Allergy Asthma Immunol Res. 2023 Jul;15(4):473-495
https://doi.org/10.4168/aair.2023.15.4.473
pISSN 2092-7355·eISSN 2092-7363

Allergy, Asthma & Immunology Research AAIR

Original Article

Global Disease Burden and Attributable Risk Factor Analysis of Asthma in 204 Countries and Territories From 1990 to 2019

Hailing Liu [1†] **Jing Zhang** [2†] **Li Liu** [1] **Guoli Lian** [1] **Ruiming Shi** [1] **Man Xu** [1] **Juan Yang** [3,4*] **Xiaohong Liu** [1*]

[1]Department of Pediatrics, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, P. R. China
[2]Department of Cardiovascular Medicine, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, P. R. China
[3]Department of Cell Biology and Genetics, School of Basic Medical Sciences, Xi'an Jiaotong University Health Science Center, Xi'an, P. R. China
[4]Key Laboratory of Environment and Genes Related to Diseases, Ministry of Education of China, Xi'an Jiaotong University, Xi'an, P. R. China

Received: Jan 30, 2022
Revised: Dec 21, 2022
Accepted: Dec 28, 2022
Published online: Apr 21, 2023

Correspondence to
Juan Yang, PhD
Department of Cell Biology and Genetics, School of Basic Medical Sciences, Xi'an Jiaotong University Health Science Center; Key Laboratory of Environment and Genes Related to Diseases, Ministry of Education of China, Xi'an Jiaotong University, No. 28 Xianning West Road, Xi'an 710061, P. R. China.
Tel: +86-29-82655077
Fax: +86-29-88965077
Email: yangjuan0112@mail.xjtu.edu.cn

Xiaohong Liu, PhD
Department of Pediatrics, The First Affiliated Hospital of Xi'an Jiaotong University, No. 277 West Yanta Road, Xi'an 710061, P. R. China.
Tel: +86-29-85323820
Fax: +86-29-85263190
Email: liuxiaoh@mail.xjtu.edu.cn

†Hailing Liu and Jing Zhang have contributed equally to this work.

ABSTRACT

Purpose: Asthma is a common chronic inflammatory respiratory tract disease with high morbidity and mortality. The global trends in asthma burden remain poorly understood, and asthma incidence has increased during the worldwide coronavirus disease 2019 (COVID-19) pandemic. This study aimed to provide a comprehensive view of the global distribution of asthma burden and its attributable risk factors from 1990 to 2019.
Methods: Based on the Global Burden of Disease Study 2019 Database, asthma incidence, deaths, disability-adjusted life years (DALYs), the corresponding age-standardized incidence rate (ASIR), age-standardized death rate (ASDR), age-standardized DALY rate, and estimated annual percentage change were analyzed according to age, sex, sociodemographic index (SDI) quintiles, and locations. Risk factors contributing to asthma deaths and DALYs were also investigated.
Results: Globally, the asthma incidence increased by 15%, but deaths and DALYs decreased. The corresponding ASIR, ASDR, and age-standardized DALY rate also decreased. The high SDI region had the highest ASIR, and the low SDI region had the highest ASDR. The ASDR and age-standardized DALY rate were negatively correlated with the SDI. The low-middle SDI region, particularly South Asia, showed the highest asthma-related deaths and DALYs. The incidence peak was under 9 years old, and more than 70% of all deaths occurred in the population over 60 years old. Smoking, occupational asthmagens, and a high body mass index were the main risk factors for asthma-related mortality and DALYs, and their distributions varied between sexes.
Conclusions: Globally, the asthma incidence has increased since 1990. The greatest asthma burden is borne by the low-middle SDI region. The 2 groups that need special attention are those under 9 years old and those over 60 years old. Targeted strategies are needed to reduce the asthma burden based on geographic and sex-age characteristics. Our findings also provide a platform for further investigation into the asthma burden in the era of COVID-19.

Keywords: Asthma; global burden of disease; risk factors; incidence; death; disability-adjusted life years

ORCID iDs

Hailing Liu
https://orcid.org/0000-0003-1094-4753
Jing Zhang
https://orcid.org/0000-0002-3577-4677
Li Liu
https://orcid.org/0000-0001-6064-1342
Guoli Lian
https://orcid.org/0000-0002-6650-5015
Ruiming Shi
https://orcid.org/0000-0002-9609-6806
Man Xu
https://orcid.org/0000-0003-1092-8964
Juan Yang
https://orcid.org/0000-0001-9965-0836
Xiaohong Liu
https://orcid.org/0000-0001-5583-5839

Disclosure

There are no financial or other issues that might lead to conflict of interest.

INTRODUCTION

Asthma is a common chronic airway disease which is characterized by variable airflow obstriction, airway hypersensitivity, airway wall thickening, and increased mucus hypersecretion. It is a heterogeneous disease with several different clinical manifestations, which varies in the exacerbation rate, response to treatment, and remission rate.[1] Asthma attack is characterized by an acute exacerbation of asthma symptoms due to exposure to allergens, viral infections, environmental irritants (including pollution and cigarette smoke), or a combination of these factors. Asthma is a major worldwide public health problem with high morbidity and mortality,[2] affecting an estimated 339 million people worldwide. The asthma prevalence varies widely across countries at different levels of development, up to 21-fold among 70 countries.[3] The asthma prevalence in the United States (US) is higher than the world average: an estimated 8.4% of the US population has asthma, while 4.3% of the world's population is affected.[4] However, the asthma prevalence continues to rise both in the US and worldwide.[5]

As the number of asthma cases increases each year, so do the economic costs as confirmed by data from studies of asthma in the US.[6] Asthma brought an obvious economic burden, costing 81.9 billion dollars in 2013 including costs caused by absenteeism and death. This figure likely undervalues the current financial cost of asthma treatment, as the number of prescriptions for novel and expensive medications targeting biological pathways is rising.[7] From 2008 to 2018, the cost of asthma continued to rise, and this trend indicated that the economic burden of asthma continued to increase. The prevention and treatment of asthma are not perfect,[8,10] and the burden of asthma deserves our attention.

In the current worldwide pandemic of coronavirus disease 2019 (COVID-19), some studies have shown that COVID-19 does not induce severe asthma exacerbations or increase the risk of worse clinical outcomes of COVID-19[11,12]; however, a study showed that asthmatic patients infected with COVID-19 were likely to have worse outcomes.[13] Therefore, fundamental data on the burden of asthma before the COVID-19 pandemic are valuable to investigate the impact of COVID-19 on the prospective asthma burden.

A few previous studies have reported the burden of asthma. Achakulwisut *et al.*[14] reported on the burden of asthma incidence attributable to ambient NO_2 pollution and described that reducing NO_2 exposure could help prevent a substantial portion of new pediatric asthma cases. Liu *et al.*[15] reported that the global asthma burden associated with obesity increased in absolute value, but the standardized burden decreased slightly. Zhang *et al.*[16] focused on the burden of childhood asthma and showed that a high body mass index was a stronger risk factor than occupational asthmagens for childhood asthma. However, to date, no studies have examined changes in the burden of asthma in all age groups and provided a detailed analysis of asthma associated with risk factors over the past 30 years for the entire world. Therefore, synthetically analyzing the burden of asthma from different levels and dimensions is necessary.

According to the Global Burden of Disease (GBD) Study 2019 dataset, we analyzed the burden of asthma: incidence, mortality, disability-adjusted life year (DALY: its classic definition refers to all healthy life years lost from onset to death, estimated as the sum of years of life lost and years lived with disability) by region, age, and sex to assess change trends globally from 1990 to 2019. Moreover, the asthma burden distribution based on the sociodemographic index (SDI) quintile was calculated. Furthermore, the influence

https://doi.org/10.4168/aair.2023.15.4.473

of multiple risk factors on asthma-related mortality and DALY was analyzed. This study provides a scientific basis for the global healthcare system to establish asthma prevention and treatment strategies by providing a multi-index and multilevel detailed understanding of the global burden of asthma.

MATERIALS AND METHODS

Data sources

In this study, detailed data on all asthma studies from 1990 to 2019 were obtained through the Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool). The GBD 2019 dataset provides the burden of 364 diseases and injuries, 87 risk factors, and 18 causes in 204 countries and territories. Our study followed the Guidelines for Accurate and Transparent Health Estimates Reporting statement.[17] First, considering the impact of age and sex on the global disease burden of asthma, data for different age ranges and sexes were extracted for analysis. Previous studies have shown that different sociodemographic characteristics considerably impact the GBD.[18,19] Therefore, to understand the burden of asthma in different developing regions, all detailed data extraction referenced 4 dimensions: global, SDI quintiles, 21 GBD regions, and 204 countries and territories. This study used the SDI as a covariate and conducted correlation analysis. The SDI is a comprehensive index combining 3 components—the total fertility rate for those younger than 25 years of age, per capita income, and average educational attainment for those older than 15 years of age. The SDI is divided into 5 grades: high, high-middle, middle, low-middle, and low levels.[20] Finally, the age-standardized incidence rate (ASIR), age-standardized death rate (ASDR), and age-standardized DALY rate in 204 countries and territories were used to reflect the asthma burden in the form of tables and world maps.

Statistical analysis

To objectively compare the asthma burden of different population structures or age changes at different time points in the same population, we used the following indicators: ASIR, ASDR, and age-standardized DALY rate. The age-standardized rate (ASR) is calculated based on the age structure of the standard population. ASR (per 100,000 population) is a crucial and representative indicator when there are differences in the age structure of multiple populations. We used the estimated annual percentage change (EAPC) based on ASRs, including ASIR, ASDR, and age-standardized DALY rate, to reflect the change trends of the asthma burden. EAPC is a recognized method to describe the changing trend of ASR with a regression model,[21] which quantitatively calculates the average annual rate of change in ASR in all specific intervals. Consequently, a regression line is fit to the natural logarithm of the rates: $y = \alpha + \beta x + \varepsilon$, where y means ln(ASR), and x means the calendar year. The EAPC value calculation formula is EAPC = $100 \times (\exp(\beta) - 1)$. If the EAPC value and its 95% confidence interval (CI) are more than zero, the corresponding ASR is defined as a rising trend. In contrast, when the EAPC value and its 95% CI are less than 0, the ASR indicates a downward trend. Others represent a relatively stable ASR over time. To explore the correlation between ASR change trends and social development degrees, Pearson correlation analysis was used to evaluate the correlation between the EAPCs and SDI values in 2019. Finally, risk factors for asthma death and DALY were retrieved from the GBD database and visualized. P values less than 0.05 were defined as statistically significant differences.

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Data visualization

We used R software (version 3.6.3; R Core Team, R Foundation, Vienna, Austria) to analyze all the data and perform data visualization using packages such as world maps and ggplot2. World heatmaps were used to visualize the asthma burden in 204 countries and territories. Histograms were used to demonstrate the global asthma burden with different sexes and age groups in 1990 and 2019. Scatter diagrams were used to show the distribution of the asthma burden in different SDI regions.

