

ORIGINAL ARTICLE

Atopic Dermatitis, Urticaria and Skin Disease

Global, regional, and national burden of allergic disorders and their risk factors in 204 countries and territories, from 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019

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Abstract

Background: Asthma and atopic dermatitis (AD) are chronic allergic conditions, along with allergic rhinitis and food allergy and cause high morbidity and mortality both in children and adults. This study aims to evaluate the global, regional, national, and temporal trends of the burden of asthma and AD from 1990 to 2019 and analyze their associations with geographic, demographic, social, and clinical factors.

Methods: Using data from the Global Burden of Diseases (GBD), Injuries, and Risk Factors Study 2019, we assessed the age-standardized prevalence, incidence, mortality, and disability-adjusted life years (DALYs) of both asthma and AD from 1990 to 2019, stratified by geographic region, age, sex, and socio-demographic index (SDI). DALYs were calculated as the sum of years lived with disability and years of life lost to premature mortality. Additionally, the disease burden of asthma attributable to high body mass index, occupational asthmagens, and smoking was described.

Results: In 2019, there were a total of 262 million [95% uncertainty interval (UI): 224–309 million] cases of asthma and 171 million [95% UI: 165–178 million] total cases

Abbreviations: AD, atopic dermatitis; DALYs, disability-adjusted life years; GBD, Global Burden of Diseases; ICD, International Classification of Disease; SDI, socio-demographic index; ISAAC, International Study of Asthma and Allergies in Childhood; QoL, quality of life; 95% UI, 95% uncertainty interval; YLDs, years lived with disability; YLLs, years of life lost.

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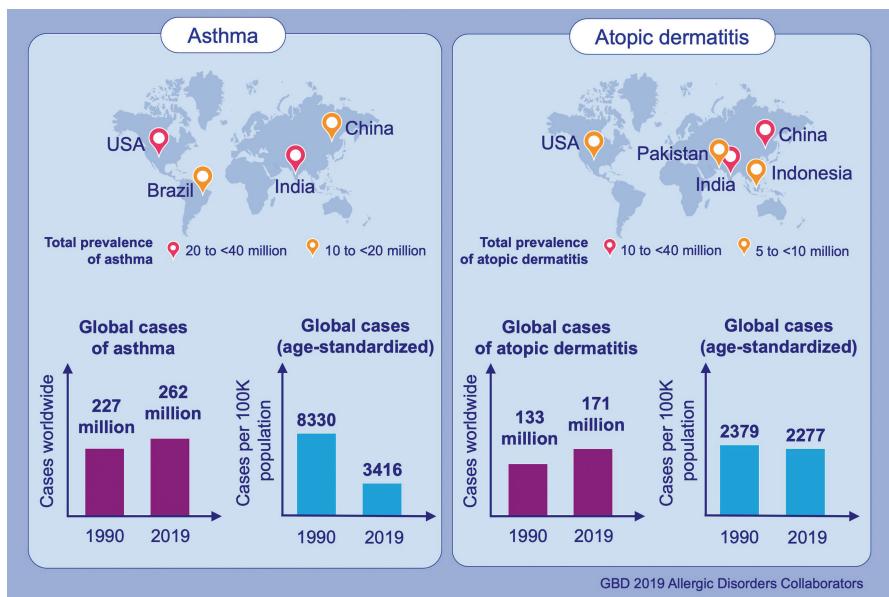
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of AD globally; age-standardized prevalence rates were 3416 [95% UI: 2899–4066] and 2277 [95% UI: 2192–2369] per 100,000 population for asthma and AD, respectively, a 24.1% [95% UI: −27.2 to −20.8] decrease for asthma and a 4.3% [95% UI: 3.8–4.8] decrease for AD compared to baseline in 1990. Both asthma and AD had similar trends according to age, with age-specific prevalence rates peaking at age 5–9 years and rising again in adulthood. The prevalence and incidence of asthma and AD were both higher for individuals with higher SDI; however, mortality and DALYs rates of individuals with asthma had a reverse trend, with higher mortality and DALYs rates in those in the lower SDI quintiles. Of the three risk factors, high body mass index contributed to the highest DALYs and deaths due to asthma, accounting for a total of 3.65 million [95% UI: 2.14–5.60 million] asthma DALYs and 75,377 [95% UI: 40,615–122,841] asthma deaths.

Conclusions: Asthma and AD continue to cause significant morbidity worldwide, having increased in total prevalence and incidence cases worldwide, but having decreased in age-standardized prevalence rates from 1990 to 2019. Although both are more frequent at younger ages and more prevalent in high-SDI countries, each condition has distinct temporal and regional characteristics. Understanding the temporospatial trends in the disease burden of asthma and AD could guide future policies and interventions to better manage these diseases worldwide and achieve equity in prevention, diagnosis, and treatment.

KEY WORDS

asthma, atopic dermatitis, disability-adjusted life years, eczema, epidemiology, global burden, mortality



GRAPHICAL ABSTRACT

Using data from the Global Burden Disease 2019 study, we assessed the total cases and age-standardized prevalence of both asthma and atopic dermatitis in 204 countries and territories from 1990 to 2019. In 2019, there were a total of 262 million [95% uncertainty interval (UI): 224–309 million] cases of asthma and 171 million [95% UI: 165–178 million] cases of AD globally; age-standardized prevalence rates were 3416 [95% UI: 2899–4066] and 2277 [95% UI: 2192–2369] per 100,000 population for asthma and atopic dermatitis, respectively, a 24.1% [95% UI: −27.2 to −20.8] decrease for asthma and a 4.3% [95% UI: 3.8–4.8] decrease for atopic dermatitis compared to baseline in 1990.

Asthma and atopic dermatitis continue to cause significant morbidity worldwide, having increased in total prevalence and incidence cases worldwide, but having decreased in age-standardized prevalence rates from 1990 to 2019.

Abbreviations: GBD, Global Burden Disease; UI, uncertainty interval

1 | INTRODUCTION

Although allergic disorders such as asthma and atopic dermatitis (AD) are frequently dismissed as diseases of childhood, they are chronic diseases that can cause significant morbidity having long-term effects even into adulthood.^{1,2} The prevalence of physician-diagnosed allergic diseases has significantly increased over time, currently affecting approximately 10% to 30% of the global population.^{3–5} These diseases, including asthma and AD, lead to substantial direct healthcare costs, as well as indirect costs due to their impact on quality of life, work, school, and productivity.⁶

Asthma and AD were once characterized as frequent diseases in high-income countries, with affluent countries reporting higher prevalence rates and the “hygiene hypothesis” suggesting that transfer of early childhood infections among siblings is associated with protection against allergies later in life.⁷ However, the hypothesis that unhygienic conditions protect individuals against allergic illness has been criticized and expanded to encompass a complex interplay between genetic predisposition and the range of environmental exposures.⁸ On an individual level, lower socioeconomic status has been associated with higher disease burden—increased severity and poorer control of asthma and AD⁹; racial and ethnic disparities also exist.^{9,10} Health inequalities regarding these diseases have been further accentuated recently, as novel and targeted treatment options, such as biologics, have been gaining popularity. In this regard, numerous reports have called attention to disparities in access and efficacy of these emerging options.¹¹ Allergic diseases such as both asthma and AD are now recognized as major public health problems that greatly impact low-and-middle income countries as well as high-income countries.^{9,10} Therefore, it is of clinical importance to provide more precise epidemiological evidence that integrates data from around the world and across socio-demographic levels.

