated before initiation of biologics and monitored over the course of the treatment.[111,136,137] Unfortunately, access to affordable GINA-recommended asthma care is limited even for basic preparations.[138–141] The GAN phase 1 study found that inhaled corticosteroid is not used by 60% of adolescents and 56% of adults with asthma even among individuals with frequent severe symptoms. Use of inhaled corticosteroid was the greatest in high-income countries. A 2023 survey of the availability, cost, and affordability of WHO essential asthma medicines across 60 LMICs found that inhaled short-acting β-agonist was the most available and affordable, followed by inhaled corticosteroid, with low availability and affordability of the combination inhaled corticosteroid–formoterol.[138,142] In keeping with the GAN phase 1 study data, there was an association between availability and affordability of inhaled corticosteroid-containing inhalers and socioeconomic status of the LMIC. Inhaled corticosteroid–formoterol is the core component of GINA track I recommendations across all steps of treatment (anti-inflammatory reliever and

MART); therefore, the low availability and affordability of this therapy is a source of great concern.[111,143] Basic effective initial treatment with the use of inhaled corticosteroid is key to the delivery of affordable asthma care and the minimisation of treatment-related adverse effects, including adverse effects associated with systemic corticosteroids. Use of oral corticosteroids for the management of asthma outside exacerbations is strongly discouraged due to their high toxicity and low efficacy.

Other atopic conditions, such as allergic rhinitis and food allergies, are increasing in prevalence in LMICs, with increasing severity of reported symptoms in these settings.[144] Allergic rhinitis is a condition commonly treated in primary care in high-income settings; over-the-counter medications, such as oral antihistamines and intra-nasal corticosteroids, are often used. However, the accessibility of these treatments in LMICs is unknown. It is recognised that in patients with allergic asthma, managing allergic rhinitis can improve asthma control by reducing inflammation.[143]

Since 2020, several publications and initiatives have sought to highlight the insufficient access to basic asthma care in low-resource settings (mainly in LMICs but also affecting underserved populations in high-income countries).[141,143–146] Infrastructure to support diagnosis and a secure supply of cost-effective drugs is often insufficient in LMICs which affects many people with chronic non-communicable lung diseases such as asthma.[147,148] GINA authors have set out the case for the widespread adoption of anti-inflammatory reliever and MART in LMICs.[143] The International Union Against Tuberculosis and Lung Disease led a consultation on improving access to affordable quality-assured inhaled medicines in LMICs and described some of the main challenges and suggestions for possible solutions.[149] GAN undertook a Delphi exercise to develop clinical standards for the management of asthma in low-resource LMIC settings, providing practical guidance for the reality facing clinicians in these settings, where at best only WHO essential medicines might be available.[145] In some LMICs, such as The Gambia, continued use of oral short-acting β-agonist therapy is affected by local beliefs about the harms of inhaled medicine. In 2024, GAN held an international symposium to build on the network's work over the last decade, including the Global Asthma Report 2022.[6] The symposium highlighted the need to improve access to affordable asthma medicines for all (figure 6).[146] Testimonies from children, adolescents, and adults with asthma were heard and summarised in a 2024 publication.[150]

WHO has a mandate to improve access to affordable asthma care as part of its non-communicable disease (NCD) agenda. The WHO Global Action Plan for the Prevention and Control of NCDs (2013–2030) includes a (voluntary) target of 80% availability of affordable essential medicines for NCDs, including asthma, in public and private health-care facilities.[151] Inhaled medicines for anti-inflammatory reliever and MART are included in the WHO Model List of Essential Medicines,[152] and are therefore covered by this target. Achieving this target is relevant to the attainment of the 2030 Sustainable Development Goal for health, including target 3.4 (NCD prevention and treatment) and target 3.8 (universal health coverage and access to essential medicines).[153]

Most of global burden of asthma morbidity and mortality discussed earlier in this paper could be overcome by improved access to and use of affordable inhaled medicines for anti-inflammatory, reliever therapy and MART. However, local beliefs about the effectiveness and addictive potential of inhaled medicines also need to be addressed. This effort requires highly effective and safe technology developed several

Panel 3: Areas of future research into improving the understanding of asthma

- Components of urbanisation that lead to increasing rates of asthma.
- Dietary determinants of asthma.
- The role of socioeconomic factors, obesity, physical inactivity, and sedentary lifestyle in asthma aetiology and management.
- Economics of accessible essential asthma medicines.
- Implementation strategies for improving access to evidence-based asthma care.
- Establishing and evaluating national asthma programmes.
- The pathophysiology and management of late-onset asthma.
- How biological therapies can be made affordable and accessible to all who would benefit from them.

The challenge is in conducting this work in countries that have the greatest mortality burden from asthma where the potential effect of the interventions is greatest.

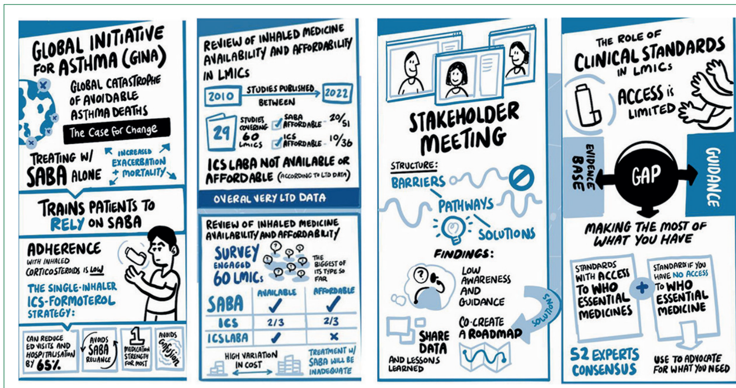

Figure 6: **Visual summary from the Global Asthma Network Symposium 2024**[146]
Adapted from the material of the Global Asthma Network Symposium 2024.

