

Is the Asthma Epidemic Still Ascending?

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KEYWORDS

• Asthma • Prevalence • Evolution • Air pollution • Passive smoking • Hygiene hypothesis • Lifestyle

KEY POINTS

- Asthma is one of the most prevalent chronic conditions affecting, approximately 300 million people worldwide, up to 1 in 10 adults and 1 in 3 children in some countries.
- Asthma is a complex disease that it still not fully understood. The type of asthma definition adopted has influenced knowledge about asthma distribution and etiology.
- In the case of asthma prevalence, accurate estimation has been hindered by varying definitions of asthma and methods of data collection, each combining to make data comparison across studies difficult, with the exception of International Study of Asthma and Allergy in Childhood and European Community Respiratory Health Survey, which unfortunately have not used biologic and clinical markers of the disease.
- Although treatment for asthma has improved substantially, the prevalence of asthma continues to increase, particularly in low and middle income countries, or in some ethnic groups in which prevalence was previously low.
- Observed spatio-temporal variations in the increased prevalence of asthma depend on exposure to environmental factors such as allergens (because of new conditions of exposure).

INTRODUCTION

Asthma is a phenotypically heterogeneous disorder of multifactorial origins resulting from complex interactions between genetic and environmental determinants. So far, several genes and environmental factors have been associated with an increased risk of developing asthma and may play a major role in asthma susceptibility. Evidence is strong for an increased risk of asthma associated with allergenic exposure, respiratory infections, air pollutants, tobacco smoke, and allergic rhinitis (AR).

Asthma is considered as a major public health problem in most countries, regardless of their level of development. According to the World Health

Organization (WHO), globally there are at least 300 million people suffering from asthma and more than 250,000 asthma-related deaths each year.¹ In the United States, the annual cost of asthma is estimated to be nearly \$18 billion. Direct costs account for nearly \$10 billion (hospitalizations are the single largest portion of direct cost), and indirect costs account for \$8 billion (lost earnings due to illness or death). This is the consequence of marked changes in asthma distribution and burden observed in the past decades. Asthma prevalence has been increasing since the early 1980s across all age, sex, and racial groups. Moreover, the asthma mortality rate has risen in some ethnic groups (African Americans in the United States) and individuals age 85 years and

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older. This increase is of particular concern, because it comes at a time when mortality rates from most natural causes are on the decline in several countries and because asthma death is in principle avoidable. Rising numbers and rates of asthma-related hospitalizations, especially in children and in some ethnic groups (African Americans in the United States) are also alarming.

Despite the growing understanding of asthma pathophysiology, much remains to be learned about the exact causes responsible for asthma development and the ways to prevent this condition. This article reviews data on asthma prevalence trends and associated risk factors in the past decades, with emphasis on childhood asthma for which data are more abundant and for which misclassification is reduced. Important unanswered research questions are raised to explain the observed trends, and suggestions for future research are provided.

IN SEARCH OF AN ASTHMA DEFINITION

Asthma is characterized by varying degrees of allergic responses, airflow obstruction, and airway inflammation causing a range of symptoms including cough, wheezing, chest tightness, and shortness of breath. In spite of this diversity, the definitions that have been applied at the population level to count the number of asthmatics and follow its progression have been based uniquely on asthma-like symptoms and diagnosis. To date, most population-based studies have used self-administered questionnaires on symptoms to distinguish between asthmatic and nonasthmatic subjects. Indeed, this method represents clear advantages in terms of cost, convenience, and the resulting optimization of sample sizes and response rates. Most studies of asthma in children are based on the definitions of asthma (a doctor's diagnosis of asthma ever) and asthma-like symptoms based on the International Study of Asthma and Allergy in Childhood (ISAAC) validated questionnaire.² The epidemiologic study of asthma in adults presents additional difficulties, which include the duration of the disease, the type/duration of treatment, occupational exposure, environmental exposure, smoking, and comorbidities. Worldwide epidemiologic surveys on adult asthma have been mainly performed using the European Community Respiratory Health Survey (ECRHS) questionnaire, conceived to standardize the epidemiologic investigation of asthma and allergies in adults. Although standardized questionnaires allow prevalence comparisons and assessment of trends across studies worldwide, these symptom questionnaires have potential

issues arising from subjective symptom recognition and because they are dependent on the interpretation and judgment of the person responding to the questionnaire.³ Recently this problem has been overcome by the introduction of asthma phenotypes or endotypes based on several entities of the diseases.⁴