Further, it is critical at this time to comprehensively analyze data to represent a global picture regarding the disease burden and time trends of allergic diseases (i.e., asthma and AD). There have been isolated studies detailing the global prevalence and disease burden of asthma and AD using the Global Burden of Disease (GBD) 2017,^{12,13} but there has not yet been an up-to-date study encompassing asthma and AD utilizing the recently released dataset from 2019. Moving forward from scattered systematic reviews regarding the global distribution of these allergic diseases,¹⁴ the present study aims to provide a bird's eye view of the global distribution of asthma and AD by analyzing data from the GBD study from 1990 to 2019 and discussing temporospatial trends in association with country-level socioeconomic development to aid future public health interventions.

2 | METHODS

2.1 | Overview

Data utilized in this paper were obtained from the GBD 2019 Results Database which provides data on health loss from hundreds of

diseases, injuries, and risk factors, from 204 countries and territories from 1990 to 2019. Our analysis was performed as part of the GBD Collaborator Network and complied with the Guidelines for Accurate and Transparent Health Estimates Reporting ([Supplementary Method](#)). A comprehensive methodology for the estimation models has been published elsewhere.^{15,16}

2.2 | Case definition

In the GBD 2019 list of causes, asthma corresponds to the International Classification of Disease 10th revision (ICD-10) codes J45 and J46 and ICD-9 code 493.^{13,17,18} Asthma was defined as a chronic lung disease involving bronchospasm and shortness of breath due to allergic reactions or hypersensitivity, adjudicated by physician diagnosis and wheezing in the past year. However, studies that are not population-based, such as hospital or clinic-based studies, or those that do not provide primary data on epidemiological parameters, such as commentary pieces, and those with a sample size of less than 150, are not included. We also added new data for Wave 7 of the English Longitudinal Study of Ageing (ELSA). Surveys carried out as part of the International Study of Asthma and Allergies in Childhood (ISAAC) collaboration are the most important source of prevalence data in children.^{15,16,19} AD, consistent with ICD-10 code L20 and ICD-9 code L691, was defined as relapsing dermatitis, either localized or widespread, associated with pruritus, elevated serum immunoglobulin E, and immune dysregulation.^{1,12} However, the potential variation in the accuracy of physician diagnosis and symptom data across regions and differences in healthcare access, diagnostic criteria, and medical knowledge may result in under- or over-diagnosis of diseases. Cases were selected through a literature review with a physical examination and claim data and then further stratified into three severity levels with different disability weights according to physical deformity and pain/itch.

2.3 | Data acquisition and processing

The main data inputs for assessing the prevalence of asthma and AD were population representative surveys, limited prevalence investigations in the literature described by a systematic review of the literature, health service visits, surveillance data, survey data, and medical claims information. Estimates for prevalence, incidence, and disease burden were modeled through three main standardized tools, namely (1) Cause of Death Ensemble model, an optimized tool for assessing the cause of death by collecting an ensemble of different modeling methods with varying choices of covariates for high predictive validity; (2) Spatiotemporal Gaussian Process Regression, a model for analyzing and comparing temporal and regional estimates between different groups; and (3) Disease Modeling-Meta regression 2.1, a Bayesian meta-regression tool, utilized to provide consistency between epidemiological parameters including prevalence, incidence, remission, and mortality by adjusting variations of heterogeneous

datasets from various modeling methods.¹⁵ The Comprehensive R Archive Network (version 4.2.1; r-project.org, R Foundation, Vienna, Austria) was used to generate all tables and figures.

2.4 | Estimators of disease burden

For this study, we obtained the publication estimates of prevalence, incidence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs) for asthma and AD, respectively, for each 5-year age group, sex, year, and location from GBD 2019. Briefly, age-standardized rates per 100,000 population were computed by the direct method to the GBD population standard.¹³ YLLs were defined as the product of the number of deaths and the remaining life expectancy per age group, as per the GBD standard life table; YLDs were calculated as the product of the prevalence estimate and disability weights for that specific condition, in this case, asthma and AD. DALYs were computed by the summation of YLLs and YLDs, representing the health loss due to a specific cause; in this case, asthma and AD. Estimates for disease burden were reported with 95% uncertainty intervals (UIs), defined as the 25th and 75th values of 1000 samples drawn for each variable. A detailed description of the methods can be found in the literature.²⁰

2.5 | Socio-demographic index

The development status of each country was graded based on the socio-demographic index (SDI) as defined in the GBD study in 2017, which is a composite score from 0 to 1 based on the total fertility under age 25 years, average education in those over age 15 years, and lag-distributed income per person.^{15,20} In our analysis, we classified countries into quintiles of ranked SDI values as low, low-middle, middle, high-middle, and high SDI as obtained from the GBD 2019 data.

2.6 | Risk factors

DALYs and deaths for asthma attributable to three risk factors: namely, high body mass index (BMI), occupational asthmagens, and smoking, as classified in GBD 2019,^{15,20,21} were obtained and further stratified by region and sex. Initially, we utilized a framework for risk assessment to determine the level of attribution of each risk factor, by conducting a comprehensive review of prior studies and incorporating pairs of risks and outcomes. Subsequently, we estimated the relative risk in relation to exposure and meta-regression assumptions, and computed the distribution of exposure for each risk factor by age, sex, location, and year using Bayesian meta-regression modeling (DisMod-MR 2.1).^{21,22} Thirdly, we established the theoretical minimum risk exposure level and assessed the population attributable fraction and attributable burden. Lastly, we combined various risk factors through other factors. A high BMI

was defined as a BMI over 25.0 kg/m² for adults, which is considered overweight or obese, and as being overweight or obese for children (ages 1–19) on International Obesity Task Force standards. Occupational asthmagens were defined as airborne substances that cause asthma, such as dust, chemicals, and fumes and smoking was defined as current or past smoking status.²¹ Attributable risk factors for AD could not be evaluated from the current GBD database at this time.

2.7 | Role of the funding source

The funders of this study had no role in study design, data collection, data analysis, data interpretation, or the writing of the report.

3 | RESULTS

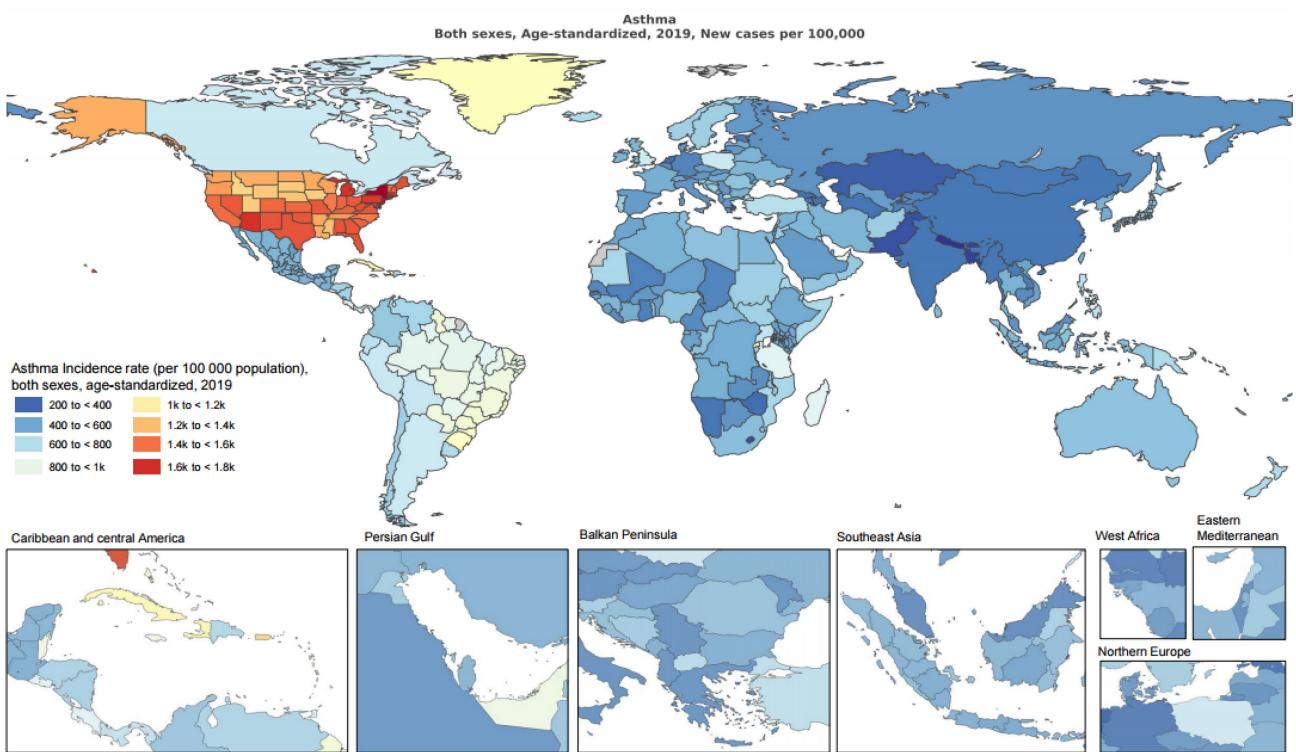
3.1 | Global and regional burden of asthma