RESULTS

The incidence rate of asthma

Globally, the incidence of asthma was 3,697.9 × 10^4 in 2019, with an insignificant increase of 15.0% from 3,216.32 × 10^4 in 1990. The incidence of asthma was slightly higher in males than in females. However, the ASIR decreased globally from 580.09/100,000 persons (95% urinary incontinence [UI] = 378.49, 579.59) in 1990 to 504.28/100,000 persons (95% UI = 216.71, 343.38) in 2019, EAPC = −0.47 (95% UI = −0.67, −0.27) (**Table 1**). Concerning all 5 SDI regions, except for the high-middle region, the incidence of asthma increased in the other 4 SDI regions. The middle SDI region had the highest number of asthma cases (952.99 × 10^4 in 1990 and 1,010.92 × 10^4 in 2019) (**Fig. 1A**). The ASIRs of the 5 SDI regions all showed downward trends, and the ASIR in the high SDI region maintained the highest level (**Fig. 2A**). At the 21 GBD region level, the highest number of asthma cases were observed in South Asia, high-income North America, and East Asia (South Asia: 543.80 × 10^4 in 2019; high-income North America: 436.64 × 10^4 in 2019; East Asia: 397.99 × 10^4 in 2019). The ASIR in high-income North America showed the most mushrooming rise during the past 30 years, with an EAPC = 1.12 (95% UI = 0.68, 1.56). We found that the ASIR of 21 GBD regions increased with increasing SDI values (**Fig. 3A**). At the country and territory levels, India, the USA, China, and Brazil had the highest number of asthma cases (453.34 × 10^4, 414.31 × 10^4, 376.13 × 10^4, and 162.32 × 10^4 in 2019, respectively) (**Fig. 4A**). The USA had the highest age-standardized ASIR, 1,547.24/100,000 persons in 2019 (**Fig. 4B**). In the past 30 years, the ASIR in Japan had the fastest decrease (EAPC = −2.5; 95% UI = −2.89, −2.10) and that in the USA had the promptest increase (EAPC = 1.20; 95% UI = 0.73, 1.69) (**Fig. 4C**).

The mortality rate of asthma

Globally, the number of deaths slightly increased during the past 30 years (460.01 × 10^3 in 1990 and 461.07 × 10^3 in 2019), whereas the ASDR decreased (**Table 2**). Given the sociodemographic factors, more than half of the total asthma death cases occurred in the low-middle and middle SDI regions. The low-middle SDI region had the most deaths until 2019 (**Fig. 1B**). The ASDRs of 5 SDI regions exhibited a downward trend, with the high SDI region showing the most obvious decline (EAPC = −5.35; 95% UI = −5.76, −4.93) (**Fig. 2B**). For 21 GBD regions, South Asia and Southeast Asia were the top 2 countries with the highest death cases (South Asia: 232.19 × 10^4 in 2019; Southeast Asia: 72.06 × 10^4 in 2019). From 1990 to 2019, asthma death cases increased in 5 of the 21 GBD regions and decreased to varying degrees in other regions. ASDR showed a downward trend with increasing SDI value. The ASDR declined in all 21 GBD regions, with the most remarkable decline in high-income Asia Pacific (EAPC = −8.69; 95% UI = −9.24, −8.14), followed by Eastern Europe and Central Europe (**Fig. 3B**). Subgroup analysis by 204 countries and territories revealed that India, Indonesia, and China accounted for the highest number of deaths (**Supplementary Fig. S1A**). Kiribati was the country with the highest ASDR, 80.50/100,000 persons (95% UI = 59.22,

https://doi.org/10.4168/aair.2023.15.4.473

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Table 1. The incident cases and age-standardized incidence rate of asthma between 1990 and 2019 and its temporal trends from 1990 to 2019

Characteristics	1990	1990	2019	2019	1990–2019
	Incident cases, No. ×10^4 (95% UI)	ASR per 100,000, No. (95% UI)	Incident cases, No. ×10^4 (95% UI)	ASR per 100,000, No. (95% UI)	EAPC, No. (95% UI)
Overall	3,216.32 (2,575.28, 4,051.31)	580.09 (474.68, 715.04)	3,697.93 (2,960.2, 4,592.81)	504.28 (400.64, 633.26)	−0.47 (−0.67, −0.27)
Sex					
Male	1,628.01 (1,282.9, 2,100.9)	577.74 (466.39, 721.91)	1,862.72 (1,469.48, 2,364.98)	505.76 (394.92, 649.36)	−0.40 (−0.60, −0.19)
Female	1,588.31 (1,295.51, 1,970.68)	582.27 (480.29, 709.48)	1,835.21 (1,495.63, 2,237.83)	501.55 (402.41, 621.43)	−0.55 (−0.75, −0.34)
Sociodemographic index					
Low	376.30 (296.68, 482.53)	594.50 (491.39, 718.57)	655.77 (506.74, 848.56)	511.23 (415.12, 624.63)	−0.31 (−0.44, −0.19)
Low-middle	568.25 (452.33, 722.52)	475.36 (395.35, 574.04)	697.63 (563.06, 863.36)	409.29 (335.58, 505.67)	−0.39 (−0.62, −0.17)
Middle	952.99 (735.79, 1,246.65)	523.33 (417.01, 662.57)	1,010.92 (796.43, 1,275.85)	471.75 (366.17, 607.69)	−0.28 (−0.49, −0.07)
High-middle	624.27 (502.08, 787.63)	559.79 (446.64, 704.44)	537.36 (432.19, 667.92)	470.70 (356.3, 609.99)	−0.83 (−1.08, −0.58)
High	692.00 (572.97, 841.07)	933.66 (749.54, 1,169.89)	705.61 (590.01, 840.68)	897.36 (711.33, 1,111.67)	0.18 (−0.08, 0.44)
Region					
Central Asia	29.96 (23.21, 38.95)	406.44 (328.07, 503.31)	35.37 (27.27, 45.98)	379.29 (293.17, 489.20)	−0.43 (−0.54, −0.32)
Central Europe	86.05 (72.31, 103.42)	714.15 (592.85, 873.9)	58.70 (48.67, 70.48)	616.99 (483.35, 789.96)	−0.69 (−0.77, −0.61)
Eastern Europe	143.34 (115.97, 177.06)	655.11 (519.74, 826.37)	75.53 (58.61, 96.63)	461.89 (338.65, 613.63)	−1.63 (−1.82, −1.44)
Australasia	13.79 (11.08, 16.63)	784.22 (622.41, 957.42)	13.99 (11.16, 17.51)	615.20 (473.25, 790.74)	−1.35 (−1.56, −1.14)
High-income Asia Pacific	137.13 (115.24, 164.67)	852.87 (707.47, 1,042.26)	79.59 (66.40, 95.14)	554.49 (421.06, 724.34)	−2.02 (−2.31, −1.72)
High-income North America	336.88 (267.85, 431.51)	1,351.69 (1,038.96, 1,769.35)	436.64 (365.33, 520.76)	1,474.11 (1,188.89, 1,810.73)	1.12 (0.68, 1.56)
Southern Latin America	36.84 (30.77, 45.12)	729.20 (612.38, 887.35)	45.37 (37.03, 55.97)	742.26 (592.41, 935.55)	−0.02 (−0.05, 0.02)
Western Europe	225.13 (192.29, 262.84)	627.59 (526.75, 750.60)	178.55 (147.21, 213.06)	512.21 (397.33, 640.62)	−0.79 (−0.89, −0.68)
Andean Latin America	47.28 (35.09, 61.26)	928.50 (698.16, 1,197.35)	48.42 (36.07, 65.22)	760.27 (565.28, 1,022.67)	−1.06 (−1.27, −0.85)
Caribbean	39.62 (31.46, 49.38)	1,008.24 (804.93, 1,253.61)	40.33 (32.15, 50.23)	938.42 (741.65, 1,178.96)	−0.30 (−0.35, −0.25)
Central Latin America	143.56 (108.92, 185.18)	717.59 (561.67, 909.60)	137.26 (101.59, 182.39)	583.29 (427.80, 775.69)	−0.95 (−1.19, −0.70)
Tropical Latin America	184.17 (133.85, 248.40)	1,045.37 (769.77, 1,384.46)	168.65 (121.47, 221.02)	916.11 (645.54, 1,218.08)	−0.97 (−1.15, −0.80)
North Africa and Middle East	239.78 (187.36, 305)	613.97 (502.26, 748.23)	348.81 (276.77, 435.43)	589.78 (473.10, 728.85)	−0.28 (−0.36, −0.21)
South Asia	390.16 (318.51, 491.99)	388.17 (325.47, 459.44)	543.80 (452.54, 658.72)	329.58 (274.87, 394.58)	0.08 (−0.32, 0.48)
East Asia	471.88 (354.47, 636.12)	400.46 (301.23, 534.05)	397.99 (308.29, 517.98)	361.24 (264.84, 499.83)	−0.58 (−1.20, 0.03)
Oceania	5.33 (4.33, 6.51)	781.11 (662.50, 910.50)	9.15 (7.61, 11.00)	665.36 (567.70, 777.32)	−0.70 (−0.78, −0.62)
Southeast Asia	289.48 (230.62, 367.68)	576.89 (474.49, 709.35)	345.10 (281.03, 427.10)	553.39 (445.75, 698.10)	−0.20 (−0.25, −0.15)
Central Sub-Saharan Africa	41.52 (31.83, 53.02)	585.13 (480.34, 707.87)	81.81 (62.91, 105.37)	518.71 (420.69, 641.53)	−0.52 (−0.56, −0.48)
Eastern Sub-Saharan Africa	186.66 (143.70, 242.65)	744.14 (605.15, 919.93)	331.91 (250.72, 434.45)	651.85 (518.29, 817.23)	−0.55 (−0.61, −0.49)
Southern Sub-Saharan Africa	32.39 (23.75, 42.49)	563.12 (429.98, 713.65)	38.54 (28.92, 50.46)	496.95 (376.47, 641.51)	−1.16 (−1.80, −0.51)
Western Sub-Saharan Africa	135.38 (102.55, 178.19)	581.54 (469.32, 726.04)	282.42 (210.29, 378.17)	514.29 (408.95, 658.46)	−0.59 (−0.67, −0.51)

UI, urinary incontinence; ASR, age-standardized rate; EAPC, estimated annual percentage change.

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104.19) in 2019 (**Supplementary Fig. S1B**). The ASDR in the Republic of Korea showed the sharpest decrease (EAPC = −9.59; 95% UI = −10.30, −8.87), and that in Zimbabwe showed the most rapid increase (EAPC = 0.39; 95% UI = 0.12, 0.67) (**Supplementary Fig. S1C**).