SPATIAL AND TEMPORAL DISTRIBUTION OF ASTHMA PREVALENCE AND RISK FACTORS

Spatial Distribution

Thanks to the multicentric epidemiologic studies based on the use of standardized and validated questionnaires and tools, an increasing amount of comparable data on asthma is available worldwide. The most up-to-date prevalence rates of childhood asthma worldwide can be obtained from the ISAAC study,⁵ conducted in representative samples of adolescents aged 13 to 14 years old in 56 countries, and the ECRHS study,⁶ conducted in representative samples of adults aged 20 to 44 years in 25 countries (mostly in Europe). Results show a great disparity in the prevalence of asthma across the world, between countries and within countries, with a trend toward more developed and westernized countries having higher rates of asthma,⁵ with as high as a 20- to 60-fold difference. Asthma symptoms were most prevalent (as much as 20%) in the United Kingdom, Australia, New Zealand, and Republic of Ireland; they were lowest (as low as 2%–3%) in Eastern Europe, Indonesia, Taiwan, Greece, Uzbekistan, India, and Ethiopia. Among European countries, the United Kingdom had the highest current prevalence of self-reported asthma symptoms among children aged 13 to 14 years, higher than other comparable European countries, such as Germany (ranked 19th) and France (ranked 20th). In Europe, the lowest prevalence of wheeze or asthma was reported in what was previously East Germany, and in Eastern countries such as Albania, indicating the possibility that the Western lifestyle may be involved. Similar geographic variations in wheezing prevalence were observed in the last 12 months among children aged 6 to 7 years old surveyed in 28 of the 56 countries of the study. Asthma symptoms were more common in boys than girls. The comparison between the ISAAC and ECRHS study in the countries where this was possible showed a good overall agreement for the distribution of wheezing and asthma prevalence between the 2 surveys, with higher figures for both adults wheezing and asthma in English-speaking countries. Globally, there is more asthma in countries with Western lifestyle compared with others. Geographic variations in asthma

prevalence certainly depend on variations in environmental risk factors. They may also in part reflect international differences in health care systems, as well as more specific differences in asthma recognition and diagnosis.

Temporal Distribution

The investigation of the sequential trends of asthma prevalence has been made possible through epidemiologic population-based studies, which employed the same methodology in similar samples, at different periods. It seems now established that the number of asthmatics, after having almost doubled over the last 30 to 40 years, might have reached a plateau in countries where asthma prevalence is the most important. However, recent data from the United States indicate a new increase in asthma prevalence.

Increase of asthma prevalence

Over the last decades, the increase in asthma prevalence has been well documented in several studies. Among them, two epidemiological studies of the Midspan Family Study Surveys were performed 20 years apart and used the same methods. They compared the prevalence of asthma in 1,708 parents and 1,124 offspring in the Renfrew and Paisley area of Scotland. At the time of assessment (1972–1976 and 1996), both populations were aged 45–54 years. The prevalence of asthma had more than doubled from 3% to 8.2% in the 20 years of survey, which was strictly independent of the genetic background because of the familial design of the study in pairs of the same sex. At least a doubling of the prevalence of asthma has also been reported in centers in Nordic countries, such as Finland and Sweden among both children⁷ and adults.^{8,9} A study undertaken by the Union Chimique Belge Institute of Allergy in Belgium concluded that the prevalence of asthma in Western Europe has doubled in the last 10 years.¹⁰ In a population-based Swedish study performed in subjects followed for 10 years, the cumulative incidence of asthma was of 3.4% among men and 4.5% among women. In addition, the incidence of asthma was higher in children than in adults (1.1% and 0.8% per year). Similarly, 25 years ago, the incidence of asthma was 2% in the Swiss population; the incidence has increased and is currently 8%.¹¹

Worldwide, rates of asthma also as assessed using national statistics and surveys have increased significantly between the 1960s and 2008.^{12,13} Some 9% of US children had asthma in 2001, compared with just 3.6% in 1980. In the United States, data from several national surveys reveal the age-adjusted prevalence of asthma

increased from 7.3 to 8.2% during the years 2001 through 2009.¹⁴ WHO reports that 10% of the Swiss population suffers from asthma today (WHO, 2007), compared with just 2% 25 to 30 years ago. In France, 4.15 million people suffered from asthma in 2006 while 3.5 million had suffered in 1998).¹⁵