	Cost per patient in 1987 (€)	Total cost in 1987 (€)	Cost per patient in 2013 (€)	Total cost in 2013 (€)	Costs in 2013 as a proportion of cost in 1987 (%)
Hospitalisation	364	30 207 488	32	7 930 223	9%
Outpatient care	310	25 506 513	119	29 486 153	38%
Medication	409	33 984 973	394	97 569 000	96%
Total direct costs	1081	89 698 974	545	133 985 376	50%
Indirect costs	1589	131 907 761	226	55 939 337	14%
Total costs	2670	221 606 735	771	189 924 713	29%

The number of registered patients with asthma in 1987 was 83 000, and in 2013 the number was 247 583. Data from Haahtela and colleagues.[154]

Table 1: **Comparison of costs (€) due to asthma in Finland in 1987 and 2013**

	ICS–LABA (200/6 μg per dose)
Pharmacy	
Availability	31 (54%) of 57
Median cost per month's supply (US$)	19·2 (IQR 9·7–27·4)
Median days of work required*	4·1 (IQR 1·9–6·9)
Health-care facility	
Availability	21 (38%) of 56
Median cost per month's supply ($)	18·4 (IQR 11·3–24·5)
Median days of work required*	3·5 (IQR 1·5–6·1)
Central medical store	
Availability	9 (20%) of 46
Median cost per month's supply ($)	7·1 (IQR 3·9–8·1)
Median days of work required*	1·52 (IQR 0·7–2·6)

ICS=inhaled corticosteroid. LABA=long-acting β-agonist. Data from Stolbrink and colleagues.[155] *Days of work required for lowest-paid government worker to pay for one month's treatment.

Table 2: **Availability and costs ($US) of fICS–formoterol (200/6 μg per dose) in selected low-income and middle-income countries**

Search strategy and selection criteria

No formal literature search was done for this Series paper. Studies included were identified by the authors based on their knowledge of asthma. The studies included and referenced were selected by the authors up to the date of submission of the first draft of the manuscript (Aug 13, 2024), based on expert opinion, to provide a comprehensive review of each topic. There were no restrictions with regard to dates of publication.

decades ago to be made universally available to all patients who need it. A proactive movement that includes representation from people affected by asthma is needed to implement this strategy without further delay. The WHO-led Global Alliance Against Chronic Respiratory Diseases is well placed to help bring individuals and organisations together behind this cause. The UN General Assembly High-Level Meeting on the Prevention and Control of NCDs in 2025 is an opportunity to take some bold steps forward and should be prioritised by the UN member states.

Asthma treatment and management has greatly improved over the last decades, with substantial decreases in mortality and morbidity, aided by the continuing development and dissemination of international guidelines. Case studies, such as the Finnish Asthma Programme (1994–2004),[154] show that national programmes focusing on both risk factors (eg, tobacco smoking) and interventions to improve both assessment and management of asthma have led to a three-times increase in the number of patients diagnosed with asthma, increased treatment rates, and substantial cost reductions per person (table 1). Treatment costs per person decreased by 50% in this study, largely due to a fall in hospital and outpatient costs, and indirect costs decreased by 86%—a highly relevant decrease with important implications for patients in many LMICs, where medication costs come from out-of-pocket expenses.

Availability of the most appropriate treatment at an affordable price and widespread knowledge of best practices remain low. Table 2 shows results from a 2024 report from an international survey of LMICs,[155] including the median cost of a month's supply of inhaled corticosteroid-formoterol (200/6 μg) and the equivalent number of days' wages it would cost the lowest-paid government employee. The median cost in a central medical store was US$7·1 (equivalent to 1·5 days' wages), $18·4 in a health-care facility, (3·5 days' wages), and $19·2 in a pharmacy (4·1 days' wages). What could feasibly be achieved is given by what was achieved by 25% of outlets, which for pharmacies is less than $10 (2 days wages) for a month's supply. For working people, these costs are likely to be within reach given that 60% of workers with moderately severe uncontrolled asthma are likely to lose at least a day a week from work. However, only 54% of pharmacies, 38% of health-care facilities, and 20% of central medical stores held the medication. This rate is far short of the objective from the WHO Global Action Plan for the Prevention and Control of NCDs 2013–20 for 80% of pharmacies and health-care facilities to hold the most effective treatments at affordable prices.

Conclusions

Asthma and other allergic diseases are the most common chronic conditions of childhood and an important cause of disability in adult life. The number of individuals with asthma is likely to increase in the coming years due to the growing population, ageing, and increasing urbanisation.

Improved maternal and child health services could help to reduce the effect of premature delivery, low birthweight, and early respiratory infections. Control of tobacco consumption, prevention of obesity, measures to address physical inactivity, and strategies to control RSV including maternal and infant vaccines could also reduce the asthma burden.