The DALY rate of asthma

At the global level, the DALY number decreased from 2,232.11 × 10^4 in 1990 to 2,155.10 × 10^4 in 2019, and the age-standardized DALY rate decreased from 476.28/100,000 persons (95% UI = 378.49, 579.59) in 1990 to 273.63/100,000 to persons (95% UI = 216.71, 343.38) in 2019,

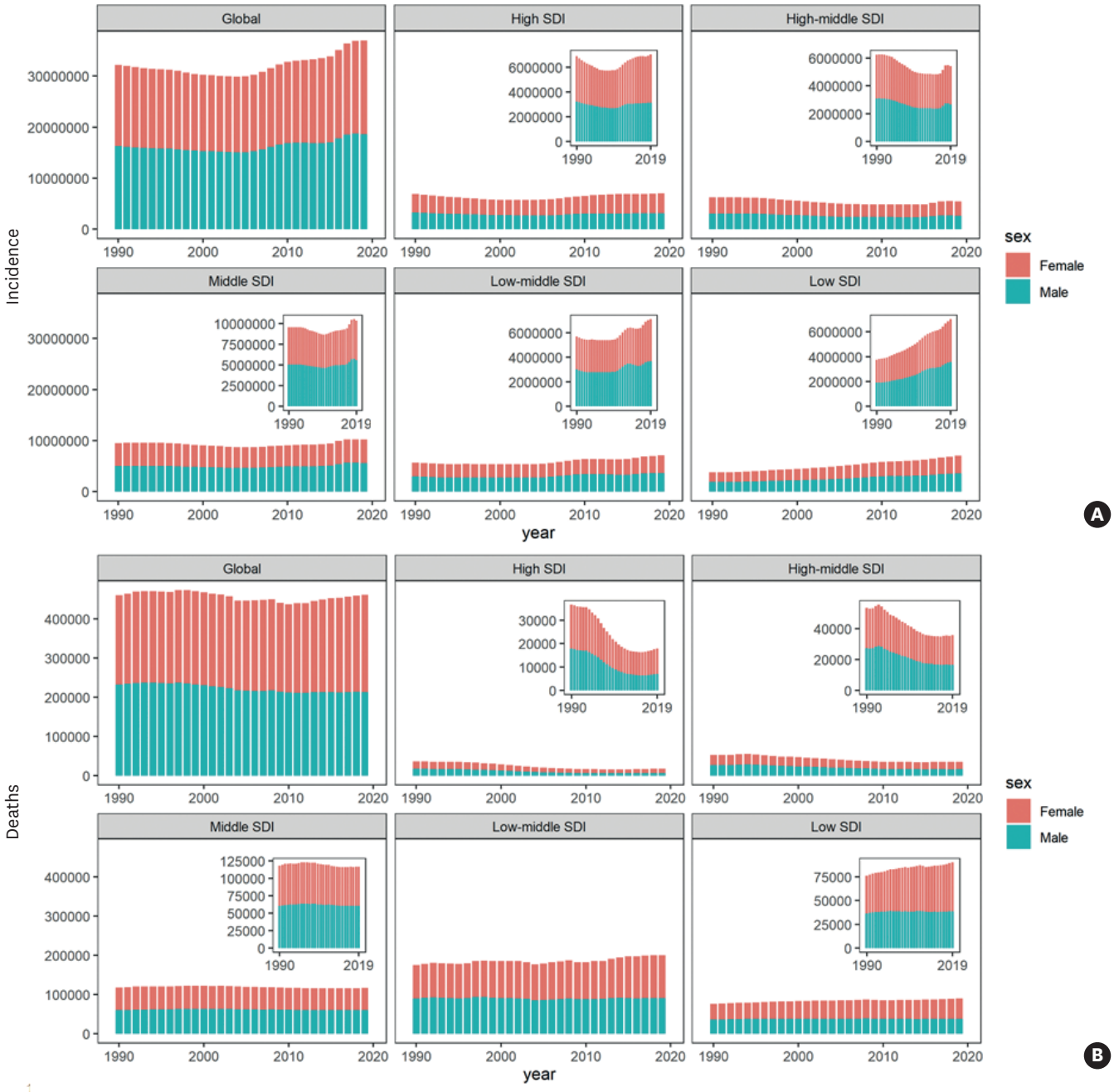

Fig. 1. Changes in (A) asthma incidence, (B) deaths, and (C) DALYs from 1990 to 2019. Blue bars represent males, and red bars represent females.
DALY, disability-adjusted life year; SDI, sociodemographic index.

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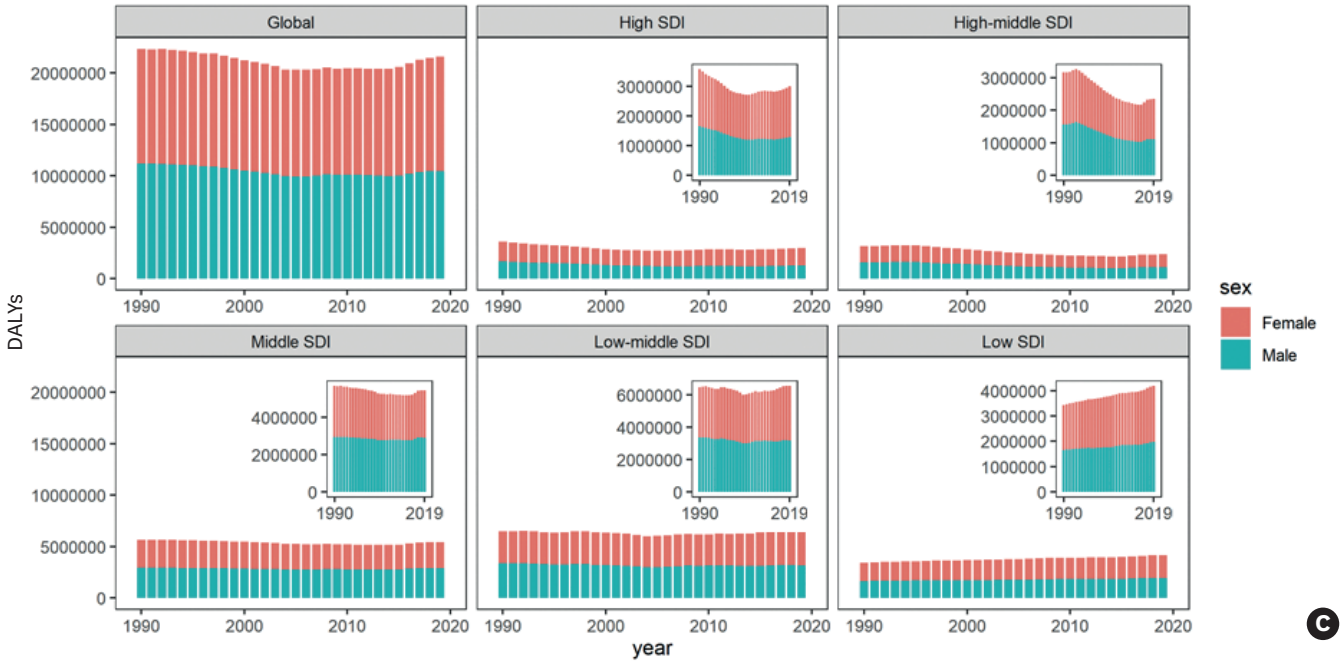

Fig. 1. (Continued) Changes in (A) asthma incidence, (B) deaths, and (C) DALYs from 1990 to 2019. Blue bars represent males, and red bars represent females.
DALY, disability-adjusted life year; SDI, sociodemographic index.

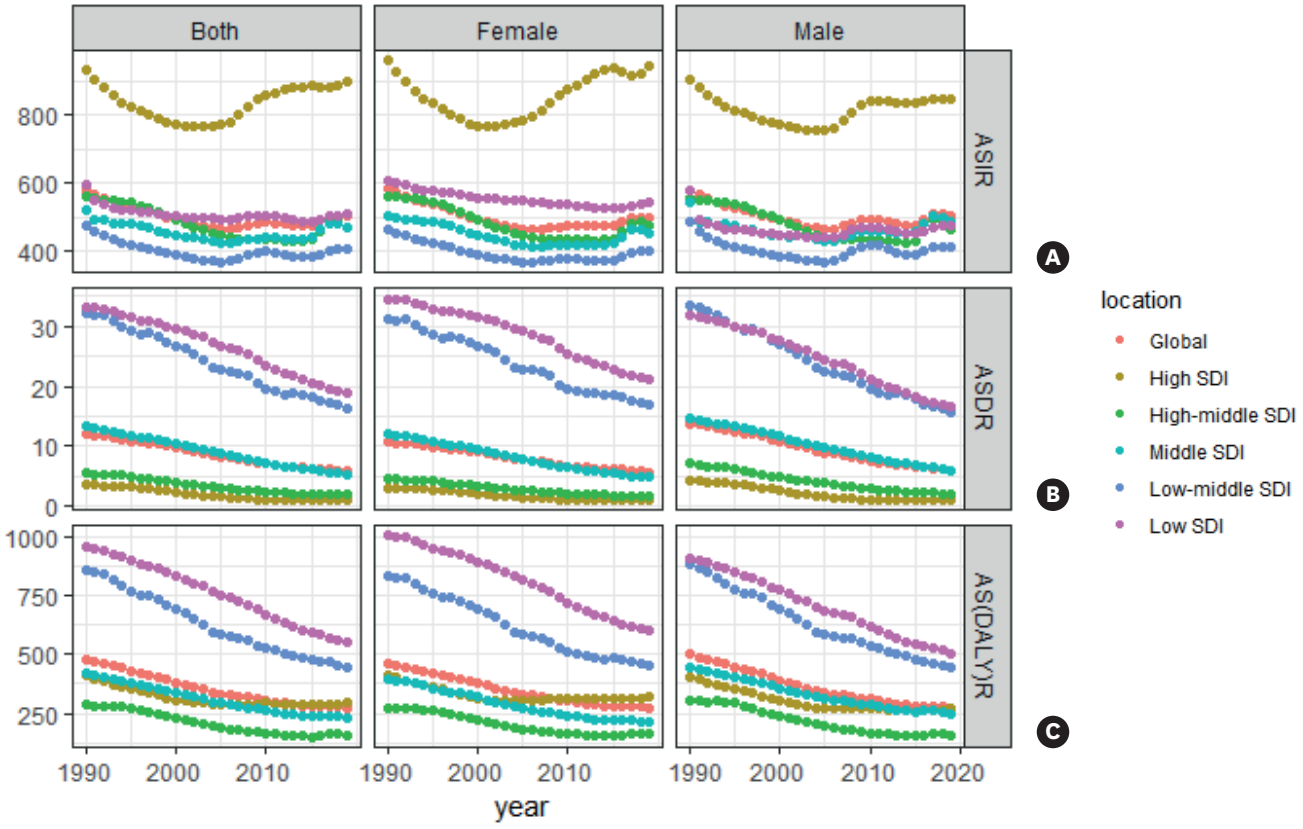

Fig. 2. The trends of (A) ASIR change, (B) ASDR, and (C) age-standardized DALY rate (per 100,000 persons) globally and among different SDI quintiles between 1990 and 2019.
ASIR, age-standardized incidence rate; ASDR, age-standardized death rate; DALY, disability-adjusted life year; SDI, sociodemographic index.