To sum up, asthma patterns vary throughout the world and considerable increases in the prevalence of asthma have occurred globally over recent decades.^{16–18}

Stagnation or decrease of asthma prevalence

Nevertheless, the last comparison of data from phases 1 and 3 of ISAAC conducted according to the same standardized methodology suggests a stagnation of asthma prevalence in children living in high-income countries, where the prevalence of asthma was already very high (**Fig. 1, Table 1**). This is consistent with von Hertzen's and Haahtela's review of reviewed studies on time trends in asthma prevalence, published between 2000 and 2004.¹⁹ Of the 20 identified investigations, 13 revealed a decreasing or stable trend for asthma or current wheeze at any time during the study period, both in adults and children. It has been emphasized in several European countries and elsewhere (eg, Australia, United States), that the rising trends in asthma prevalence among adults may have reached a plateau or may even be decreasing, following a steady increase for the past decades. In one study,²⁰ wheezing increased in the older children and decreased in the younger age group, and in another study,²¹ the prevalence of asthma increased, whereas wheezing decreased. The authors suggest that in affluent Westernized societies, the increasing trend in asthma in adults and adolescents may have plateaued or even reversed, while the situation is more ambiguous in younger children.

The fact that the prevalence of allergic rhinitis and eczema is still increasing worldwide in all classes of age suggests a separation in the course of asthma and allergic asthma, which has not been investigated so far.²

The proportion of asthma attributable to atopy in children has been estimated to be 38%, but there is significant variation between studies, ranging from 25 to 63%.²² In the ISAAC phase 2 study, it has been reported that the population fraction of asthma attributable to atopy differed greatly between countries according to economic growth, being 40.7% in study centers from high-income countries and 20.3% in centers from low-income countries.²³ A nonatopic phenotype was the most common presentation of childhood asthma in low-income populations.^{23–25}

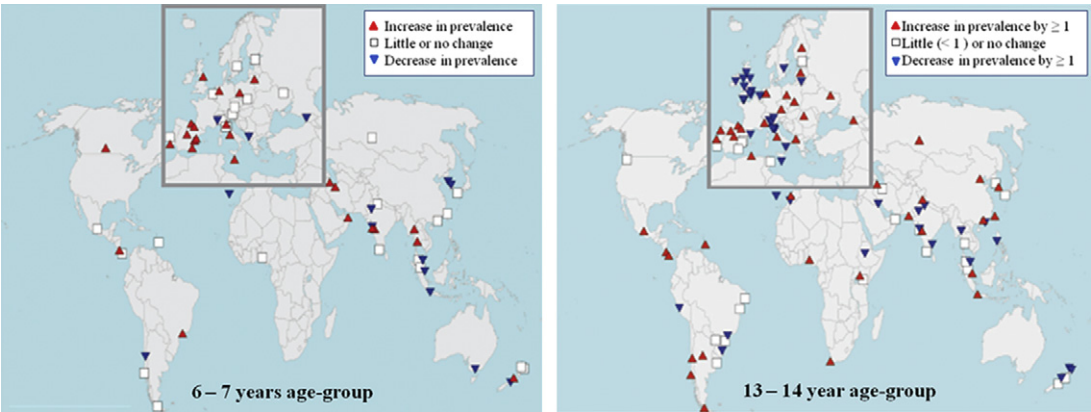


Fig. 1. World map showing direction of change in prevalence of asthma symptoms for 6- to 7-year age group and 13- to 14-year age group, on a follow-up period of 7 years (ISAAC phase 1 to phase 3). Each symbol represents a center. (From Asher MI, Montefort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 2006;368:733; with permission.)