The age-standardized rates of asthma are mapped at the country level in Figure 1. Globally, the total number of patients with asthma increased slightly from 227 million [95% UI: 195–270 million] in 1990 to 262 million [95% UI: 224–309 million] in 2019, or an increase of 15.4%. However, age-standardized prevalence rates had a 24.1% [20.8–27.2] decrease, from 4497 [3914–5224] per 100,000 population in 1990 to 3416 [2899–4066] per 100,000 population in 2019. Incidence rates of asthma showed similar trends where total incidence cases has increased from 32.2 million [25.8–40.5] to 37.0 million [29.6–45.9], whereas age-standardized incidence rates has decreased from 580.1 per 100,000 population [474.7–715.0] to 504.3 per 100,000 population [400.6–633.3] in 1990 and 2019, respectively (Figures S1–S10 and Tables S1–S4). The incidence and prevalence of asthma are significantly increased in several countries, such as India and the United States having the highest number of cases. According to the study, India has 4,533,397 cases of asthma incidence and 34,305,973 cases of asthma prevalence, while the United States has 4,143,124 cases of asthma incidence and 33,954,467 cases of asthma prevalence. China, Brazil, and Nigeria are also among the top countries with high asthma incidence and prevalence (Table S5).

3.2 | Trends in burden of asthma and AD separately by demographic factors

Asthma accounted for a total of 0.461 million [0.367–0.559] deaths in 2019, resulting in an age-standardized mortality rate of 5.8 per 100,000 population; a 51.3% decrease from 11.9 per 100,000 population in 1990. The total number of DALYs and age-standardized DALYs rates due to asthma decreased from 1990 to 2019 (Figure 2). In particular, age-standardized DALYs rates underwent a steep decrease of 42.5% [-48.5 to -36.6] from 1990

(A)



(B)

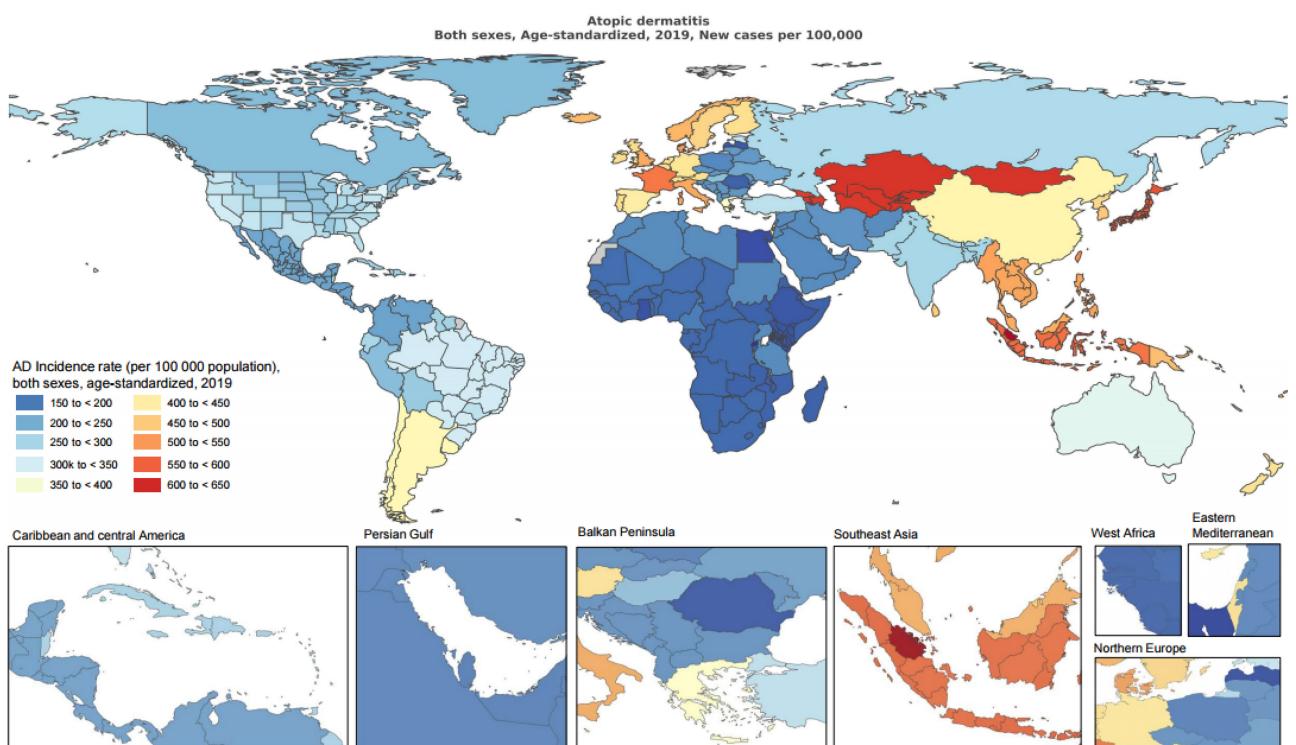


FIGURE 1 Global distribution of the age-standardized prevalence rates of asthma (A) and atopic dermatitis (B). AD = atopic dermatitis.

to 2019, with DALYs rates of 476.3 [378.5–579.6] per 100,000 population in 1990 to 273.6 [216.7–343.4] per 100,000 population in 2019.

High-income North America and Australasia regions had the highest and second-highest age-standardized prevalence of asthma at 9848 [8624–11,312] and 8393 [6909–10,347] per 100,000

population in 2019, respectively. Notably, the high-income North America region had a 9.6% [1.2–19.2] increase from 1990, with the United States contributing most of the increase at 10.9% [2.0–21.4] from 1990 to 2019; Australasia, had a 30.6% [18.5–40.6] decrease from its rate in 1990, a finding consistent with most regions and the global trend.

East, Central, and South Asia were the regions with the lowest age-standardized prevalence of asthma, at 2026 [1577–2631], 2277 [1883–2788], and 2443 [2030–2910] per 100,000 population, respectively, in 2019. The lowest age-standardized prevalence rates of asthma were reported in Nepal and Bangladesh, at 1073 [932–1215] and 1391 [1217–1574] per 100,000 population.

DALYs rates showed a somewhat different regional trend, with Oceania reporting the highest DALYs rates of 1102 [864–1431] per 100,000 population, and East Asia reporting the lowest DALYs rates of 106.4 [75.3–152.1] per 100,000 population.