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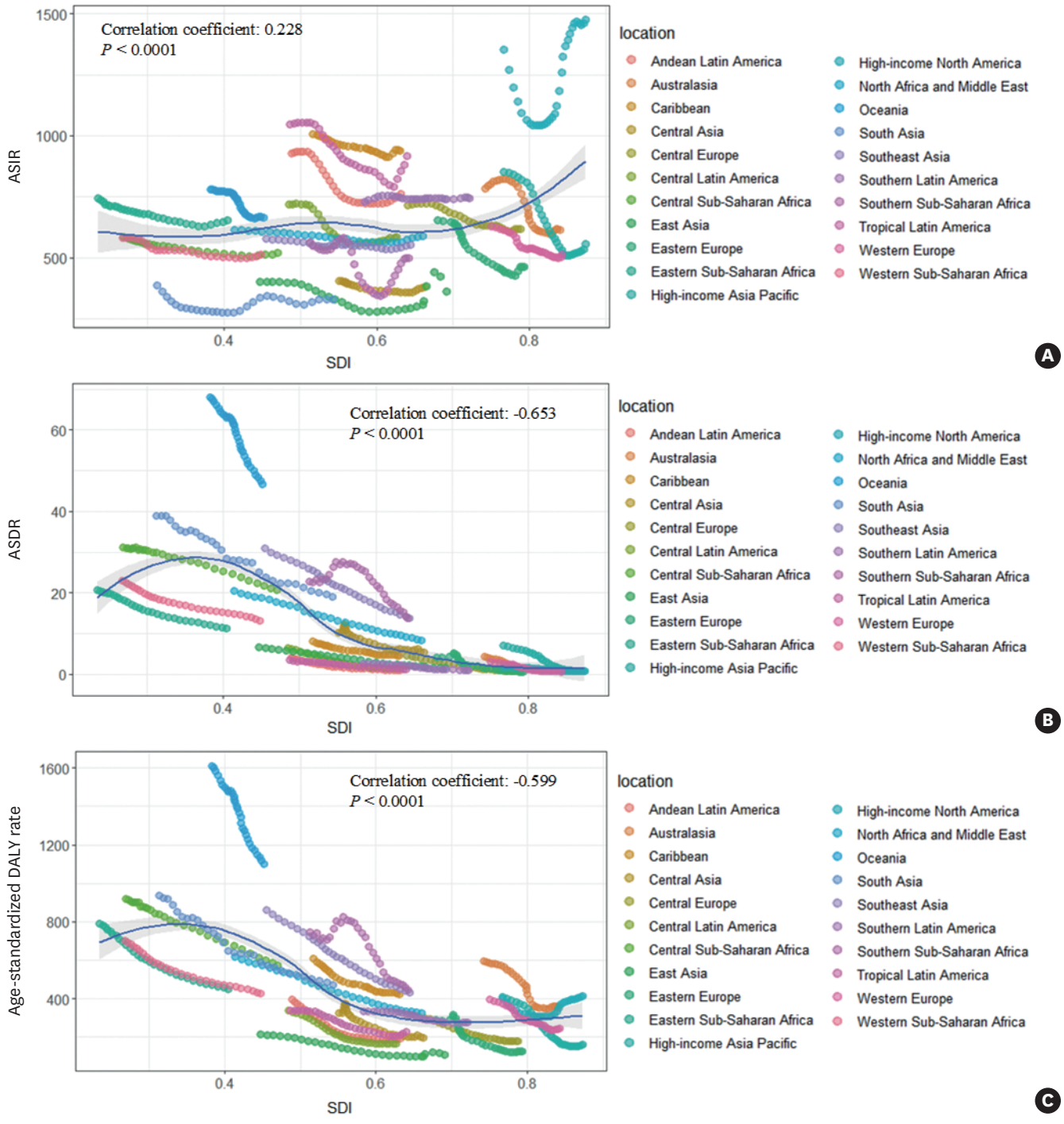

Fig. 3. The change trends and correlation analyses of age-standardized rates and SDI (2019) from 1990 to 2019 in 21 Global Burden of Disease regions. (A) ASIRs-SDI (2019). (B) ASDRs-SDI (2019). (C) Age-standardized DALY rates-SDI (2019).
ASIR, age-standardized incidence rate; ASDR, age-standardized death rate; DALY, disability-adjusted life year; SDI, sociodemographic index.

EAPC = −2.05 (95% UI = −2.16, −1.94) (**Table 3**). Subgroup analysis by sociodemographic factor showed that only the DALY numbers in the low SDI and low-middle SDI regions increased from 1990 to 2019 (**Fig. 1C**). The age-standardized DALY rates in the 5 SDI regions all decreased and were most serious in the high-middle SDI region, with an EAPC of −2.52

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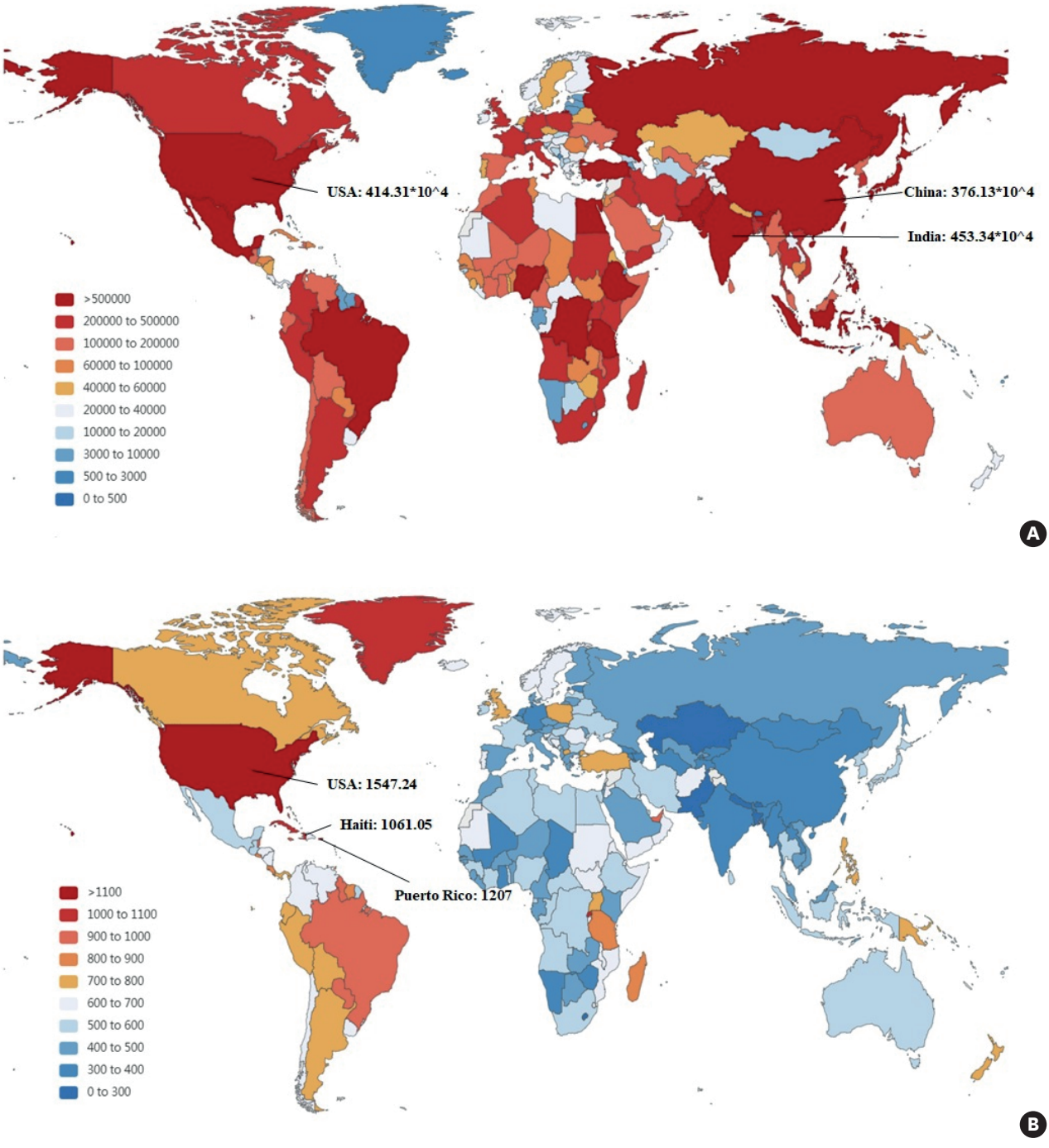

Fig. 4. The global disease burden of asthma in 204 countries or territories. (A) The absolute number of asthma cases in 2019. (B) The ASIR (per 100,000 persons) of asthma in 2019. (C) The EAPCs in asthma ASIRs between 1990 and 2019.
ASIR, age-standardized incidence rate; EAPC, estimated annual percentage change.

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(95% UI = −2.76, −2.27) (**Fig. 2C**). In the subgroup analysis of 21 GBD regions, the top 2 highest DALY numbers were observed in South Asia and Southeast Asia (South Asia: 690.76 × 10^4 in 2019; Southeast Asia: 267.87 × 10^4 in 2019). The age-standardized DALY rate in high-income North America was the only one showing an upward trend with an EAPC = 0.74 (95% UI = 0.34, 1.15), and that in high-income Asia Pacific displayed the greatest decrease with

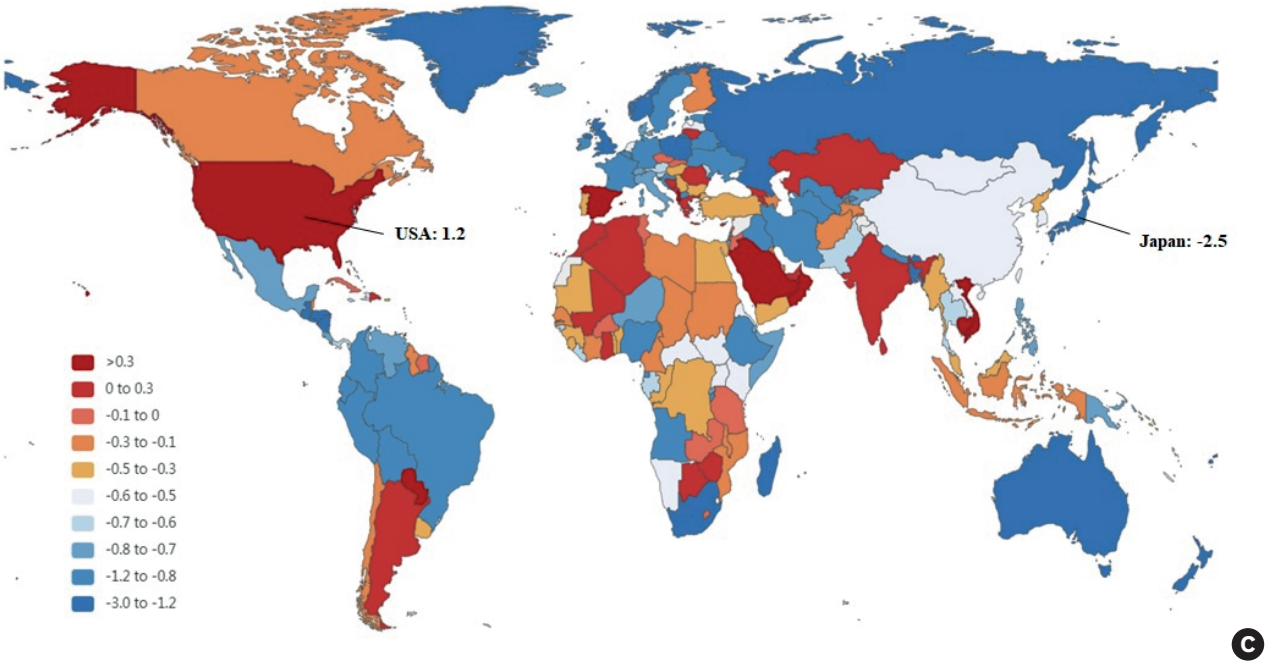

Fig. 4. (Continued) The global disease burden of asthma in 204 countries or territories. (A) The absolute number of asthma cases in 2019. (B) The ASIR (per 100,000 persons) of asthma in 2019. (C) The EAPCs in asthma ASIRs between 1990 and 2019.
ASIR, age-standardized incidence rate; EAPC, estimated annual percentage change.