Improving the understanding of asthma management by all stakeholders and increasing the availability (to at least 80% of pharmacies and health-care facilities) and affordability of the most effective treatments are achievable goals. Finding ways of further reducing treatment costs, particularly for children, individuals without paid employment, and other vulnerable groups, should be a further priority.

Contributors

All authors drafted the original paper, suggested revisions, and approved the final draft.

Declaration of interests

SMJ is funded by National Institute of Health Research as a clinical lecturer. JBS has received grants from Chiesi, GSK, Linde, and Novartis granted to Hospital Universitario de La Princesa; and participated in presentations, advisory committees, and consultancies for Air Liquide, Almirall, AstraZeneca, Boehringer Ingelheim, CHEST, Chiesi, Comité Nacional para la Prevención del Tabaquismo, European Respiratory Society, FTH, Gebro, Grifols, GSK, Institute for Health Metrics and Evaluation, Laminar Pharma, Linde, Lipopharma, Menarini, Mundipharma, Novartis, Organisation Mondiale de la Santé/WHO, Pfizer, ResApp, Research in Real Life, ROVI, Sociedad Española de Neumología y Cirugía Torácica, Seqirus, WHO Europe, Takeda, and Zambon. RM has received advisory board fees, grants, or speaker fees from AstraZeneca, GSK, Organon, and Sanofi. GD, NS, and PB declare no competing interests. KM has received advisory board fees, grants, and sponsorship from AstraZeneca and GSK relevant to the content of this paper. Editorial note: The Lancet Group takes a neutral position with respect to territorial claims in published maps.

References

1 Porsbjerg C, Melén E, Lehtimäki L, Shaw D. Asthma. *Lancet* 2023; **401:** 858–73.

2 Mosnaim G. Asthma in adults. *N Engl J Med* 2023; **389:** 1023–31.

3 Antó JM, Pearce N, Douwes J, et al. Why has epidemiology not (yet) succeeded in identifying the origin of the asthma epidemic? *Int J Epidemiol* 2023; **52:** 974–83.

4 Asher MI, Keil U, Anderson HR, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995; **8:** 483–91.

5 Beasley R, Keil UE, von Mutius E, Pearce N. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet 1*998; **351:** 1225–32.

6 The Global Asthma Network. The global asthma report 2022. *Int J Tuberc Lung Dis* 2022; **26** (suppl 1**):** 1–104.

7 Burney PG, Luczynska C, Chinn S, Jarvis D. The European Community Respiratory Health Survey. *Eur Respir J* 1994; **7:** 954–60.

8 Burney P, Chinn S, Jarvis D, Luczynska C, Lai E. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). *Eur Respir J* 1996; **9:** 687–95.

9 de Marco R, Accordini S, Marcon A, et al. Risk factors for chronic obstructive pulmonary disease in a European cohort of young adults. *Am J Respir Crit Care Med* 2011; **183:** 891–97.

10 Marcon A, Locatelli F, Dharmage SC, et al. The coexistence of asthma and COPD: risk factors, clinical history and lung function trajectories. *Eur Respir J* 2021; **58:** 2004656.

11 Ellwood P, Asher MI, Billo NE, et al. The Global Asthma Network rationale and methods for phase I global surveillance: prevalence, severity, management and risk factors. *Eur Respir J* 2017; **49:** 1601605.

12 García-Marcos L, Asher MI, Pearce N, et al. The burden of asthma, hay fever and eczema in children in 25 countries: GAN phase I study. *Eur Respir J* 2022; **60:** 2102866.

13 Mortimer K, Lesosky M, García-Marcos L, et al. The burden of asthma, hay fever and eczema in adults in 17 countries: GAN phase I study. *Eur Respir J* 2022; **60:** 2102865.

14 Pearce N, Sunyer J, Cheng S, et al. Comparison of asthma prevalence in the ISAAC and the ECRHS. ISAAC Steering Committee and the European Community Respiratory Health Survey. *Eur Respir J* 2000; **16:** 420–26.

15 van Schayck OC. Global strategies for reducing the burden from asthma. *Prim Care Respir J* 2013; **22**: 239–43.

16 Accordini S, Calciano L, Marcon A, et al. Incidence trends of airflow obstruction among European adults without asthma: a 20-year cohort study. *Sci Rep* 2020; **10:** 3452.

17 Jarvis D, Newson R, Janson C, et al. Prevalence of asthma-like symptoms with ageing. *Thorax* 2018; **73:** 37–48.

18 Magwenzi P, Rusakaniko S, Sibanda EN, Gumbo FZ. Challenges in the diagnosis of asthma in children, what are the solutions? A scoping review of 3 countries in sub-Saharan Africa. *Respir Res* 2022; **23**: 254.

19 Masekela R, Zurba L, Gray D. Dealing with access to spirometry in Africa: a commentary on challenges and solutions. *Int J Environ Res Public Health* 2018; **16:** 62.

20 Binegdie AB, Meme H, El Sony A, et al. Chronic respiratory disease in adult outpatients in three African countries: a cross-sectional study. *Int J Tuberc Lung Dis* 2022; **26:** 18–25.

21 Zar HJ, Ehrlich RI, Workman L, Weinberg EG. The changing prevalence of asthma, allergic rhinitis and atopic eczema in African adolescents from 1995 to 2002. *Pediatr Allergy Immunol* 2007; **18:** 560–65.