Table 1 Direction of change in prevalence of childhood asthma for 6- to 7-year age group and 13- to 14-year age group, on a follow-up period of 7 years (ISAAC phase 1 to phase 3).			
Region	Asthma Symptoms		
	Increase	Decrease	Little or No Change
6 to 7-years age group			
English-speaking Africa	0	0	1
Asia-Pacific	2	5	5
Eastern Mediterranean	4	0	0
Indian subcontinent	2	2	2
Latin America	2	1	4
North America	1	0	1
Northern and eastern Europe	2	2	5
Oceania	1	2	2
Western Europe	11	2	7
Total	25	14	27
13- to 14-year age group			
Africa (English and French-speaking)	5	2	2
Asia-Pacific	6	4	5
Eastern Mediterranean	2	2	2
Indian subcontinent	2	4	2
Latin America	7	3	5
North America	1	0	1
Northern and eastern Europe	9	2	1
Oceania	0	3	2
Western Europe	10	20	4
Total	42	40	24

From Asher MI, Montefort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 2006;368:733; with permission.

All together these findings indicate that international differences in asthma symptom prevalence have reduced, particularly in the 13- to 14-year age group, with decreases in prevalence in English-speaking countries and Western Europe and increases in prevalence in regions where prevalence was previously low. In addition, these findings suggest that, although asthma symptom prevalence is no longer increasing in most English-speaking and Western European countries, its global burden may continue to rise.²⁶

Recent trends

Recently, the US Centers for Diseases Control and Prevention (CDC) reported that asthma prevalence increased from 7.3% in 2001 to 8.4% in 2010, when 25.7 million persons had asthma, and prevalence is now at its highest level in the United States. For the period 2008 to 2010, asthma prevalence was higher among children than adults, and among multiple-race, black, and American Indian or Alaska Native persons than white persons. People of multiple races had an incidence of 14.1%, while Asians had the lowest incidence (5.2%). Blacks had an incidence of 11.2%, while whites had an incidence of 7.7%. Hispanics of Puerto Rican descent had the highest prevalence, 16.1%. Children (9.5%) having a higher asthma prevalence than adults (7.7%) suggests that the disease will become a greater problem in the future. From 2001 to 2009, health care visits for asthma per 100 persons with asthma declined in

primary care settings, while asthma emergency department (ED) visits and hospitalization rates were stable. For the period 2007 to 2009, black persons had higher rates for asthma ED visits and hospitalizations per 100 persons with asthma than white persons, and a higher asthma death rate per 1000 persons with asthma. Compared with adults, children had higher rates for asthma primary care and ED visits, similar hospitalization rates, and lower death rates. Obesity, which has increased dramatically in the United States in the past decades could explain the rise in asthma prevalence because of the well-known relationship between obesity and asthma. In this respect, it would be interesting to stratify the prevalence of asthma according to body mass index (BMI).

FACTORS RESPONSIBLE FOR TRENDS IN ASTHMA PREVALENCE

Factor Explaining Asthma Increase

Because the rise of asthma prevalence has been far too rapid to implicate any genetic basis for change and because of the great disparities in asthma prevalence and severity of the disease on a worldwide scale and between individuals with similar genetic background and living in different environments, the intervention of environmental and lifestyle factors that have shown marked changes in the past decades has been evoked for the asthma prevalence increase, among which the ones related to the so-called hygiene hypothesis (Table 2).¹⁶

Table 2
Factors responsible for increase or stagnation in asthma prevalence

Factors Responsible for an Increase	Factors Responsible for a Stagnation in High-Income Countries
Environmental factors • Allergens (because of new exposure conditions) • Parental smoking, since in utero life • Outdoor and indoor air pollution • Excess of hygiene • Diet • Stress Increased host susceptibility • Excess of hygiene • Decreased number of miscarriages and perinatal morbimortality • In utero events (maternal hormone and medication intake during pregnancy, fetal distress...)^a • Prematurity, low birth weight • Diet • Stress	• Cohort effect: Western lifestyle more efficient in the 1960s than since the 2000s^a • Efficiency of asthma treatments, resulting in a decrease of consultations for asthma and asthma prevalence^a • Increased professional awareness of the disease^a • No more people susceptible to develop asthma because of environmental influences (of the past decades)^a

^a Few or no data.