an EAPC = −3.99 (95% UI = −4.38, −3.59). Similar to the ASDR, the age-standardized DALY rate tended to decrease with increasing SDI values (**Fig. 3C**). At the level of 204 countries and territories, India, the USA, China, and Indonesia had the most DALY numbers (583.88×10^4, 141.32×10^4, 141.46×10^4, and 104.50×10^4 in 2019, respectively) (**Supplementary Fig. S2A**). Kiribati had the highest age-standardized DALY rate, 2,630.86/100,000 persons (95% UI = 2,187.96, 3,178.83) in 1990 and 1,795.09/100,000 persons (95% UI = 1,411.44, 2,242.16) in 2019 (**Supplementary Fig. S2B**). In the past 30 years, the age-standardized DALY rate in the Maldives showed the fastest decrease (EAPC = −5.42; 95% UI= −5.81, −5.04), and that in the USA showed the most pronounced increase (EAPC = 0.83; 95% UI = 0.40, 1.26) (**Supplementary Fig. S2C**).

Age and sex distribution of asthmatic patients

Globally, over the past 30 years, although the number of asthma cases was higher in males than in females, deaths and DALYs in females gradually exceeded those in males. The peak incidence of asthma occurred in those aged younger than 5 years, and the asthma incidence aged between 5 and 9 years was also extremely high (**Fig. 5A**). The ratio of patients aged younger than 24 years to total individuals was approximately 66% in 2019. Before the age of 9 years, the asthma incidence in male individuals was higher, and the reverse was true thereafter. The number of asthma deaths remained at a stable low level between the ages of 5 and 29 years, with a gradual upward trend from the age of 35 years until the peak at 80 plus years. Worryingly, the deaths of children under 5 years were also not low (**Fig. 5B**). Regarding the number of DALY in 2019, 2 peaks were observed: children (younger than 9 years old) and the elderly (60 to 64 years old). The DALY cases were higher in females than in males aged 20 to 49 years in 1990, and they were higher in females than in males after the age of 25 years in 2019 (**Fig. 5C**). We analyzed changes in the incidence, death, and DALY rates of asthma in different age groups during the past 30 years and found that compared with older

https://doi.org/10.4168/aair.2023.15.4.473

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Table 2. The death cases and age-standardized incidence rate of asthma between 1990 and 2019 and its temporal trends from 1990 to 2019

Characteristics	1990	1990	2019	2019	1990–2019
	Death cases, No. ×10^3 (95% UI)	ASR per 100,000, No. (95% UI)	Death cases, No. ×10^3 (95% UI)	ASR per 100,000, No. (95% UI)	EAPC, No. (95% UI)
Overall	460.01 (342.62, 599.60)	11.91 (8.80, 15.86)	461.07 (366.58, 559.01)	5.80 (4.62, 7.03)	−2.65 (−2.73, −2.57)
Sex					
Male	232.93 (168.39, 323.36)	13.76 (9.82, 19.51)	213.67 (174.06, 260.24)	5.93 (4.84, 7.21)	−3.06 (−3.14, −2.98)
Female	227.08 (152.95, 313.98)	10.67 (7.15, 14.80)	247.40 (179.85, 320.09)	5.72 (4.16, 7.39)	−2.32 (−2.41, −2.24)
Sociodemographic index					
Low	75.92 (52.69, 102.49)	33.26 (22.16, 49.06)	90.18 (65.75, 127.84)	18.94 (13.35, 28.66)	−2.03 (−2.16, −1.90)
Low-middle	175.69 (118.67, 247.70)	32.29 (21.25, 48.01)	200.06 (143.31, 257.38)	16.29 (11.60, 21.33)	−2.46 (−2.55, −2.36)
Middle	118.02 (92.35, 150.27)	13.26 (10.19, 17.46)	116.85 (100.29, 131.92)	5.33 (4.55, 6.02)	−3.25 (−3.34, −3.15)
High-middle	53.39 (45.39, 64.00)	5.50 (4.64, 6.65)	35.68 (30.69, 40.38)	1.83 (1.57, 2.07)	−4.16 (−4.32, −4.00)
High	36.67 (32.6, 39.1)	3.57 (3.17, 3.81)	17.96 (15.62, 20.18)	0.96 (0.86, 1.07)	−5.35 (−5.76, −4.93)
Region					
Central Asia	4.47 (3.68, 5.32)	10.26 (8.30, 12.43)	3.34 (2.87, 4.05)	5.42 (4.69, 6.54)	−2.96 (−3.34, −2.59)
Central Europe	6.36 (5.78, 6.82)	4.63 (4.20, 5.00)	1.78 (1.51, 2.14)	0.81 (0.69, 0.98)	−6.52 (−6.87, −6.17)
Eastern Europe	11.36 (9.33, 12.43)	4.20 (3.43, 4.62)	2.33 (1.96, 3.41)	0.70 (0.59, 1.02)	−7.62 (−8.16, −7.09)
Australasia	0.98 (0.88, 1.06)	4.33 (3.88, 4.67)	0.54 (0.45, 0.64)	1.14 (0.96, 1.31)	−4.93 (−5.61, −4.26)
High-income Asia Pacific	12.38 (9.71, 13.50)	7.03 (5.44, 7.69)	4.95 (3.76, 6.27)	0.83 (0.66, 1.04)	−8.69 (−9.24, −8.14)
High-income North America	5.53 (5.10, 6.36)	1.65 (1.53, 1.88)	4.37 (3.59, 4.70)	0.83 (0.70, 0.88)	−2.96 (−3.26, −2.67)
Southern Latin America	1.26 (1.10, 1.41)	2.79 (2.45, 3.12)	0.88 (0.73, 1.01)	1.07 (0.89, 1.21)	−3.61 (−3.80, −3.42)
Western Europe	17.56 (15.99, 19.07)	3.11 (2.83, 3.36)	6.90 (5.73, 7.83)	0.70 (0.61, 0.79)	−5.74 (−6.17, −5.30)
Andean Latin America	1.29 (0.91, 1.61)	4.13 (3.09, 5.01)	0.52 (0.40, 0.66)	0.95 (0.73, 1.19)	−4.97 (−5.17, −4.77)
Caribbean	2.39 (1.88, 2.91)	8.06 (6.35, 10.09)	2.23 (1.69, 2.83)	4.54 (3.43, 5.83)	−1.96 (−2.09, −1.84)
Central Latin America	5.75 (4.90, 6.17)	6.52 (5.64, 7.02)	3.42 (2.81, 4.05)	1.49 (1.23, 1.76)	−5.55 (−5.83, −5.27)
Tropical Latin America	3.28 (2.88, 3.59)	3.45 (3.01, 3.79)	2.94 (2.61, 3.45)	1.28 (1.14, 1.50)	−3.64 (−3.84, −3.44)
North Africa and Middle East	32.42 (26.00, 42.14)	20.45 (15.90, 28.03)	32.08 (26.20, 38.35)	8.39 (6.86, 9.92)	−3.16 (−3.23, −3.09)
South Asia	185.11 (118.30, 278.67)	38.82 (24.26, 61.63)	232.19 (160.83, 316.30)	18.95 (12.92, 26.43)	−2.61 (−2.75, −2.47)
East Asia	43.49 (33.08, 61.96)	6.60 (4.92, 9.65)	27.21 (22.73, 33.03)	1.59 (1.33, 1.93)	−5.18 (−5.40, −4.96)
Oceania	1.60 (1.26, 2.12)	67.94 (51.62, 94.50)	2.56 (1.89, 3.45)	46.76 (34.38, 63.61)	−1.29 (−1.37, −1.20)
Southeast Asia	72.71 (55.59, 86.99)	30.93 (22.89, 38.63)	72.06 (61.16, 81.55)	13.79 (11.64, 15.64)	−2.74 (−2.81, −2.67)
Central Sub-Saharan Africa	7.10 (4.64, 10.33)	31.20 (18.83, 55.74)	9.79 (6.18, 17.11)	20.63 (12.04, 41.64)	−1.38 (−1.60, −1.16)
Eastern Sub-Saharan Africa	18.63 (14.01, 22.32)	20.73 (15.29, 28.44)	19.76 (15.36, 28.24)	11.29 (8.54, 17.52)	−2.23 (−2.30, −2.15)
Southern Sub-Saharan Africa	6.39 (5.50, 7.60)	22.72 (19.10, 27.97)	7.11 (6.30, 8.29)	13.78 (12.14, 16.11)	−1.80 (−2.40, −1.19)
Western Sub-Saharan Africa	19.95 (15.91, 23.96)	23.04 (18.35, 28.45)	24.11 (19.91, 29.11)	13.13 (10.95, 15.72)	−1.83 (−1.87, −1.79)

UI, urinary incontinence; ASR, age-standardized rate; EAPC, estimated annual percentage change.