22 Kirenga BJ, Chakaya J, Yimer G, et al. The burden of severe asthma in sub-Saharan Africa: findings from the African Severe Asthma Project. *J Allergy Clin Immunol Glob* 2024; **3:** 100209.

23 Population Reference Bureau. African overview. https://www.prb.org/international/ (accessed Aug 17, 2021).

24 National Center for Health Statistics. 2022 NHIS adult summary health statistics. U.S. Department of Health and Human Services. 2023. https://catalog.data.gov/dataset/nhis-adult-summary-health-statistics-b5ce9 (accessed Feb 9, 2025).

25 Singh S, Salvi S, Mangal DK, et al. Prevalence, time trends and treatment practices of asthma in India: the Global Asthma Network study. *ERJ Open Res* 2022; **8:** 00528-2021.

26 Partridge MR, Alwan A. Prevention of asthma and approaches for enhanced care in the Eastern Mediterranean region. *Eastern Med Health J 1997;* **3:** 133–42.

27 Sony AE, Mohammad Y. Asthma in the eastern Mediterranean region. *Int J Tuberc Lung Dis* 2022; **26:** 48–55.

28 Speizer FE, Doll R, Heaf P. Observations on recent increase in mortality from asthma. *BMJ* 1968; **1:** 335–39.

29 Fok AO, Wong GW. What have we learnt from ISAAC phase III in the Asia-Pacific rim? *Curr Opin Allergy Clin Immunol* 2009; **9:** 116–22.

30 Thomsen SF. Genetics of asthma: an introduction for the clinician. *Eur Clin Respir J* 2015; **2:** 24643.

31 Demenais F, Margaritte-Jeannin P, Barnes KC, et al. Multiancestry association study identifies new asthma risk loci that colocalize with immune-cell enhancer marks. *Nat Genet* 2018; **50:** 42–53.

32 Ali FR. Does this patient have atopic asthma? *Clin Med* 2011; **11:** 376–80.

33 Holgate ST. Genetic and environmental interaction in allergy and asthma. *J Allergy Clin Immunol* 1999; **104:** 1139–46.

34 UN, Department of Economic and Social Affairs, Population Division. World urbanization prospects: the 2018 revision. 2019. https://www.un.org/en/desa/2018-revision-world-urbanization-prospects (accessed Feb 9, 2025).

35 Godfrey RC. Asthma and IgE levels in rural and urban communities of The Gambia. *Clin Allergy* 1975; **5:** 201–07.

36 Anderson HR. The epidemiological and allergic features of asthma in the New Guinea Highlands. *Clin Allergy* 1974; **4:** 171–83.

37 van Niekerk CH, Weinberg EG, Shore SC, et al. Prevalence of childhood asthma in Africa. *Lancet* 1977; **1:** 96–97.

38 Waite DA, Eyles EF, Tonkin SL, O'Donnell TV. Asthma prevalence in Tokelauan children in two environments. *Clin Allergy* 1980; **10:** 71–75.

39 Keeley DJ, Neill P, Gallivan S. Comparison of the prevalence of reversible airways obstruction in rural and urban Zimbabwean children. *Thorax* 1991; **46:** 549–53.

40 Merrett TG, Merrett J, Cookson JB. Allergy and parasites: the measurement of total and specific IgE levels in urban and rural communities in Rhodesia. *Clin Allergy* 1976; **6:** 131–34.

41 Perzanowski MS, Ng'ang'a LW, Carter MC, et al. Atopy, asthma, and antibodies to *Ascaris* among rural and urban children in Kenya. *J Pediatr* 2002; **140:** 582–88.

42 Calvert J, Burney P. *Ascaris*, atopy, and exercise-induced bronchoconstriction in rural and urban South African children. *J Allergy Clin Immunol* 2010; **125:** 100–05.e5.

43 Calvert J, Burney P. Effect of body mass on exercise-induced bronchospasm and atopy in African children. *J Allergy Clin Immunol* 2005; **116:** 773–79.

44 Hooper R, Calvert J, Thompson RL, Deetlefs ME, Burney P. Urban/rural differences in diet and atopy in South Africa. *Allergy* 2008; **63:** 425-31.

45 Weinmayr G, Weiland SK, Björkstén B, et al. Atopic sensitization and the international variation of asthma symptom prevalence in children. *Am J Respir Crit Care Med* 2007; **176:** 565–74.

46 Flohr C, Weiland SK, Weinmayr G, et al. The role of atopic sensitization in flexural eczema: findings from the International Study of Asthma and Allergies in Childhood phase two. *J Allergy Clin Immunol* 2008; **121:** 141–47.e4.

47 Büchele G, Genuneit J, Weinmayr G, et al. International variations in bronchial responsiveness in children: findings from ISAAC phase two. *Pediatr Pulmonol* 2010; **45:** 796–806.

48 von Mutius E, Martinez FD, Fritzsch C, Nicolai T, Roell G, Thiemann HH. Prevalence of asthma and atopy in two areas of West and East Germany. *Am J Respir Crit Care Med* 1994; **149:** 358–64.

49 Gassner M. Immunologisch-allergologische reaktionen unter veränderten umweltbedingungen. *Schweiz Rundsch Med Prax* 1992; **81:** 426–30.

50 Braun-Fahrländer C, Gassner M, Grize L, et al. Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community. *Clin Exp Allergy* 1999; **29:** 28–34.