Environmental factors initially proposed to explain the increased global prevalence of asthma include increased prevalence of maternal smoking,^{27,28} increased air pollution,^{29,30} changed diet,^{31–34} and stress.³⁵

Passive smoking

Building upon previous findings from 79 prospective studies, a recent meta-analysis showed that exposure to passive smoking increases the incidence of wheeze and asthma in children and young people by at least 20% and that preventing parental smoking is crucially important to the prevention of asthma.³⁶ Exposure to pre- or post-natal passive smoke exposure was associated with a 30% to 70% increased risk of incident wheezing (strongest effect from postnatal maternal smoking on wheeze in children aged 2 years or younger, odds ratio [OR] = 1.70, 95% confidence interval [CI] = 1.24–2.35, 4 studies) and a 21% to 85% increase in incident asthma (strongest effect from prenatal maternal smoking on asthma in children aged 2 years or younger, OR = 1.85, 95% CI = 1.35–2.53, 5 studies).

Outdoor and indoor air pollution

Whereas it is well established that short-term exposure to air pollution is related to an increase in asthma hospitalization, visits and medication, data on the causal role of chemical air pollution in the development of asthma are considered by some authors as still insufficient. Long-term exposure to ozone may increase the prevalence of asthma and asthmatic symptoms.^{37–39} Long-term exposure to outdoor residential nitrogen dioxide (NO₂) was associated with a history of doctor-diagnosed asthma in children in the 6 Cities Study⁴⁰ and adults in the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults study.⁴¹ A Japanese cohort study also reported an association between NO₂ levels and asthma incidence.⁴² In contrast, a Norwegian study found no association between modeled NO₂ exposure at the birth address and doctor-diagnosed asthma in a large cohort of children.⁴³ There is evidence that living near high-traffic roads is associated with asthma (<http://www.healtheffects.org/>). First, McConnell and colleagues³⁸ observed that the incidence of new diagnoses of asthma in children is associated with physical exercise in areas with high concentrations of ozone and particulate matter. Since then, other prospective cohort studies have indicated that long-term exposure to traffic pollution could contribute to the development of asthma-like symptoms and allergic sensitization in children.⁴⁴ In the French Etude des Déterminants

pré et post-natal du développement et de la santé de l'Enfant birth cohort (<http://eden.vjf.inserm.fr/>), it was found that among modifiable environmental exposures, the impact of traffic-related air pollution was greater than that of passive smoking and molds.⁴⁵

Fewer data concern exposure to indoor air and asthma. The most consistent finding for asthma induction in childhood is related as previously said to exposure to environmental tobacco smoke and to living in homes close to busy roads, and to exposure to dampness. In the case of measurement-based exposure assessments of chemical air pollutants, relationships have been found between fine particulate matter and several volatile organic compounds (VOCs).⁴⁶ Evident dampness or mold has consistent positive associations with asthma.⁴⁷ However, limited associations exist in the case of measured microbiologic agents or microbial VOCs as objective assessments of mold contamination.⁴⁸ These findings are critical, because indoor exposure to air pollutants has been assessed only for short periods. No robust data exist on temporal trends of aeroallergens, well-known risk factors of asthma and allergies, although individual exposure in indoor settings has been modified by modern lifestyle. The upsurge in the prevalence of allergies is observed as societies become more affluent and urbanized. In many low-income and middle-income countries, including rural areas in India, people rely on solid fuel (wood, cow dung, or crop residues) that they burn in simple stoves or open fires for domestic energy.⁴⁹ Secondhand smoke has become more common as parents become affluent enough to buy cigarettes. Together, these factors generate indoor air pollution that is estimated to be as much as 5 times as severe in poor countries as in rich ones.⁵⁰

Climate change

Climate change provides an additional plausible explanation for both increasing asthma susceptibility and increasing severity observed over several decades.⁵¹ There are many types of asthma, and climate change may explain the component of the increase that is allergic asthma, particularly pollen-induced asthma. Indeed climate change significantly affects plant distribution and pollination, as well as mold proliferation. This is likely to be a significant proportion of asthma cases. For example, Grossman⁵² suggests that up to 78% of people with asthma also suffer from allergic rhinitis. Furthermore, although the hypothesis that trends in air pollution have been major determinants for the rise in prevalence of asthma and allergic disease in recent decades is now generally disproved,^{53,54} air pollution is likely to have its own effects on pollen

production.⁵⁵ Moreover, climate change, change in ambient temperatures, and changes in weather during pollen seasons can cause both biologic and chemical changes to pollens and have direct adverse consequences on human health by inducing disease exacerbations, especially in urban and polluted regions.