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Table 3. The DALYs and age-standardized DALY rate of asthma between 1990 and 2019 and its temporal trends from 1990 to 2019

Characteristics	1990	1990	2019	2019	1990–2019
	DALY cases, No. ×10^4 (95% UI)	Age-standardized DALY rate per 100,000, No. (95% UI)	DALY cases, No. ×10^4 (95% UI)	Age-standardized DALY rate per 100,000, No. (95% UI)	EAPC, No. (95% UI)
Overall	2,232.11 (1,790.95, 2,734.42)	476.28 (378.49, 579.59)	2,155.10 (1,714.16, 2,697.2)	273.63 (216.71, 343.38)	−2.05 (−2.16, −1.94)
Sex					
Male	1,118.99 (896.42, 1,392.93)	498.88 (392.53, 620.97)	1,043.47 (831.89, 1,305.02)	272.16 (216.88, 340.92)	−2.22 (−2.33, −2.10)
Female	1,113.12 (854.82, 1,393.92)	461.30 (353.71, 579.02)	1,111.63 (867.46, 1,407.52)	275.24 (214.89, 349.63)	−1.94 (−2.05, −1.84)
Sociodemographic index					
Low	342.34 (264.04, 407.69)	958.70 (705.09, 1,243.84)	418.87 (332.02, 525.88)	553.90 (434.74, 726.78)	−1.99 (−2.07, −1.91)
Low-middle	647.86 (486.57, 802.91)	859.43 (615.47, 1,143.21)	655.82 (519.11, 797.41)	445.90 (348.53, 546.29)	−2.36 (−2.44, −2.28)
Middle	566.51 (463.59, 691.22)	419.94 (341.9, 508.8)	542.95 (436.30, 675.84)	230.64 (183.79, 290.27)	−2.20 (−2.29, −2.11)
High-middle	316.31 (245.87, 410.70)	286.79 (224.27, 369.40)	235.39 (176.17, 316.81)	158.33 (114.00, 220.25)	−2.52 (−2.76, −2.27)
High	357.27 (263.10, 483.65)	409.25 (295.92, 561.89)	300.22 (209.17, 420.21)	293.69 (200.72, 419.44)	−1.10 (−1.36, −0.85)
Region					
Central Asia	17.48 (14.36, 21.24)	324.22 (270.15, 387.10)	16.07 (12.66, 20.47)	197.95 (160.01, 246.02)	−2.45 (−2.76, −2.15)
Central Europe	42.59 (32.15, 56.97)	317.67 (236.94, 429.27)	22.63 (15.72, 31.84)	180.45 (119.9, 263.92)	−2.27 (−2.48, −2.07)
Eastern Europe	72.43 (56.56, 92.70)	288.54 (221.46, 374.87)	26.08 (18.44, 36.39)	124.09 (84.15, 182.59)	−3.78 (−4.09, −3.47)
Australasia	12.08 (8.90, 16.22)	593.53 (433.65, 802.06)	10.11 (6.92, 14.49)	359.99 (239.04, 527.64)	−2.28 (−2.52, −2.03)
High-income Asia Pacific	74.19 (55.81, 98.14)	409.49 (306.25, 543.25)	33.58 (23.72, 46.49)	160.29 (105.89, 237.58)	−3.99 (−4.38, −3.59)
High-income North America	112.01 (78.38, 157.65)	401.62 (276.72, 570.29)	148.46 (102.18, 205.73)	412.95 (282.52, 584.39)	0.74 (0.34, 1.15)
Southern Latin America	16.24 (11.72, 22.12)	333.79 (242.27, 454.37)	19.06 (13.04, 27.12)	275.77 (188.18, 399.41)	−0.88 (−0.95, −0.81)
Western Europe	176.88 (129.03, 241.52)	396.41 (284.2, 551.61)	115.01 (78.58, 164.12)	245.62 (162.85, 361.91)	−1.79 (−1.95, −1.63)
Andean Latin America	18.37 (13.12, 24.63)	396.37 (290.64, 521.9)	12.16 (7.86, 18.56)	192.28 (124.91, 291.95)	−2.78 (−3.13, −2.42)
Caribbean	21.74 (16.29, 27.56)	608.76 (462.11, 763.86)	19.30 (14.62, 24.99)	422.79 (315.68, 553.54)	−1.25 (−1.37, −1.14)
Central Latin America	52.91 (40.52, 69.98)	337.68 (271.21, 429.32)	40.39 (28.31, 57.46)	166.15 (116.28, 237.45)	−2.75 (−3.05, −2.45)
Tropical Latin America	53.57 (37.98, 76.89)	340.11 (250.73, 473.47)	46.60 (32.18, 68.55)	227.28 (154.5, 339.89)	−2.03 (−2.22, −1.84)
North Africa and Middle East	152.44 (124.45, 182.69)	618.12 (513.67, 757.56)	167.78 (131.81, 212.26)	324.16 (259.23, 397.53)	−2.38 (−2.45, −2.31)
South Asia	610.59 (428.46, 820.81)	935.82 (632.71, 1,352.04)	690.76 (520.56, 869.53)	472.00 (350.52, 601.23)	−2.44 (−2.51, −2.36)
East Asia	213.84 (160.83, 280.15)	215.90 (165.88, 279.90)	152.81 (114.20, 206.25)	106.42 (75.33, 152.05)	−2.87 (−3.30, −2.43)
Oceania	6.23 (5.11, 7.79)	1,610.92 (1,286.27, 2,090.81)	9.50 (7.41, 12.22)	1,102.21 (863.7, 1,431.32)	−1.30 (−1.38, −1.23)
Southeast Asia	296.37 (245.48, 341.1)	860.93 (699.29, 995.38)	267.87 (225.29, 316.45)	433.23 (365.45, 509.73)	−2.37 (−2.40, −2.34)
Central Sub-Saharan Africa	36.53 (25.88, 45.29)	920.05 (640.15, 1,325.52)	47.95 (34.14, 65.87)	572.95 (389.25, 907.95)	−1.64 (−1.82, −1.46)
Eastern Sub-Saharan Africa	122.82 (96.13, 149.56)	790.39 (622.07, 947.47)	145.06 (112.06, 185.67)	450.86 (356.42, 582.77)	−2.07 (−2.12, −2.02)
Southern Sub-Saharan Africa	29.37 (25.01, 34.92)	744.87 (640.15, 871.84)	29.90 (24.90, 36.62)	446.49 (378.51, 530.69)	−1.97 (−2.45, −1.49)
Western Sub-Saharan Africa	93.44 (77.18, 110.39)	704.15 (582.61, 830.73)	134.01 (108.09, 167.04)	425.22 (354.05, 508.79)	−1.75 (−1.80, −1.70)

DALY, disability-adjusted life year; UI, urinary incontinence; EAPC, estimated annual percentage change.

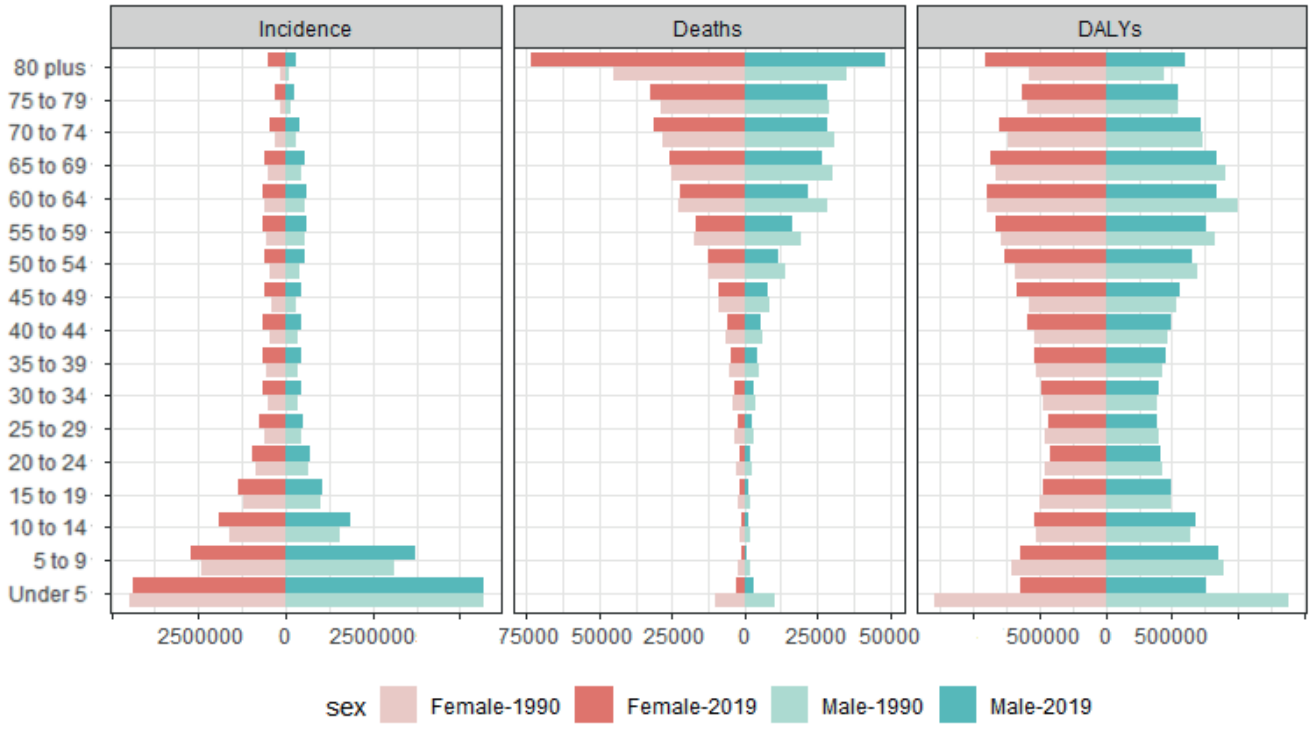

Fig. 5. The global burden of asthma in both sexes and different age groups in 1990 and 2019. (A) The absolute number of asthma cases. (B) The absolute number of deaths. (C) The absolute number of DALYs. Blue bars represent male individuals, and red bars represent female individuals; light bars represent 1990, and dark bars represent 2019.
DALY, disability-adjusted life year.

patients, the death and DALY rates of younger patients younger than 50 years were lower than those of ASDR and the age-standardized DALY rate, respectively. In addition, the death and DALY rates of patients older than 50 years decreased more significantly over the year (**Supplementary Fig. S3**).

Correlations between the SDI and asthma burden

First, we calculated the correlation coefficients between the SDI in 2019 and EAPC values of the ASIR, ASDR, and age-standardized DALY rate in 204 countries and territories. The correlations between the SDI and EAPCs of ASIR and age-standardized DALY rate were not statistically significant, whereas the EAPC of the ASDR was markedly negatively correlated with the SDI (correlation coefficient of EAPC = −0.572; $P < 0.0001$) (**Fig. 6**). To further evaluate the association between the SDI and asthma burden, we investigated the correlation between the SDI and ASIR, ASDR and age-standardized DALY rate in 21 GBD regions worldwide from 1990 to 2019. The ASIR value was positively correlated with the SDI (correlation coefficient of the ASIR = 0.228; $P < 0.0001$); however, the ASDR and age-standardized DALY rate values were negatively correlated with the SDI (correlation coefficient of the ASDR = −0.653; correlation coefficient of the age-standardized DALY rate = −0.599; $P < 0.0001$) (**Fig. 3**).