In most countries, age-standardized DALYs rates had a precipitous decrease over time, the drop in DALYs rates being as large as 72.3% [60.8–79.2] in the Republic of Korea; the only exceptions

were Montenegro, the United States, and Paraguay, with a 6.7% [−1.3 to 15.9], a 4.4% [−3.4 to 12.9], and a 3.1% [−7.8 to 13.7] increase in DALYs from 1990 to 2019, respectively.

3.3 | Global and regional burden of AD

In 2019, the number of AD cases worldwide was 171 million [165–178], which represents an increase of 28.6% from 133 million [128–138] cases in 1990; in contrast, the global age-standardized rates of AD had a slight decrease of −4.3% [−4.8 to −3.8] to 2277 [2193–2369] per 100,000 population in 2019 (Figure 1). Similar to asthma, total incidence cases rose approximately 27.1% from 19.2 million [18.3–20.2] in 1990 to 24.4 million [23.3–25.6] in 2019, but age-standardized incidence rates dropped slightly (−4.2% [−4.8 to −3.6] change).

As no deaths were directly attributable to AD, DALYs for AD were the same as the YLDs. DALYs rates due to AD showed the same trend as prevalence and incidence; the total number of DALYs rose steeply from 5.827 million [3.090–9.784] in 1990 to 7.480 million

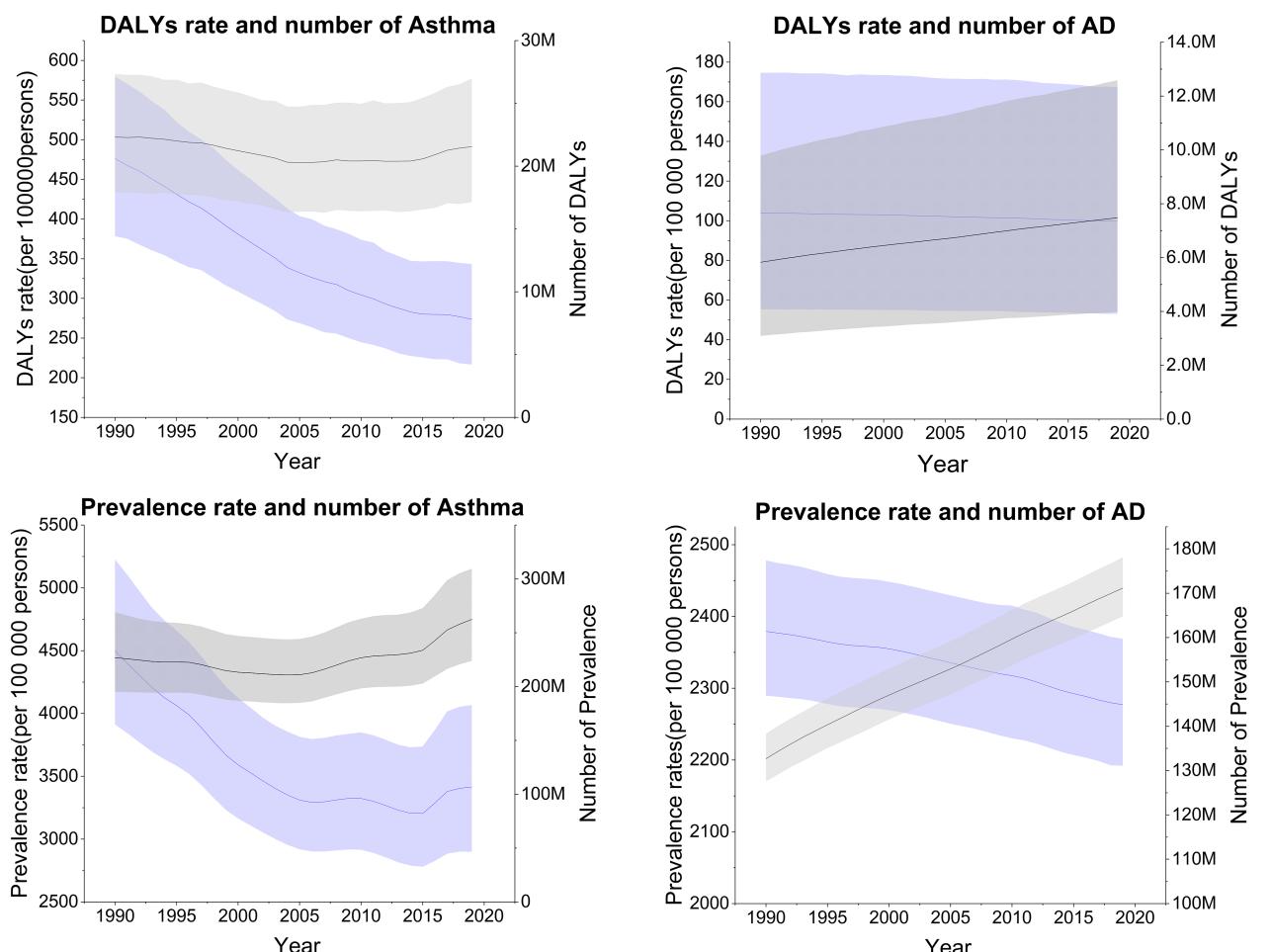


FIGURE 2 Global prevalence and disability-adjusted life years of asthma and atopic dermatitis, 1990–2019. AD = atopic dermatitis. DALYs = disability-adjusted life years.

[3.987–12.580] in 2019, whereas age-standardized rates had a slight drop of 4.1% [−4.8 to −3.5] to 99.7 per 100,000 population.

Based on the 2019 GBD data, the significant contributors to the incidence/prevalence of AD are China (with 5,837,355 incident cases and 35,583,695 prevalent cases), followed by India (with 3,739,094 incident cases and 25,923,780 prevalent cases), Indonesia (with 1,437,343 incident cases and 9,679,480 prevalent cases), the United States (with 888,977 incident cases and 8,610,796 prevalent cases), and Pakistan (with 782,596 incident cases and 4,972,106 prevalent cases) (**Table S5**). The prevalence rates of AD did not vary as drastically between regions as those of asthma, but there were still some regional trends. The highest prevalence rates of AD were reported in the high-income Asia Pacific region at 4876 [4639–5113] per 100,000 population and Central Asia at 4678 [4210–5192] per 100,000 population; the lowest prevalence rates of AD were reported in African countries, including Central, Eastern, Southern, and Western Sub-Saharan Africa, with 1081 [1009–1162], 1082 [1035–1132], 1083 [1027–1140], and 1102 [1054–1149] per 100,000 population, respectively (**Table S5**). In most regions, prevalence rates of AD remained stable from 1990 to 2019; the steepest increase was observed in Kenya at merely 5.3% [2.0–8.2], and the largest decrease in the Maldives at a similar percentage of 6.6% [−7.2 to −6.0] (**Table S6**). The DALYs rates of AD had a similar regional distribution with prevalence rates of AD, with the highest DALYs rates in the high-income Asia Pacific region and lowest DALYs rates in the Sub-Saharan Africa (**Figures S11–S18** and **Tables S5–S8**).

3.4 | Trends according to demographic factors

From 1990 to 2019, the total number of incident cases and age-standardized incidence rates of asthma were similar between females and males, whereas those of AD were substantially higher in females than in males (**Figure 3A**). Both total incidence and incidence rates of asthma down-trended slightly from 1990 to 2005, then increased from 2005 to 2019, drawing a slight V-shape over time. In contrast, the total incidence of AD increased steadily from 1990 to 2019, while age-standardized rates decreased slightly over the same period. Time trends were similar in both sexes (**Figure 3B**).