Diet

In the past 2 decades, increasing evidence has suggested that modern diets may contribute to the increase in the prevalence of asthma.⁵⁶ Modern diets in most westernized countries differ considerably from those of previous generations, in which asthma prevalence was lower. In contrast with traditional diets, which mainly consist of locally produced, fresh, seasonal and less processed food, modern diets predominantly consist of processed foods that have been modified, stored, and transported over long distances. In addition, because of changes in agricultural techniques and increased storage and transportation, nutritional content has changed. For example, it was reported that mineral content of vegetables, fruit, and meat has declined.⁵⁷ From the supplementation point of view, the available epidemiologic evidence is weak but nonetheless supportive with respect to the association between deficiencies of the nutrients selenium; zinc; vitamins A, C, D, and E and low fruit and vegetable intake and the development of asthma and allergic disorders as shown by a recent meta-analysis.⁵⁸ In addition, a Mediterranean diet has been proposed for the prevention of asthma. Experimental studies of these exposures, randomized-controlled trials in particular, are warranted.

Stress

Stress is also considered to affect the expression of asthma and thus its prevalence through multidimensional endocrine, neural, immune, and behavioral processes. There is observational evidence that severe negative life events may increase the risk of children's asthma attacks over subsequent weeks³⁵ and may be associated with asthma symptoms among adolescents.⁵⁹ The association between stressful life events and an increased risk of asthma has also been reported in retrospective studies^{60–62} and in at least one prospective study⁶³ among adults.

Hygiene hypothesis

Further potential explanatory factors of the increase in asthma prevalence come under the hygiene hypothesis, which proposes that greater risk of atopy results from altered challenges to the immune system in early life, particularly reduced infections, and the consequent development of a bias toward

T-helper type 2 immune response over T-helper type 1.⁶⁴ Specific factors proposed under the hygiene hypothesis include changed immunization practices,^{65,66} changed living conditions and increased exposure to indoor allergens,⁶⁷ increased use of antibiotics,^{68–70} and reduced exposure to endotoxins.^{71–73} Furthermore, studies examining the hygiene hypothesis have not been entirely consistent, with some showing no effects of these exposures on subsequent development of asthma.⁷⁴ Inconsistencies may result from different social trends that alter exposures in more than one direction. Although the hygiene hypothesis has been proposed as one explanation for the increases in symptom prevalence, it does not appear entirely to account for the time trends, since the increases have occurred for both nonatopic (noneosinophilic) and atopic (eosinophilic) asthma, whereas the hygiene hypothesis would only explain trends for atopic asthma.⁷⁵ The hygiene hypothesis is also unlikely to explain the considerably higher prevalence of asthma in many Latin American countries and in US inner cities, which are more consistent with changes in environmental exposures other than hygiene.^{24,76,77} Although some trends may have reduced potentially protective exposures (increased urbanization, reduced family size, and increased maternal work stress during pregnancy), others (eg, greater use of formal child care) may increase the protective exposures. However, it is well established that respiratory infections are a risk factor for asthma exacerbations.

Other factors

Among the most recent factors proposed to explain asthma increase, there is the use of paracetamol during pregnancy, which has been associated with an increased risk of childhood asthma with a pooled OR for the risk of current wheeze in the children of women who were exposed to any paracetamol during any stage of pregnancy of 1.21 (95% CI 1.02–1.44).⁷⁸ This is consistent with the fact that asthma increase is paralleled by aspirin decrease. However, other studies are needed to better estimate this risk.

Host susceptibility

It has also been suggested that the increase in asthma could be due to a more susceptible population in the past decades (see **Table 2**). Susceptibility would have increased as the result of early life events. Indeed, there is epidemiologic evidence for multiple prenatal factors impacting early life respiratory morbidity.^{79,80} In utero exposures including tobacco smoke exposure, dietary exposures including vitamin D, and prenatal infections and exposure to microbial products may modulate

both atopy and respiratory disease. In addition, there is recent evidence that in utero exposures can affect the children's health through its impact on the newborn's immune system.⁸¹

Similarly, there exists significant association between asthma and the caesarean sections and other prenatal events such as the decreased number of miscarriages and prematurity and low birth weight.⁸² Diet and stress could also contribute to individual susceptibility. The mechanisms of action of these factors need further investigation and may act via various pathways, including effects on lung development, allergic and nonallergic inflammation, and airway remodeling. It remains to be determined also if some of these early life factors that predispose to wheezing will all translate into increased risk of asthma. Indeed several studies have shown the existence of nontransient wheezing in early life.