Asthma-related death and DALY attributable risk factors from 1990 to 2019

We searched the GBD database for potential asthma-related risk factors for deaths and DALYs. The leading risk factors for deaths and DALYs due to asthma were smoking, occupational asthmagens, and high body mass index. From 1990 to 2019, globally, the

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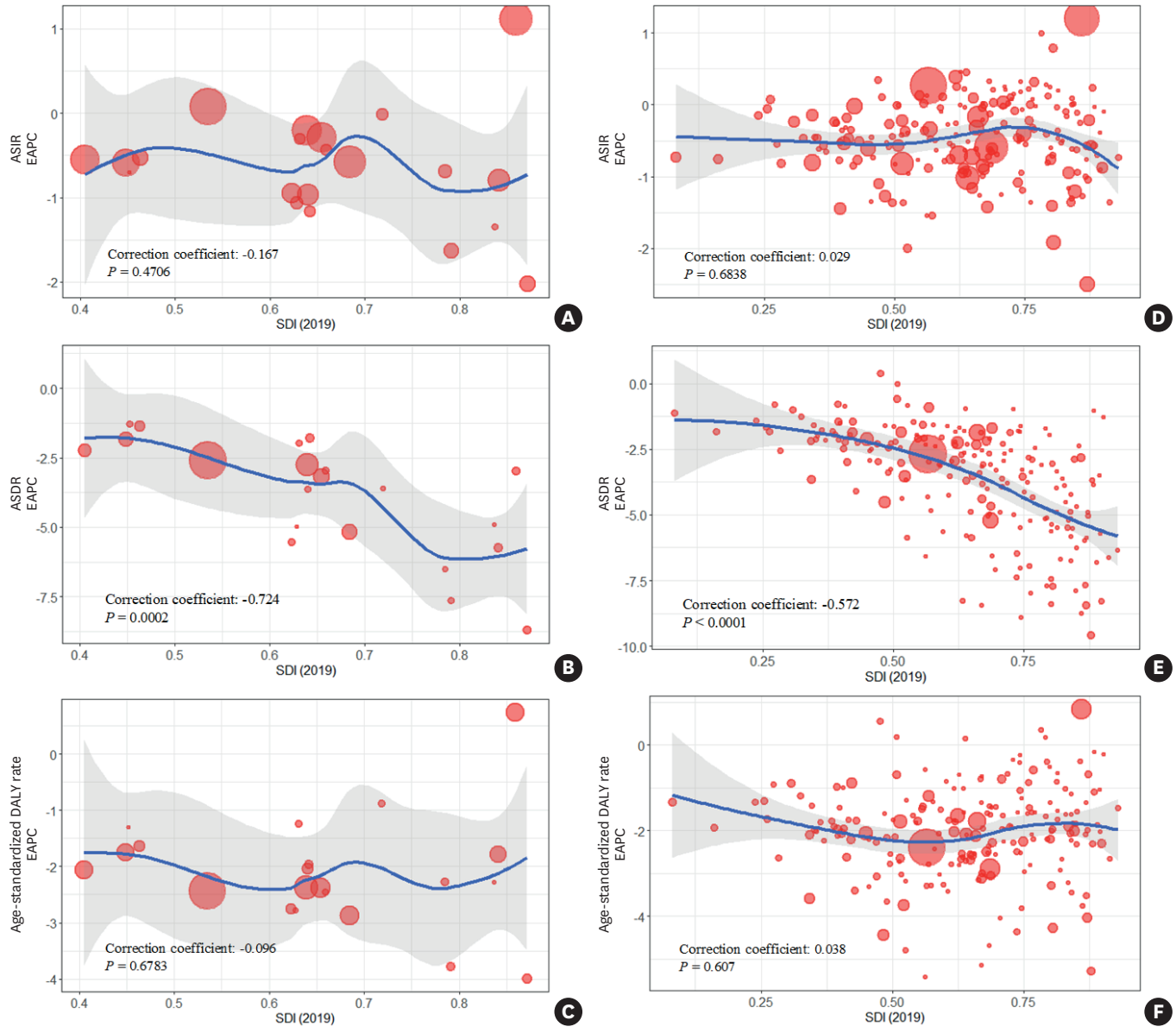

Fig. 6. Correlation analyses of EAPCs-SDI (2019). EAPCs of (A) ASIR-SDI (2019), (B) ASDR-SDI (2019), and (C) age-standardized DALY rate-SDI (2019) in 21 GBD regions; EAPCs of (D) ASIR-SDI (2019), (E) ASDR-SDI (2019), and (F) age-standardized DALY rate-SDI (2019) in 204 countries or territories. The size of the circle represents the quantity of asthma patients in a single region/country or territory.
ASIR, age-standardized incidence rate; ASDR, age-standardized death rate; DALY, disability-adjusted life year; EAPC, estimated annual percentage change; SDI, sociodemographic index.

proportion of asthma deaths/DALYs attributable to smoking declined, and the proportion of patients with a high body mass index increased. For occupational asthmagens, the proportion of asthma deaths also decreased; however, the proportion of asthma DALYs showed no obvious change law.

Smoking-related asthma deaths/DALYs showed a downward trend in all SDI quintiles, most notably in the high SDI region. The proportions of asthma deaths/DALYs attributable to a high body mass index showed an upward trend in all SDI quintiles, most significantly in the high SDI region. At the same time, we found that the higher the SDI was, the higher the

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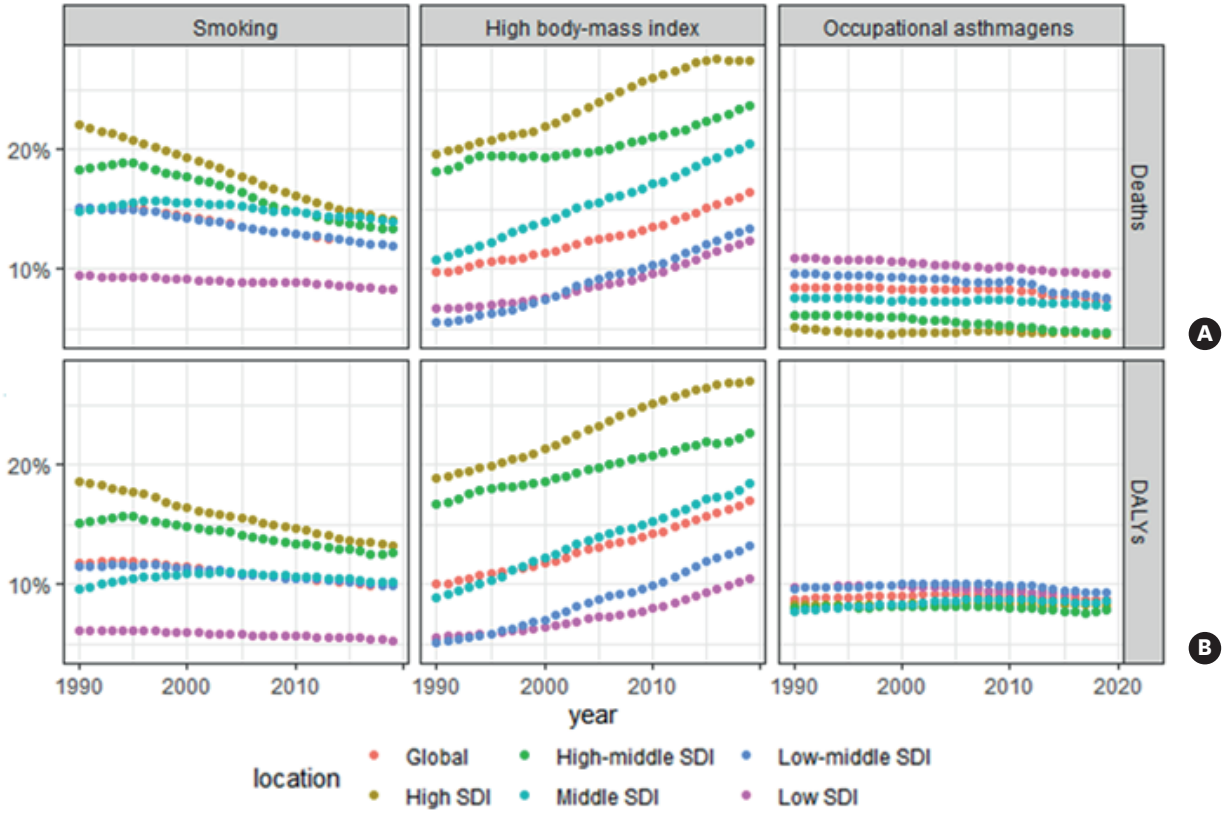

Fig. 7. Risk factors for asthma-related deaths and DALYs. (A) The proportions of the 3 risk factors contributing to asthma-related deaths from 1990 to 2019 globally and in different regions. (B) The proportions of the 3 risk factors contributing to asthma-related DALYs from 1990 to 2019 globally and in different regions.
DALY, disability-adjusted life year; SDI, sociodemographic index.

proportion of asthma deaths/DALYs attributed to smoking/high body mass index, but that for occupational asthmagens was almost the opposite (**Fig. 7**).

For 21 GBD regions, the percentage of asthma deaths/DALYs attributable to smoking/occupational asthmagens was much higher in males than in females; however, that for high body mass index was reversed. It is important to note that in all GBD regions, the percentage of asthma deaths/DALYs attributable to high body mass index increased in 2019 when compared with 1990 in both sexes (**Supplementary Fig. S4**). At all ages, the percentage of asthma deaths/DALYs attributable to smoking/occupational asthmagens was significantly higher in males than in females. For high body mass index, the percentage was much higher in females than in males and higher in 2019 than in 1990 (**Supplementary Fig. S5**).

To determine the relationship between risk factors associated with asthma deaths/DALYs and the SDI, we also calculated the correlation coefficient between the SDI and percentage of asthma-related risk factors in 204 countries and territories. By analyzing the data on risk factors associated with asthma deaths, the proportion of high body mass index/smoking increased as the SDI value increased, showing a positive correlation (correlation coefficient of high body mass index = 0.66; $P < 0.0001$ in 2019; correlation coefficient of smoking = 0.511; $P < 0.0001$ in 2019). However, our findings demonstrated a negative correlation between the proportion of asthma-related occupational asthmagens and the SDI (correlation coefficient of occupational asthmagens = −0.692; $P < 0.0001$ in 2019). The relationship between the proportion of DALYs attributable to high body mass index/smoking and SDI was similar to that between

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the proportion of high body mass index/smoking attributable to asthma deaths and the SDI; however, the association between the proportion of occupational asthmagens contributing to asthma DALYs and the SDI was not statistically significant (**Supplementary Fig. S6**).

DISCUSSION

Understanding the temporal trends of the asthma burden facilitates the initiation of more targeted public health strategies. The present study comprehensively reflected the latest global burden of asthma by analyzing data on the incidence, death, DALY, and most relevant risk factors for asthma from 1990 to 2019. Although the incidence and death rate of asthma slightly increased (15% and 0.2%, respectively) during the past 30 years, the overall ASIR, ASDR, and age-standardized DALY rate relatively decreased and showed a declining trend with negative EAPC values. This phenomenon might be attributable to the population size and distribution structure and the changes in diagnostic methods from clinical to laboratory examination—for example, lung function tests. In addition, variabilities in region, sex, and age played important roles in the asthma incidence and mortality. The incidence, death, and DALY of asthma were heterogeneous among people in different age groups and from country to country.