When stratified by age, in 2019, the total number of prevalence cases peaked at ages 5–9 years, down-trended to reach a plateau at ages 25–69 years, and then decreased in the older age groups (**Figure 4A**). In contrast, the age-specific prevalence rate of asthma had an N-shaped distribution, with prevalence rates peaking in ages 5–9 years, reaching the lowest at ages 25–29 years, then increasing continuously in the following groups. Total age-specific prevalence cases and prevalence rates of asthma were higher in males up to the 15–19 age group; afterward, the trend reversed with higher prevalence in females.

Total cases of AD according to age groups showed similar trends as those of asthma, having a distribution heavily skewed in infancy and early childhood with a peak in the 5–9 age group and a steep

decrease thereafter (**Figure 4B**). Age-specific prevalence of AD was characterized by an earlier peak in the 1–4 and 5–9 age groups and a later trough at ages 35–44 years. For AD, both age-specific prevalence rates and total number of prevalence cases were higher for females in all age groups, with the difference being almost two-fold in young adulthood (ages 25–45 years; **Figure 4B**).

3.5 | Burden of asthma and AD separately in accordance with SDI

Age-standardized DALYs rates of asthma decreased steadily from 1990 to 2005 across all SDI quintiles, with the exception of the high SDI quintile, for which the DALYs rates increased slightly since 2005 (**Figure 5**). Higher SDI levels tended to have lower DALYs rates, with high, high-middle, and middle SDI quintiles having substantially lower DALYs rates than low and low-middle quintiles consistently over the study period, and with the low SDI quintile having the highest, and the high-middle quintile having the lowest DALYs rates from 1990 to 2019 (553.9 [434.7–726.8] and 158.3 [114.0–220.2] per 100,000 population, respectively, in 2019). On the contrary, the high SDI quintile had the highest age-standardized prevalence, incidence, and YLDs rates of asthma across the study period, compared to lower SDI quintiles. The highest SDI quintile had a prevalence rate of 6855 [5877–8058] per 100,000 population; at the same time, the high and high-middle SDI quintiles experienced the largest decrease in asthma prevalence of 17.7% [14.2–20.9] and 26.8% [22.2–32.1], respectively, over the study period. Although the mortality rate decreased for all SDI quintiles over the study period, lower SDI quintiles having substantially higher DALYs and higher mortality.

Age-standardized DALYs rates of AD were largely stable from 1990 to 2019 in all SDI levels (**Figure S9**). Of note, we characterized the relationship between DALYs and SDI in AD as being reversed. Specifically, higher SDI levels had higher DALYs rates of AD throughout 1990–2019, with the high SDI quintile having more than doubled the DALYs rates of the low SDI quintile (155.5 [83.5–262.0] and 59.7 [32.0–100.1] per 100,000 population, respectively, in 2019). This trend was replicated in prevalence and incidence rates of AD; the high SDI quintile had the highest prevalence rate of 3540 [3376–3685] per 100,000 population, whereas the low SDI quintile had the lowest prevalence rate of 1359 [1301–1424] per 100,000 population in 2019.

3.6 | Burden of asthma attributable to risk factors

Asthma-related DALYs and deaths attributable to three risk factors: namely, body mass index (BMI), occupational asthmagens, and smoking, as classified in GBD 2019, were collected and further stratified by region (**Figure 6A**) and sex (**Figure 6B**). At this time, the current GBD database was not used to evaluate attributable risk factors for AD.

Globally, high BMI contributed to the most DALYs and deaths due to asthma in 2019, followed by smoking and occupational

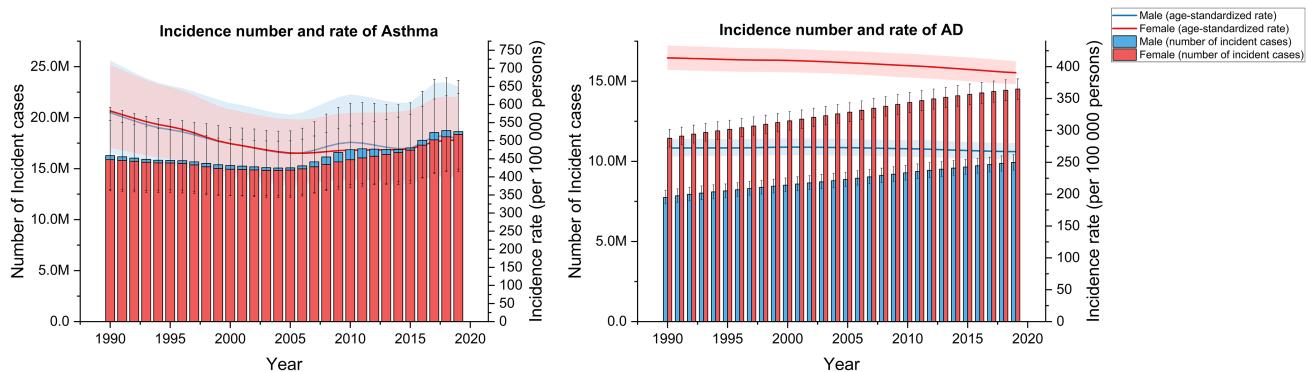


FIGURE 3 Total number of incident cases and global incidence rates of asthma (left [A]) and atopic dermatitis (right [B]) by sex, 1990–2019.

asthmagens, with a total of 3.65 million [2.14–5.60], 2.12 million [1.13–3.01], and 1.90 million [1.51–2.33] asthma DALYs, and a total of 75,377 [40,615–122,841], 54,849 [29,149–78,006] and 34,395 [27,828–42,614] deaths attributable to each risk factor, respectively (Figures S19–S28). In both men and women, South Asia had the highest number of asthma DALYs attributable to all three risk factors (0.910 million [0.447–1.587] for high BMI, 0.622 million [0.475–0.818] for occupational asthmagens, and 0.689 million [0.333–1.044] for smoking), mirroring the number of total DALYs due to asthma. South Asia was followed by the North Africa and the Middle East, high-income North America, and Southeast Asia, for the highest asthma DALYs due to high BMI; the trend was slightly different for occupational asthmagens and smoking, for which the second and third highest asthma DALYs occurred in Southeast Asia and Eastern Sub-Saharan Africa for occupational asthmagens and Southeast Asia and East Asia for smoking, respectively.

Consistent with the high absolute numbers of attributable DALYs, high BMI accounted for nearly 30% of asthma DALYs in the North Africa and the Middle East (27.9% [18.3–38.8]) and Southern Sub-Saharan Africa (27.7% [18.3–38.0]), but only 9.6% [5.0–6.6] in the high-income Asia Pacific. In most regions, females had a higher proportion of asthma DALYs attributable to high BMI, with the exception of the high-income Asia Pacific and the East Asia regions. These two regions also had the lowest percentages of DALYs due to high BMI.

Eastern, Western, and Central Sub-Saharan Africa had a substantially higher percentage of asthma DALYs due to occupational asthmagens compared to other regions, which were 13.3% [11.8–14.8], 11.9% [10.5–13.3], and 10.8% [9.0–12.4], respectively. Further, the percentage of asthma DALYs attributable to occupational asthmagens were higher in males than in females in all regions.

The highest asthma DALYs attributable to smoking occurred in Central Europe (12.7% [7.2–17.8]) and Western Europe (12.2% [6.7–17.0]), and the lowest in Andean Latin America (1.3% [0.5–2.1]). Notably, the percentage of DALYs attributable to smoking was substantially higher in males in most regions with the exception of high-income North America, Southern Latin America, and Australasia,

which had some of the highest proportions of DALYs due to smoking in females nearing 10%.