Factor Explaining Asthma Prevalence Stagnation

Just as it is not known why prevalence has increased since the 1950s so far, it is not known why prevalence should now be decreasing.²¹ The latest data on temporal trends in the prevalence of asthma are in favor of stagnation or decrease of the number of asthmatics in high-income countries due to the cessation of environmental influences. Perhaps the most striking finding is the apparent decline in symptom prevalence in English-speaking countries. This contrasts with the hygiene hypothesis, as it does not seem apparent that the English-speaking language countries have become less hygienic in recent decades, although increases in infant and childhood infections could have occurred due to specific factors such as increased use of childcare facilities.⁸³ Other established asthma risk factors do not appear to explain the worldwide asthma prevalence patterns^{31,70,84–86} or time trends, particularly the decline in English-speaking countries. It also seems unlikely that the decline in symptom prevalence is due to decreased recognition and labeling of asthma symptoms, given that the prevalence of asthma ever has increased. This could explain why, in some countries, symptom prevalence has not increased or has even declined, but the prevalence of asthma ever has increased. It should also be noted that the findings for asthma ever are to some extent reassuring with regard to the findings for current asthma symptoms, since they indicate that increased recognition and diagnosis of asthma have not been accompanied by an increase in reporting of asthma symptoms; such an increase would have been expected if the symptom

prevalence patterns were entirely due to differences in recognition and labeling of symptoms. Further results of population-based studies showed a stagnation of asthma prevalence combined with an increase in the use of inhaled corticosteroids (ICs) in industrialized countries.⁸⁷ Although the use of IC may explain the reduction of asthma-related symptoms and hospitalizations, it only influences the decrease in asthma prevalence to a negligible extent. Moreover, we observed a decline in the prevalence of allergic rhinitis and emphysema, for which ICs are not prescribed.

One plausible hypothesis that may explain this decrease is that genetic potential could not be further expressed in the absence of important environmental changes, as observed in industrialized countries (see **Table 2**). Indeed, environmental influences may have reached their maximum expression in inducing disease in susceptible individuals. However, it remains difficult to assess the validity of this hypothesis from the epidemiologic point of view. Additional factors that may explain the reversing trend prevalence of asthma are (see **Table 2**):

- An increased professional awareness of the disease, which can reduce overdiagnosis in children.
- The implementation of national and global asthma prevention and management guidelines that have led to earlier detection and improved treatment of asthmatics.
- Changes in disease severity may be one potential factor and as a result, asthma may have become milder, independent of increased use of inhaled corticosteroids, which may be reflected in changed trends of prevalence.

SUMMARY

Asthma is one of the most prevalent chronic conditions, affecting approximately 300 million people worldwide, up to 1 in 10 adults and 1 in 3 children in some countries. However, asthma is a complex disease that it still not fully understood. The type of asthma definition adopted has influenced knowledge on asthma distribution and etiology. In the case of asthma prevalence, accurate estimation has been hindered by varying definitions of asthma and methods of data collection, each combining to make data comparison across studies difficult, with the exception of ISAAC and ECRHS, which unfortunately have not used biologic and clinical markers of the disease. For instance, the use of incomplete definitions of asthma has led to an underestimation of asthma prevalence and

resulted in gaps in the identification of asthma-related risk and protective factors.

Although treatment for asthma has improved substantially, the prevalence of asthma continues to increase, particularly in low- and middle-income countries, or in some ethnic groups in which prevalence was previously low. Observed spatio-temporal variations in the increased prevalence of asthma depend on exposure to environmental factors such as allergens (because of new conditions of exposure), parental smoking, air pollution, excess of hygiene, and more in general lifestyle. Recently, several arguments are also in favor of the involvement of host susceptibility and stress in the observed increase of asthma prevalence.

Further investigations are needed to better understand asthma development, mechanisms of exacerbation, and its evolution worldwide. In particular, gene-environment interactions starting in early life using the epigenetic approach should be explored to better understand asthma epidemiologic evolution.

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