51 Midodzi WK, Rowe BH, Majaesic CM, Senthilselvan A. Reduced risk of physician-diagnosed asthma among children dwelling in a farming environment. *Respirology* 2007; **12:** 692–99.

52 Strachan DP. Hay fever, hygiene, and household size. *BMJ* 1989; **299:** 1259–60.

53 von Mutius E. The microbial environment and its influence on asthma prevention in early life. *J Allergy Clin Immunol* 2016; **137:** 680–89.

54 Krämer U, Heinrich J, Wjst M, Wichmann HE. Age of entry to day nursery and allergy in later childhood. *Lancet* 1999; **353:** 450–54.

55 Svanes C, Jarvis D, Chinn S, Burney P. Childhood environment and adult atopy: results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1999; **103:** 415–20.

56 Svanes C, Jarvis D, Chinn S, Omenaas E, Gulsvik A, Burney P. Early exposure to children in family and day care as related to adult asthma and hay fever: results from the European Community Respiratory Health Survey. *Thorax* 2002; **57:** 945–50.

57 Woodcock A, Lowe LA, Murray CS, et al. Early life environmental control: effect on symptoms, sensitization, and lung function at age 3 years. *Am J Respir Crit Care Med* 2004; **170:** 433–39.

58 Calvert J, Burney P. Effect of body mass on exercise-induced bronchospasm and atopy in African children. *J Allergy Clin Immunol* 2005; **116:** 773–79.

59 Lack G, Fox D, Northstone K, Golding J. Factors associated with the development of peanut allergy in childhood. *N Engl J Med* 2003; **348:** 977–85.

60 Du Toit G, Katz Y, Sasieni P, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. *J Allergy Clin Immunol* 2008; **122:** 984–91.

61 Fox AT, Sasieni P, du Toit G, Syed H, Lack G. Household peanut consumption as a risk factor for the development of peanut allergy. *J Allergy Clin Immunol* 2009; **123:** 417–23.

62 Turner S, Prabhu N, Danielan P, et al. First- and second-trimester fetal size and asthma outcomes at age 10 years. *Am J Respir Crit Care Med* 2011; **184:** 407–13.

63 den Dekker HT, Jaddoe VWV, Reiss IK, de Jongste JC, Duijts L. Fetal and infant growth patterns and risk of lower lung function and asthma. The Generation R Study. *Am J Respir Crit Care Med* 2018; **197:** 183–92.

64 Håland G, Carlsen KC, Sandvik L, et al. Reduced lung function at birth and the risk of asthma at 10 years of age. *N Engl J Med* 2006; **355:** 1682–89.

65 Martinez FD, Morgan WJ, Wright AL, Holberg C, Taussig LM. Initial airway function is a risk factor for recurrent wheezing respiratory illnesses during the first three years of life. *Am Rev Respir Dis* 1991; **143:** 312–16.

66 Bisgaard H, Jensen SM, Bønnelykke K. Interaction between asthma and lung function growth in early life. *Am J Respir Crit Care Med* 2012; **185:** 1183–89.

67 Turner SW, Palmer LJ, Rye PJ, et al. The relationship between infant airway function, childhood airway responsiveness, and asthma. *Am J Respir Crit Care Med* 2004; **169:** 921–27.

68 Sonnenschein-van der Voort AMM, Arends LR, de Jongste JC, et al. Preterm birth, infant weight gain, and childhood asthma risk: a meta-analysis of 147,000 European children. *J Allergy Clin Immunol* 2014; **133:** 1317–29.

69 Been JV, Lugtenberg MJ, Smets E, et al. Preterm birth and childhood wheezing disorders: a systematic review and meta-analysis. *PLoS Med* 2014; **11:** e1001596.

70 Mebrahtu TF, Feltbower RGG, Greenwood DC, Parslow RC. Birth weight and childhood wheezing disorders: a systematic review and meta-analysis. *J Epidemiol Community Health* 2015; **69:** 500–08.

71 Meme H, Amukoye E, Bowyer C, et al. Preterm birth, birth weight, infant weight gain and their associations with childhood asthma and spirometry: a cross-sectional observational study in Nairobi, Kenya. *BMJ Open Respir Res* 2023; **10:** e001895.

72 WHO. WHO recommendations on antenatal care for a positive pregnancy experience. 2016. https://www.who.int/publications/i/item/9789241549912 (accessed Feb 9, 2025).

73 Khosa JK, Louie S, Lobo Moreno P, et al. Asthma care in the elderly: practical guidance and challenges for clinical management—a framework of 5 "Ps". *J Asthma Allergy* 2023; **16:** 33–43.

74 Hegendörfer E, Degryse JM. Breathlessness in older adults: what we know and what we still need to know. *J Am Geriatr Soc* 2023; **71:** 2082–95.

75 Safiri S, Karamzad N, Kaufman JS, et al. Prevalence, deaths and disability-adjusted-life-years (DALYs) due to type 2 diabetes and its attributable risk factors in 204 countries and territories, 1990–2019: results from the Global Burden of Disease Study 2019. *Front Endocrinol* 2022; **13:** 838027.

76 Lemanske RF Jr, Jackson DJ, Gangnon RE, et al. Rhinovirus illnesses during infancy predict subsequent childhood wheezing. *J Allergy Clin Immunol* 2005; **116:** 571–77.

77 Jackson DJ, Gangnon RE, Evans MD, et al. Wheezing rhinovirus illnesses in early life predict asthma development in high-risk children. *Am J Respir Crit Care Med* 2008; **178:** 667–72.