4 | DISCUSSION

Asthma and AD increased in total prevalence and incidence worldwide; however, age-standardized prevalence rates decreased from 1990 to 2019. The increase in total prevalence and incidence could be largely due to population growth, rather than an actual increase in the proportion of individuals affected by these conditions. It could also suggest that improvements in health care and public health measures may have had some effect on reducing the burden of asthma and AD. Both conditions seem to peak at ages 5–9 years in terms of incidence; however, prevalence continues to increase in later adulthood. These diseases tend to have a higher prevalence in countries with higher SDI, but for asthma, lower SDI was associated with higher mortality and DALYs rates; further, disease burden varied substantially across geographic regions. Further epidemiologic studies of asthma and AD spanning the globe are warranted to initiate actions targeting the decrease of disease burden, equity in prevention, diagnosis, and treatment regarding these allergic diseases.

Asthma and AD are atopic diseases that can affect individuals throughout their life course and have major repercussions both on population health and on the global economy. However, reflecting heightened awareness from early in life, improved diagnostic capacity, and perceptions that affluent populations are prone to allergic diseases, mounting studies have focused on high-income countries, such as the United Kingdom, the European Union countries, and the United States.^{13,23–25} Furthermore, as these diseases have been considered as pediatric conditions, most studies have leaned toward children.²⁶ To provide a global bird's eye view regarding the true public health impact of these diseases across the lifespan, we utilized the most up-to-date data from the GBD 2019 study to describe the global prevalence, incidence, and disease burden of asthma and AD and

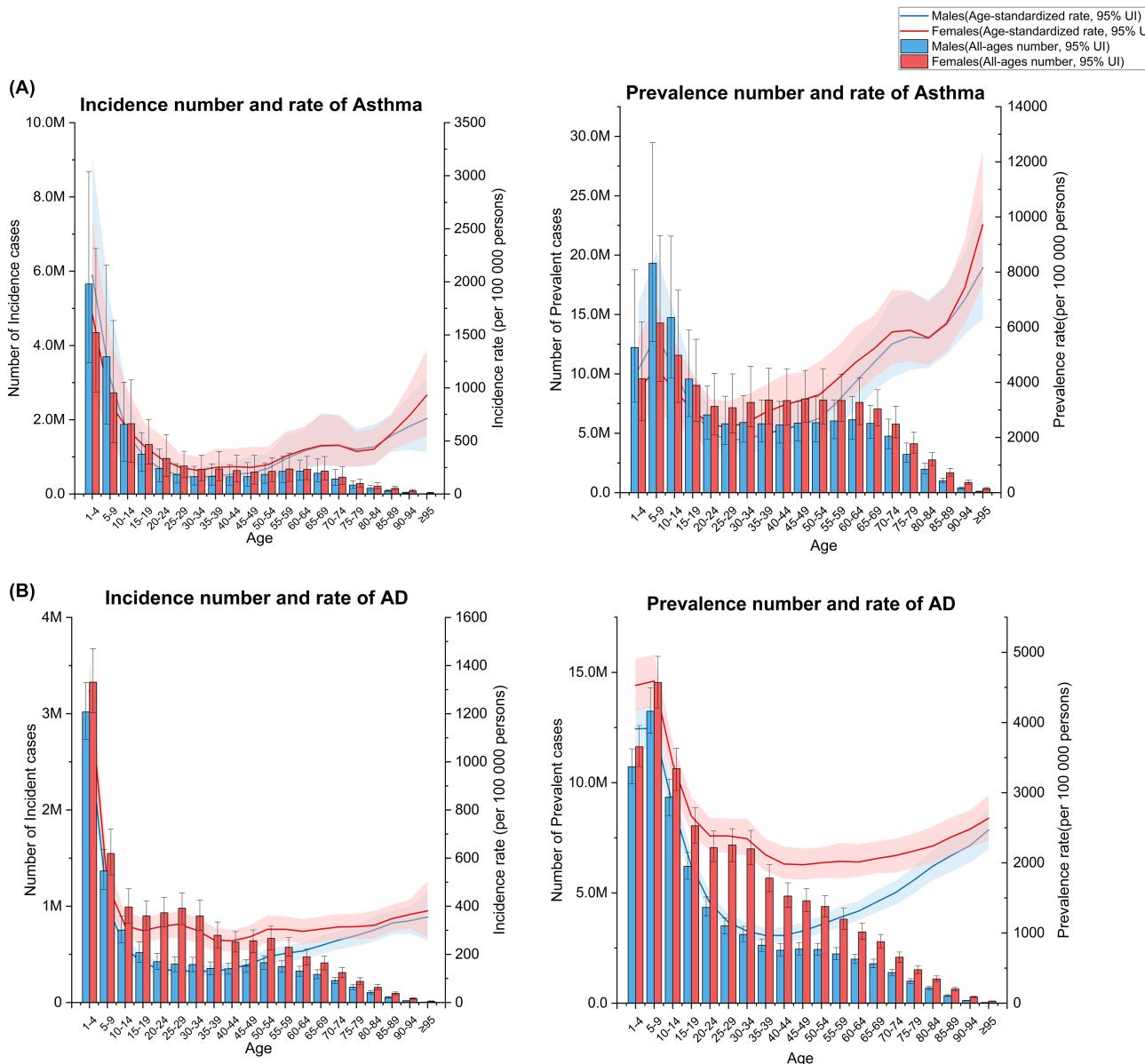


FIGURE 4 Total number of prevalent cases and global prevalence rates of asthma (A) and atopic dermatitis (B) by age, 1990–2019.

analyzed their associations with geographic region, demographic characteristics, SDI, and risk factors.

In 2019, there were 262 million [224–309] total cases (2.4%) of asthma globally across all ages, the percentage less than other studies from the World Health Survey (4.3% in adults), Global Asthma Network (10.4% in adolescents and 9.9% in children), and the International Study of Asthma and Allergies in Childhood (13.7% in age 13–14 years and 11.6% in age 6–7 years).^{27–29} This discrepancy may be explained by differences in included countries and age groups, especially considering the significant variation in asthma prevalence among countries and along the life course evident in the GBD data and in the other worldwide studies. While the total number of asthma patients increased, age-standardized prevalence rates had a large decrease of 24.1% globally, with incident cases and

incidence rates mirroring the same trend, which suggests that the increase in number was in part due to population expansion. Likewise, the prevalence rate of asthma decreased in most regions. However, a few regions, such as the United States, had a rise in asthma prevalence; this increase could be attributed to increased awareness and diagnostic availability of asthma due to public health campaigns such as the National Asthma Education and Prevention Program and, in part, due to over-diagnosis.³⁰

The disease burden of asthma is represented by age-standardized DALYs rates, and its mortality rates also underwent a steep decrease of 42.5% and 51.3% from 1990 to 2019, respectively. This finding may reflect the establishment of cornerstone guidelines (e.g., the National Heart, Lung, and Blood Institute guidelines, first issued in 1991, and the Global Initiative for Asthma guidelines, first published

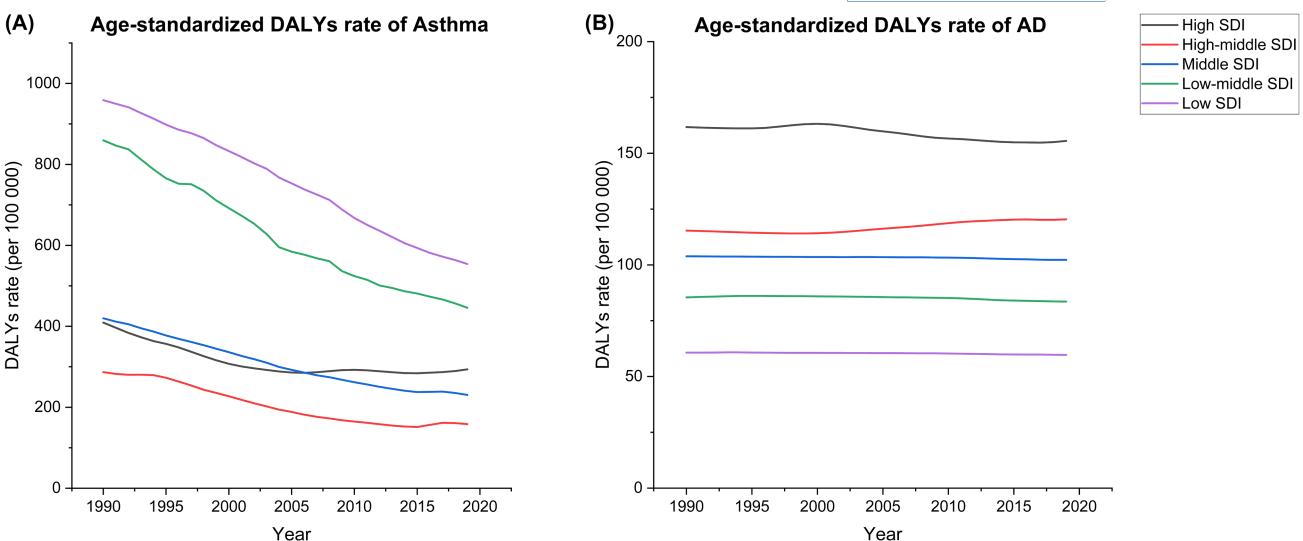


FIGURE 5 Age-standardized DALYs rates of asthma (A) and atopic dermatitis (B) according to SDI, 1990–2019. DALYs, disability-adjusted life years; SDI, socio-demographic index.

in 1995), heightened awareness and better management of asthma globally, and the development and popularization of different treatment options.^{31,32} For example, the decrease in asthma DALYs was especially precipitous in some countries, reaching 72.3% in the Republic of Korea; this may be ascribed to the fact that various initiatives and cohorts were undertaken since the early 2000s, such as the Cohort for Reality and Evolution of Adult Asthma, the Korea Asthma Allergy Foundation, and the Seoul Atopy-Asthma-friendly School Project.³³ However, as there are still existed wide variations in DALYs and mortality rates around the globe and within regions, it is critical to continue efforts for better prevention and control of asthma, especially in under-resourced settings.⁹

For AD, there were 171 million total cases globally, approximately 2.23% of the population. Although the absolute number of prevalence and incident cases rose from 1990 to 2019, age-standardized prevalence and incidence rates remained relatively stable over time, undergoing only a slight drop of 4.3% and 4.2%, respectively. The prevalence and DALYs rates of AD did not vary as drastically among countries and regions as those of asthma; however, the highest prevalence and DALYs rates were reported in the high-income Pacific region, and the lowest rates were reported in the Sub-Saharan Africa regions. The low reported disease burden in African countries may be partly ascribed to differences in diet and environment, but may also be a result of under-reporting, especially as AD prevalence has recently increased in these low-and-middle income countries.³⁴ Therefore, additional epidemiologic studies should be conducted to delineate complex factors associated with the changes in different parts of the world and efforts to boost awareness and diagnostic capability in under-resourced settings should be continued.

Corresponding well with the literature and common perceptions, this study found that both asthma and AD peaked at younger ages, typically ages 5–9 years^{28,31}; however, we also found that

age-standardized rates increased throughout adulthood. In older populations, asthma and AD may be difficult to diagnose and treat due to their traditional misconceptions as being “pediatric diseases,” different clinical presentations (i.e., phenotypes) and functional characteristics. Moreover, with the presence of multiple comorbidities associated with aging, physicians should be vigilant in recognition of these conditions and their multi-dimensional management in older adults.³⁵

Higher SDI levels tended to have a higher prevalence of asthma and AD, as reported in previous international studies.^{26,28,36} Notably, however, mortality and DALYs rates had the reverse trend, with lower SDI was associated with higher mortality in all time frames. Low-resource settings have been associated with worse outcomes of asthma, mediated by socioeconomic factors including income and education, environmental allergens or pollutants, psychosocial stressors, and lack of access to health care.^{9,37} Likewise, many inner-city populations in low- and middle-income countries have a very high prevalence of asthma, but limited access to and affordability for essential medications for persistent asthma³⁸; under-treatment in these countries causes significant morbidity and mortality.³⁹ Further, the high incidence of acute respiratory infections in low- and middle-income countries can lead to asthma exacerbations as well as under-diagnosis and thus under-treatment of asthma, resulting in an under-reported prevalence and a higher morbidity.⁴⁰ These trends suggest a large potential for global and community initiatives to improve asthma outcomes in low-resource populations.^{37,41}

The trends in asthma prevalence and DALYs due to high BMI, occupational asthmagens, and smoking vary across countries and regions due to various factors including differences in lifestyle, environmental exposures, and healthcare infrastructure. South Asia had the highest number of asthma DALYs attributable to all three risk factors, followed by North Africa and the Middle East,