78 Guilbert TW, Singh AM, Danov Z, et al. Decreased lung function after preschool wheezing rhinovirus illnesses in children at risk to develop asthma. *J Allergy Clin Immunol* 2011; **128:** 532–38.

79 Gray DM, Turkovic L, Willemse L, et al. Lung function in African infants in the Drakenstein Child Health Study. Impact of lower respiratory tract illness. *Am J Respir Crit Care Med* 2017; **195:** 212–20.

80 Makrinioti H, Hasegawa K, Lakoumentas J, et al. The role of respiratory syncytial virus- and rhinovirus-induced bronchiolitis in recurrent wheeze and asthma—a systematic review and meta-analysis. *Pediatr Allergy Immunol* 2022; **33:** e13741.

81 Rosas-Salazar C, Chirkova T, Gebretsadik T, et al. Respiratory syncytial virus infection during infancy and asthma during childhood in the USA (INSPIRE): a population-based, prospective birth cohort study. *Lancet* 2023; **401:** 1669–80.

82 Anderson J, Do LAH, Wurzel D, et al. Severe respiratory syncytial virus disease in preterm infants: a case of innate immaturity. *Thorax* 2021; **76:** 942–50.

83 Quinn LA, Shields MD, Sinha I, Groves HE. Respiratory syncytial virus prophylaxis for prevention of recurrent childhood wheeze and asthma: a systematic review. *Syst Rev* 2020; **9:** 269.

84 WHO. Global report on trends in prevalence of tobacco use 2000–2030. 2024. https://www.un.org/en/desa/2018-revision-world-urbanization-prospects (accessed Feb 9, 2025).

85 Burke H, Leonardi-Bee J, Hashim A, et al. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. *Pediatrics* 2012; **129:** 735–44.

86 Li YF, Langholz B, Salam MT, Gilliland FD. Maternal and grandmaternal smoking patterns are associated with early childhood asthma. *Chest* 2005; **127:** 1232–41.

87 Magnus MC, Håberg SE, Karlstad Ø, et al. Grandmother's smoking when pregnant with the mother and asthma in the grandchild: the Norwegian Mother and Child Cohort Study. *Thorax* 2015; **70:** 237–43.

88 Devereux G, Barker RN, Seaton A. Antenatal determinants of neonatal immune responses to allergens. *Clin Exp Allergy* 2002; **32:** 43–50.

89 Hanrahan JP, Tager IB, Segal MR, et al. The effect of maternal smoking during pregnancy on early infant lung function. *Am Rev Respir Dis* 1992; **145:** 1129–35.

90 Kurihara C, Kuniyoshi KM, Rehan VK. Preterm birth, developmental smoke/nicotine exposure, and life-long pulmonary sequelae. *Children* 2023; **10**: 608.

91 Tattan-Birch H, Brown J, Shahab L, Beard E, Jackson SE. Trends in vaping and smoking following the rise of disposable e-cigarettes: a repeat cross-sectional study in England between 2016 and 2023. *Lancet Reg Health Eur* 2024; **42:** 100924.

92 Wang TW, Gentzke AS, Neff LJ, et al. Disposable e-cigarette use among U.S. youth—an emerging public health challenge. *N Engl J Med* 2021; **384:** 1573–76.

93 Li X, Zhang Y, Zhang R, Chen F, Shao L, Zhang L. Association between e-cigarettes and asthma in adolescents: a systematic review and meta-analysis. *Am J Prev Med* 2022; **62:** 953–60.

94 Thurston GD, Balmes JR, Garcia E, et al. Outdoor air pollution and new-onset airway disease. An Official American Thoracic Society workshop report. *Ann Am Thorac Soc* 2020; **17:** 387–98.

95 Royal College of Physicians. Every breath we take: the lifelong impact of air pollution. Report of a working party. 2016. https://www.rcplondon.ac.uk/projects/outputs/every-breath-we-take-lifelong-impact-air-pollution (accessed March 15, 2024).

96 Sicard P, Agathokleous E, Anenberg SC, et al. Trends in urban air pollution over the last two decades: a global perspective. *Sci Total Environ* 2023; **858:** 160064.

97 Li C, van Donkelaar A, Hammer MS, et al. Reversal of trends in global fine particulate matter air pollution. *Nat Commun* 2023; **14:** 5349.

98 Barber CM, Cullinan P, Feary J, et al. British Thoracic Society clinical statement on occupational asthma. *Thorax* 2022; **77:** 433–42.

99 Jeebhay MF, Quirce S. Occupational asthma in the developing and industrialised world: a review. *Int J Tuberc Lung Dis* 2007; **11:** 122–33.

100 Hoy R. Occupational asthma in developing countries requires further research. *Int J Tuberc Lung Dis* 2015; **19:** 372.

101 Health and Safety Executive. Substances that can cause occupational asthma. https://www.hse.gov.uk/asthma/substances.htm (accessed March 15, 2024).

102 WHO. Obesity and overweight. 2024. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight#:~:text=Worldwide (accessed March 15, 2024).

103 Egan KB, Ettinger AS, Bracken MB. Childhood body mass index and subsequent physician-diagnosed asthma: a systematic review and meta-analysis of prospective cohort studies. *BMC Pediatr* 2013; **13:** 121.

104 Parasuaraman G, Ayyasamy L, Aune D, et al. The association between body mass index, abdominal fatness, and weight change and the risk of adult asthma: a systematic review and meta-analysis of cohort studies. *Sci Rep* 2023; **13:** 7745.

105 Mosen DM, Schatz M, Magid DJ, Camargo CA Jr. The relationship between obesity and asthma severity and control in adults. *J Allergy Clin Immunol* 2008; **122:** 507–11.e6.

106 Thompson CA, Eslick SR, Berthon BS, Wood LG. Asthma medication use in obese and healthy weight asthma: systematic review/meta-analysis. *Eur Respir J* 2021; **57:** 2000612.

107 Chen Z, Salam MT, Alderete TL, et al. Effects of childhood asthma on the development of obesity among school-aged children. *Am J Respir Crit Care Med* 2017; **195:** 1181–88.

108 Baan EJ, de Roos EW, Engelkes M, et al. Characterization of asthma by age of onset: a multi-database cohort study. *J Allergy Clin Immunol Pract* 2022; **10:** 1825–34.e8.

109 Tooba R, Wu TD. Obesity and asthma: a focused review. *Respir Med* 2022; **204:** 107012.

110 van der Ploeg HP, Hillsdon M. Is sedentary behaviour just physical inactivity by another name? *Int J Behav Nutr Phys Act* 2017; **14:** 142.

111 Global Initiative for Asthma. Global strategy for asthma management and prevention, 2024. 2024. https://ginasthma.org/2024-report/ (accessed Feb 9, 2025).

112 Strain T, Flaxman S, Guthold R, et al. National, regional, and global trends in insufficient physical activity among adults from 2000 to 2022: a pooled analysis of 507 population-based surveys with 5·7 million participants. *Lancet Glob Health* 2024; **12:** e1232–43.

113 Guthold R, Stevens GA, Riley LM, Bull FC. Global trends in insufficient physical activity among adolescents: a pooled analysis of 298 population-based surveys with 1·6 million participants. *Lancet Child Adolesc Health* 2020; **4:** 23–35.

114 Shaaban R, Leynaert B, Soussan D, et al. Physical activity and bronchial hyperresponsiveness: European Community Respiratory Health Survey II. *Thorax* 2007; **62:** 403–10.

115 Xu M, Lodge CJ, Lowe AJ, et al. Are adults with asthma less physically active? A systematic review and meta-analysis. *J Asthma* 2021; **58:** 1426–43.

116 Huovinen E, Kaprio J, Koskenvuo M. Factors associated to lifestyle and risk of adult onset asthma. *Respir Med* 2003; **97:** 273–80.

117 Russell MA, Janson C, Real FG, et al. Physical activity and asthma: a longitudinal and multi-country study. *J Asthma* 2017; **54:** 938–45.

118 Bédard A, Carsin AE, Fuertes E, et al. Physical activity and lung function—cause or consequence? *PLoS One* 2020; **15:** e0237769.

119 Fuertes E, Carsin A-E, Antó JM, et al. Leisure-time vigorous physical activity is associated with better lung function: the prospective ECRHS study. *Thorax* 2018; **73:** 376–84.

120 Brumpton BM, Langhammer A, Ferreira MAR, Chen Y, Mai XM. Physical activity and incident asthma in adults: the HUNT Study, Norway. *BMJ Open* 2016; **6:** e013856.

121 Bédard A, Serra I, Dumas O, et al. Time-dependent associations between body composition, physical activity, and current asthma in women: a marginal structural modeling analysis. *Am J Epidemiol* 2017; **186:** 21–28.

122 Eijkemans M, Mommers M, Harskamp-van Ginkel MW, et al. Physical activity, sedentary behaviour, and childhood asthma: a European collaborative analysis. *BMJ Open Respir Res* 2024; **11:** e001630.

123 Cassim R, Dharmage SC, Koplin JJ, Milanzi E, Paro FM, Russell MA. Does physical activity strengthen lungs and protect against asthma in childhood? A systematic review. *Pediatr Allergy Immunol* 2019; **30:** 739–51.

124 Freeman AT, Staples KJ, Wilkinson TMA. Defining a role for exercise training in the management of asthma. *Eur Respir Rev* 2020; **29:** 190106.

125 Ordman D. An outbreak of bronchial asthma in South Africa, affecting more than 200 persons, caused by castor bean dust from an oil-processing factory. *Int Arch Allergy Appl Immunol* 1955; **7:** 10–24.

126 Antó JM, Sunyer J, Rodriguez-Roisin R, Suarez-Cervera M, Vazquez L. Community outbreaks of asthma associated with inhalation of soybean dust. *N Engl J Med* 1989; **320:** 1097–102.

127 Bellomo R, Gigliotti P, Treloar A, et al. Two consecutive thunderstorm associated epidemics of asthma in the city of Melbourne. The possible role of rye grass pollen. *Med J Aust* 1992; **156:** 834–37.

128 Targonski PV, Persky VW, Ramekrishnan V. Effect of environmental molds on risk of death from asthma during the pollen season. *J Allergy Clin Immunol* 1995; **95:** 955–61.

129 O'Hollaren MT, Yunginger JW, Offord KP, et al. Exposure to an aeroallergen as a possible precipitating factor in respiratory arrest in young patients with asthma. *N Engl J Med* 1991; **324:** 359–63.