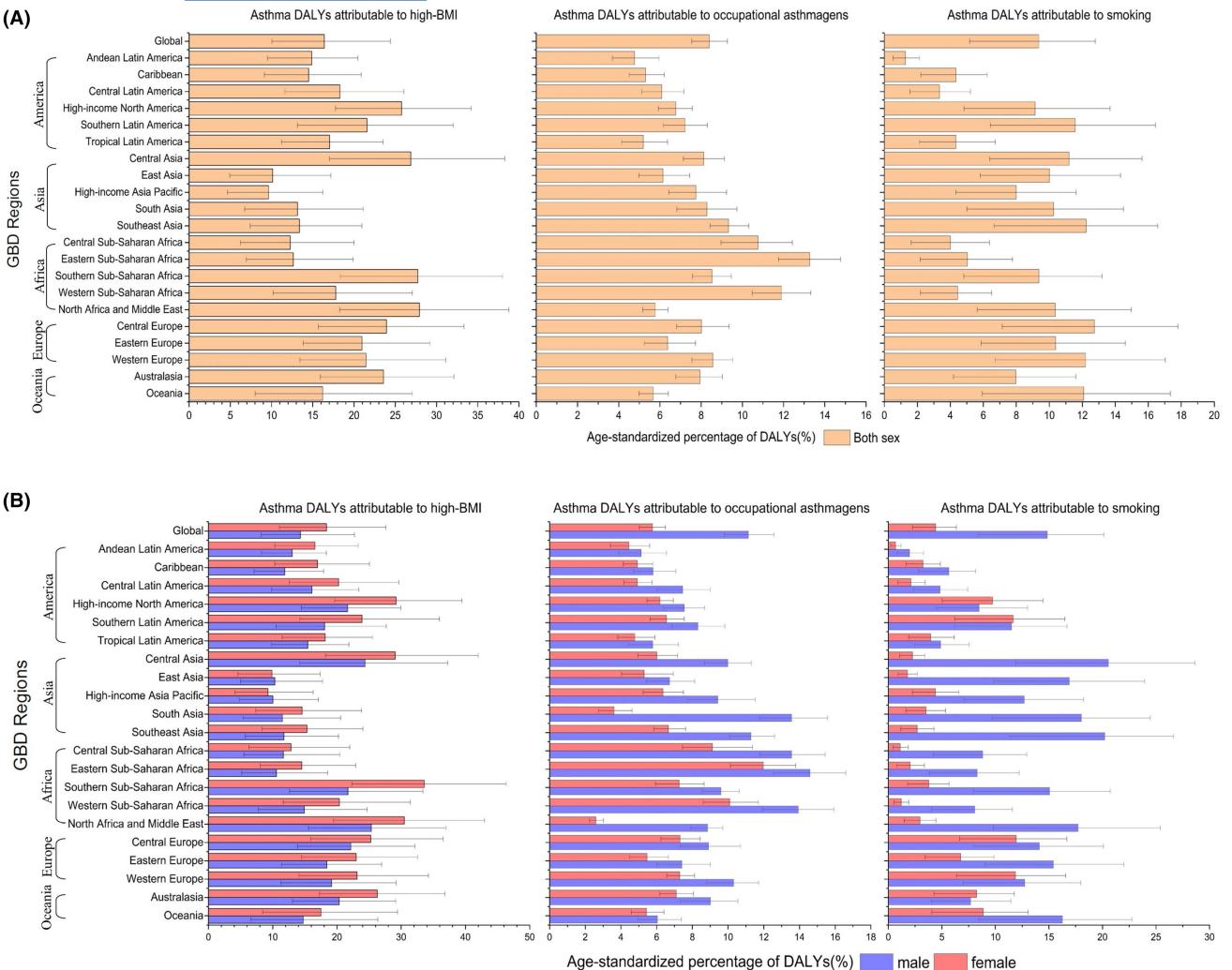


FIGURE 6 Percentage of age-standardized DALYs rates of asthma attributable to high BMI, occupational asthmagens, and smoking by geographic region; total (A) and sex-stratified (B). BMI, body mass index; DALYs, disability-adjusted life years.

high-income North America, and Southeast Asia for high BMI. The high rates of obesity in South Asia may be related to factors such as a sedentary lifestyle, unhealthy diet, and genetic factors. However, the trend was slightly different for occupational asthmagens and smoking, with the second and third highest asthma DALYs occurring in Southeast Asia and Eastern Sub-Saharan Africa for occupational asthmagens and Southeast Asia and East Asia for smoking, respectively. The high burden of occupational asthmagens in Southeast Asia and Eastern Sub-Saharan Africa could be related to the higher rates of certain occupations including farming and mining, which may expose workers to hazardous substances. The higher smoking-related asthma DALYs in Southeast Asia and East Asia may be related to the high prevalence of smoking in these regions, driven by cultural factors and the easy accessibility to tobacco products. Additionally, differences in healthcare access, quality, and healthcare-seeking behavior may contribute to the regional variation in asthma DALYs. Further research are needed to determine the underlying causes of these trends and their implications for public health interventions.

4.1 | Implication of the study

Up-to-date population-level estimates on these frequent respiratory and skin conditions is crucial for efficient policy making with the aim of increasing access to health-care and scaling of vigorous prevention strategies. This study warrants greater standardization in data collection regarding case definitions and severity distributions of asthma and AD. We call for further and revised population measurements of asthma and AD to better quantify the size of the problem and to better guide progress toward achievement of the 2030 health-related Sustainable Development Goals.

4.2 | Strengths and limitations of the study

The present study was the first to systematically assess the disease burden of asthma and AD across regions and throughout the lifespan using the most recently released GBD data. However, there are some limitations to our study. First, the definition of asthma and AD

was made mainly through physician diagnosis and symptom data, the stringency of which could have been heterogeneous across regions depending on local practices and terminology. For example, the possibility that different countries used different terms to describe symptoms of asthma or AD may lead to inconsistencies in the diagnosis and resulting prevalence estimates. Further, regional differences in under- or over-diagnosis of asthma could also contribute to discrepancies in prevalence statistics. Second, the case definition used in this study, requiring asthma to be due to "allergic reactions or hypersensitivity" and "wheezing" in the last year, may not capture all cases of asthma. As asthma is a heterogeneous disease that includes non-allergic phenotypes, this impact on generalizability should be considered. Additionally, the requirement of wheezing in the last year may exclude individuals with asthma who are on controlled medications and have no symptoms. This could explain the observed fall in asthma prevalence over time, as increased accessibility to asthma medication over the last decades has likely led to improved asthma control and a higher proportion of asymptomatic individuals who would not be captured by our definition. Third, while chronic allergic conditions encompass a variety of diseases including asthma, AD, allergic rhinitis, and food allergy, the GBD study data were unable to model these conditions comprehensively. This is due to the fact that some countries may not have had sufficient data available to accurately estimate the prevalence of these conditions, especially in cases where the disease is relatively rare or there is a lack of clear disease codes to define cases. As a result, the analysis presented in this study was limited to asthma and AD. While this represents an important contribution to understanding the global burden of these diseases, it is important to recognize that other chronic allergic conditions may also significantly impact global health and should be the focus of future research efforts. Fourth, the attributable risk factors of AD were not evaluated from the current GBD database. Fifth, as this study was driven by data from the GBD study, it includes the limitations of the GBD dataset, mainly, that some regions had low availability and quality of data, for which statistics had to rely on predictive covariates. Sixth, the study is primarily based on GBD 2019 Results Database, which relies on representative surveys, medical claims information etc. and may not take into account chronic cases that never make it to the clinics and thus go unreported. In low-income countries such as Sub-Saharan regions, it is likely that many people will resort to home-based treatments. Seventh, there may be the influence of non-modifiable factors on the results. Eighth, available data for AD has limitations; therefore, we were not able to do further analyses with AD data. Ninth, there are possibilities that data was only partially registered or underreported in low- and mid-income countries, which may bias the actual data interpretation. For example, illiteracy, lack of access to health-care facilities for all populations, economic issues, etc., may prevent people of deprived African regions from reporting the actual burden of asthma and AD. Tenth, as we compared country-level aggregate data, the trends and associations observed in the present study are subject to ecological bias. Eleventh, we were unable to consider the role of ethnicity in the burden of asthma and AD. As the GBD study was obtained from various countries with different forms of resources, the heterogeneity of the data

sources prevented us from considering racial factors in our analysis which can play a critical role in health outcomes and disease burden. Lastly, we were only able to assess the attributable risk for asthma on three risk factors (high BMI, occupational asthmagens, and smoking); more research is necessary to investigate associations with different demographic and clinical factors, and also for AD. Therefore, caution should be taken when interpreting the trends in asthma prevalence and burden presented in this study, and further research is needed to investigate the potential impact of changes in asthma management and control on the observed trends.

5 | CONCLUSION

In summary, asthma and AD are both allergic diseases that have increased in total burden worldwide, but have decreased in age-standardized prevalence rates from 1990 to 2019. Although both are prevalent at younger ages and in high-SDI countries, each condition has distinct temporal and regional trends. In addition, Eastern, Western, and Central Sub-Saharan Africa had a substantially higher percentage of asthma DALYs due to occupational asthmagens compared to other regions. This study may help assess regional and temporal trends regarding the distribution and disease burden of asthma and AD and guide interventions to better manage these diseases worldwide as well as to attain equity in prevention, diagnosis, and treatment.

AUTHOR CONTRIBUTIONS

Please see appendix for more detailed information about individual author contributions to the research, divided into the following categories: providing data or critical feedback on data sources; developing methods or computational machinery; providing critical feedback on methods or results; drafting the manuscript or revising it critically for important intellectual content; and managing the estimation or publications process. Youn Ho Shin, Jimin Hwang, Rosie Kwon, Seung Won Lee, and Min Seo Kim contributed equally to this work as first authors. Jae Il Shin and Dong Keon Yon contributed equally to this work as corresponding authors. Dong Keon Yon is a senior author.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in GBD 2019 at <https://ghdx.healthdata.org/gbd-2019>.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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