130 Burney P, Amaral AFS. Air pollution and chronic airway disease: is the evidence always clear? *Lancet* 2019; **394:** 2198–200.

131 Zureik M, Neukirch C, Leynaert B, Liard R, Bousquet J, Neukirch F. Sensitisation to airborne moulds and severity of asthma: cross sectional study from European Community Respiratory Health Survey. *BMJ* 2002; **325:** 411–14.

132 Rosenstreich DL, Eggleston P, Kattan M, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med* 1997; **336:** 1356–63.

133 Crossingham I, Turner S, Ramakrishnan S, et al. Combination fixed-dose beta agonist and steroid inhaler as required for adults or children with mild asthma. *Cochrane Database Syst Rev* 2021; **5:** CD013518.

134 Bateman ED, Reddel HK, O'Byrne PM, et al. As-needed budesonide–formoterol versus maintenance budesonide in mild asthma. *N Engl J Med* 2018; **378:** 1877–87.

135 O'Byrne PM, FitzGerald JM, Bateman ED, et al. Inhaled combined budesonide–formoterol as needed in mild asthma. *N Engl J Med* 2018; **378:** 1865–76.

136 Menzies-Gow A, Bafadhel M, Busse WW, et al. An expert consensus framework for asthma remission as a treatment goal. *J Allergy Clin Immunol* 2020; **145:** 757–65.

137 Blaiss M, Oppenheimer J, Corbett M, et al. Consensus of an American College of Allergy, Asthma, and Immunology, American Academy of Allergy, Asthma, and Immunology, and American Thoracic Society workgroup on definition of clinical remission in asthma on treatment. *Ann Allergy Asthma Immunol* 2023; **131:** 782–85.

138 García-Marcos L, Chiang CY, Asher MI, et al. Asthma management and control in children, adolescents, and adults in 25 countries: a Global Asthma Network phase I cross-sectional study. *Lancet Glob Health* 2023; **11:** e218–28.

139 Plum C, Stolbrink M, Zurba L, Bissell K, Ozoh BO, Mortimer K. Availability of diagnostic services and essential medicines for non-communicable respiratory diseases in African countries. *Int J Tuberc Lung Dis* 2021; **25:** 120–25.

140 Meghji J, Mortimer K, Agusti A, et al. Improving lung health in low-income and middle-income countries: from challenges to solutions. *Lancet* 2021; **397:** 928–40.

141 Stolbrink M, Thomson H, Hadfield RM, et al. The availability, cost, and affordability of essential medicines for asthma and COPD in low-income and middle-income countries: a systematic review. *Lancet Glob Health* 2022; **10:** e1423–42.

142 Ellwood P, Ellwood E, Rutter C, et al. Global Asthma Network phase I surveillance: geographical coverage and response rates. *J Clin Med* 2020; **9:** 3688.

143 Mortimer K, Reddel HK, Pitrez PM, Bateman ED. Asthma management in low and middle income countries: case for change. *Eur Respir J* 2022; **60:** 2103179.

144 Aït-Khaled N, Pearce N, Anderson HR, Ellwood P, Montefort S, Shah J. Global map of the prevalence of symptoms of rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC) phase three. *Allergy* 2009; **64:** 123–48.

145 Jayasooriya S, Stolbrink M, Khoo EM, et al. Clinical standards for the diagnosis and management of asthma in low- and middle-income countries. *Int J Tuberc Lung Dis* 2023; **27:** 658–67.

146 The Global Asthma Network. Global Asthma Network Symposium 2024. 2024. http://globalasthmanetwork.org/advocacy/symposium2024.php (accessed Feb 9, 2025).

147 Beran D, Zar HJ, Perrin C, Menezes AM, Burney P. Burden of asthma and chronic obstructive pulmonary disease and access to essential medicines in low-income and middle-income countries. *Lancet Respir Med* 2015; **3:** 159–70.

148 Burney P, Potts J, Aït-Khaled N, et al. A multinational study of treatment failures in asthma management. *Int J Tuberc Lung Dis* 2008; **12:** 13–18.

149 Stolbrink M, Chinouya MJ, Jayasooriya S, et al. Improving access to affordable quality-assured inhaled medicines in low- and middle-income countries. *Int J Tuberc Lung Dis* 2022; **26:** 1023–32.

150 Mortimer K, Kurtulus S, Yorgancıoğlu A, et al. Living with asthma in low- and middle-income countries in the six WHO Regions. *NEJM Evid* 2024; **3:** p2300292.

151 WHO. Global action plan for the prevention and control of noncommunicable diseases 2013–2020. 2013. https://www.who.int/publications/i/item/9789241506236 (accessed Feb 9, 2025).

152 WHO. WHO model list of essential medicines—23rd list, 2023. https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.02 (accessed Feb 9, 2025).

153 UN. Transforming our world: the 2030 Agenda for Sustainable Development, Department of Economic and Social Affairs. 2024. https://sdgs.un.org/2030agenda.2024 (accessed Feb 9, 2025).

154 Haahtela T, Herse F, Karjalainen J, et al. The Finnish experience to save asthma costs by improving care in 1987–2013. *J Allergy Clin Immunol* 2017; **139:** 408–14.e2.

155 Stolbrink M, Ozoh OB, Halpin DMG, et al. Availability, cost and affordability of essential medicines for chronic respiratory diseases in low-income and middle-income countries: a cross-sectional study. *Thorax* 2024; **79:** 676–79.