In 2019, the highest incidence was found in children aged younger than 9 years, particularly those aged 0 to 5 years, because they are vulnerable to respiratory infections and other environmental hazards.[22] In addition, the age-specific incidence was higher in boys (0–9 years old), almost equal in sex during adolescence (10–14 years old), and higher in females later, indicating a switch during puberty (**Fig. 5A**). Possibly because of the high diagnosis rate of asthma in that age group, this finding was consistent with those of some large sample studies.[23,24] Boys have higher incidences partly because of their smaller airway relative to lung size compared with girls, but this mode reverses during puberty. Additionally, a prospective study confirmed that asthma remission was more likely in boys, but less likely in girls and severe asthma or sensitization to furred animals.[25] These factors explain the high incidence of asthma in young boys. The incidence of asthma after puberty was higher in females than in males, particularly in middle-aged women, likely because of their obvious hormonal changes. Menopause, for example, was used as a forceful predictor of asthma in women not using exogenous hormones.[26]

The number of asthma deaths increased with age, and most asthma deaths occurred in people aged older than 60 years (more than 70% of all deaths) (**Fig. 5B**). One reason is the increasingly prominent aging social structure; currently, 8.5% of the world's population is aged older than 60 years.[27] Between 1990 and 2019, the number of older persons (those aged 60 years or older) in the world grew by 114%, from 483 million to more than 1.03 billion. The number of children aged younger than 14 years also showed an increasing trend (1990: 1.7 billion; 2019: 2.0 billion).[28] Thus, the ratio of elderly and pediatric patients with asthma has increased. A second reason is that some studies have shown that asthma with onset later in life has a poorer prognosis.[29,30] The pathophysiology of asthma in elderly individuals is different from that of early-onset asthma. Older individuals experience a decrease in elastic fibers, curvature in the spine, and a stiffening of the thorax because of a decline in particular movements, all of which will decrease the amount of traction on the bronchi of the lungs. For elderly patients, these events may lead to the narrowing of the bronchioles.[31] Iwanaga *et al.*[32] found that R5-R20, representing the index for the small airway, was distinctly higher in elderly asthmatic patients aged older than 65 years. Therefore, small airway disease was more

https://doi.org/10.4168/aair.2023.15.4.473

severe in elderly asthmatic patients than in younger patients with asthma. Furthermore, the disease burden is mainly focused on 2 groups of people, those aged older than 60 years and children younger than 9 years, which were the focus of our healthcare institutions.

The burden of asthma was the highest in South Asia, Southeast Asia, and East Asia, and it was higher in high-income North America, Western Sub-Saharan Africa, and Tropical Latin America. South Asia, Southeast Asia and East Asia, are the most densely populated regions in the world, home to approximately half of the world's population. The large population also contributed to the higher burden of asthma. Tropical Latin America is usually racially admixed, with heterogeneous proportions of European, Native American, and African ancestry. A study showed that African ancestry has been associated with lower lung function, leading to an increased susceptibility to asthma in these populations.[33] Therefore, it makes sense for Western Sub-Saharan Africa and Tropical Latin America to have a higher disease burden of asthma.

At the country level, except for China, India, and Indonesia, different countries faced different asthma burdens. Considering the increasing incidence of asthma in children in China, the National Clinical Research Center for Respiratory Diseases developed the Action Plan for Asthma in Children in China to improve the level of self-management of asthma in children.[34] Notably, the asthma incidence in the United States of America (USA) remained in the top 3 all along, and the ASIR not only always maintained the first place but also kept rising the fastest. Because the incidence and outcome of asthma vary widely across geographical regions, such as the greater disease burden in rural areas, rural health has become increasingly crucial in health surveillance and health equity in the US,[35] and much work has been performed to measure asthma indicators by demographic characteristics and poverty level.[36] Therefore, targeted health policy systems must be specified according to different situations.

During the past 30 years, asthma incidences have increased, particularly in high-income North America and South Asia. Moreover, our study demonstrated that the ASIR of asthma in high-income North America always remained the highest with an upward trend, such as in the USA. The region is one of the most economically developed in the world and rich in medical resources. Therefore, the screening and diagnosis of disease are timelier. Encouragingly, little increase was observed in the number of deaths and DALYs, and the ASDR and age-standardized DALY rate continued to decline, suggesting that health policy designation had a positive effect on the burden of asthma, both fatal and nonfatal. However, concerns persist about the burden of asthma in individual regions.

The difference in asthma burden changes is due to multiple factors. In addition to the health care system, it also includes biological, sociocultural, and built environments. For example, many risk alleles and loci representing almost all chromosomes in the human genome were identified by genome-wide association studies of asthma, such as 6p21, 2q12, 5q22, and 9p24. However, some studies have confirmed that every locus is not equally expressed in all populations. The 17q12-21 locus is verified as the most replicated and most distinct asthma locus and is highly associated with early-onset asthma among European, Asian, and Latino individuals. However, weak and inconsistent associations of 17q are found in Africans.[37,38] Therefore, the expression and polymorphism of asthma-related genes vary among ethnic groups, resulting in different disease occurrences and outcomes. A clear understanding of the changes in the burden of asthma and the characteristics of the disease will help policy-

https://doi.org/10.4168/aair.2023.15.4.473

makers develop more precise strategies to reduce the burden of asthma.

We demonstrated that the global distribution of asthma burden was heterogeneous and uneven. At the level of sociodemographic factors, the area with the highest disease burden of asthma was the high SDI region—for instance, the USA—likely attributable to better asthma diagnosis and registry systems, as well as increasing population size and obvious aging trends. However, in some low-SDI and middle-SDI regions with low-income countries, health resources are relatively limited, and defining asthma by reported symptoms and a clinician diagnosis could result in an underestimate of asthma incidence in those countries.[39] In addition, poverty, air pollution, climate change, exposure to indoor allergens, urbanization, and diet contribute to inadequate control and poor outcomes in developing countries.[40] In high-SDI regions with high-income countries, the burden of death and DALY was lower due to greater access to health care and better treatment options based on international asthma guidelines.[41] Therefore, the formulation of medical policies must be adjusted according to the actual local disease burden.

Our data showed that smoking, occupational asthmagens, and a high body-mass index were risk factors for asthma-caused death and DALY. A previous study showed that asthmatic patients who smoke have distinctly increased morbidity and mortality compared with nonsmokers.[42] Continued smoking is related to aggravated loss of lung function over time in adult-onset asthma.[43] Therefore, several initiatives have been implemented to reduce exposure to smoke. Some measures, such as banning advertising, creating tobacco-free spaces, inserting health warnings on the packaging of tobacco products, and increasing cigarette taxation, were advocated by the World Health Organization. The effect of high body mass index on asthma cannot be ignored. A study in the USA showed that genetic predisposition to obesity was a risk factor for asthma, particularly for childhood-onset asthma, in females[44] but not in males. Having an obese mother also increases the risk of asthma in children.[45] Obese asthma results in worse asthma control and increased healthcare utilization due to asthma.[46] We found that the higher the SDI, the higher the proportion of asthma deaths/DALYs attributed to smoking/high body mass index. Although the age-standardized global prevalence of daily smoking was 15.3%, a 29.4% decrease from 1990,[47] globally in 2019, most countries with the highest tobacco consumption per person were in the high SDI and high-middle SDI regions, such as Slovenia, Montenegro, and North Macedonia, all having consumption exceeding 2,350 cigarette equivalents per person. However, the low SDI regions, such as sub-Saharan Africa, had the lowest tobacco consumption per person.[48] Similarly, obesity is more common in developed countries than in developing countries.[49]

Occupational asthmagens, including gas, smoke or dust, organic dust, dampness and mold, cold conditions, and other agents, were associated with exacerbation of asthma. The proportion due to occupational asthmagens was much higher in the low and low-middle SDI regions, and no obvious downward trend of asthma deaths/DALYs was attributable to occupational asthmagens in either sex over time. With globalization, many manufacturing factories were relocated to underdeveloped regions; however, strict occupational protection was not fully implemented. Thus, some occupational interventions and policies to reduce work-related asthma were needed according to the SDI.

In summary, globally, the incidence of asthma has prominently increased, and children

https://doi.org/10.4168/aair.2023.15.4.473

have a higher risk of developing asthma. The number of deaths slightly increased, and more than 70% of all deaths occurred in patients aged older than 60 years. The low-middle SDI region, particularly South Asia, had the highest asthma-related death and DALY burden. The high SDI region had the highest ASIR, and the low SDI region had the highest ASDR. The ASDR and age-standardized DALY rate of asthma were negatively correlated with SDI values, indicating that the death and DALY rates were significantly higher in the developing regions than in the developed regions. Smoking, occupational asthmagen, and higher body mass index were the main risk factors contributing to asthma-related mortality and DALYs, and the effects of the 3 risk factors on asthma were different between sexes and regions. The asthma burden showed considerable spatiotemporal and sex-age heterogeneity. Globally, considering population growth and accelerated aging trends, the asthma burden might further increase. Systematic efforts must be achieved to reduce the asthma burden through ongoing efforts to identify the contribution of factors within the biological, behavioral, sociocultural, built environment, and healthcare domains to the development of asthma.

Although this study analyzed the global burden and attributable risk factors of asthma in 204 countries and territories from 1990 to 2019, it has several limitations. First, the accuracy of the GBD data used for analysis relies on the quality of the existing data in each country, and data collected by different regions and countries may vary substantially in terms of quality, comparability, accuracy, and the degree of data missing. Secondly, the lack of data on other asthma-associated risk factors limits the analysis of overall risk factors. Thirdly, our study is implemented at the regional and national levels and lacks an analysis of differences between urban and rural areas.

ACKNOWLEDGMENTS

This work were supported by The Scientific Research and Sharing Platform Construction Project of Shaanxi Province (Grant Number: 2022PT-07) and Scientific Research Foundation of The First Affiliated Hospital of Xi'an Jiaotong University (Project Number: 2021ZYTS-34).

SUPPLEMENTARY MATERIALS

Supplementary Fig. S1

Global death burden of asthma in 204 countries or territories. (A) Absolute number of asthma deaths in 2019. (B) ASDR (per 100,000 persons) of asthma in 2019. (C) Estimated annual percentage change of asthma ASDRs between 1990 and 2019.

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Supplementary Fig. S2

Global DALY burden of asthma in 204 countries or territories. (A) Absolute number of asthma DALYs in 2019. (B) Age-standardized DALY rate (per 100,000 persons) of asthma in 2019. (C) Estimated annual percentage change of asthma age-standardized DALY rate between 1990 and 2019.

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Supplementary Fig. S3

Trends of the incidence, death, and DALY rates (per 100,000 persons) among different age groups between 1990 and 2019.

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Supplementary Fig. S4

Proportion of deaths/DALYs attributable to 3 risk factors in 21 Global Burden of Disease regions in 1990 and 2019. Blue bars represent male individuals, and red bars represent female individuals; light bars represent 1990, and dark bars represent 2019.

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Supplementary Fig. S5

Proportions of deaths/DALYs attributable to 3 risk factors in different age groups in 1990 and 2019. Blue bars represent male individuals, and red bars represent female individuals; light bars represent 1990, and dark bars represent 2019.

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Supplementary Fig. S6

Correlation analyses of the proportions of 3 risk factors attributable to deaths/DALYs-SDI (2019). (A) Smoking attributable to deaths-SDI (2019) and (D) smoking attributable to DALYs-SDI (2019). (B) High body-mass index attributable to deaths-SDI (2019) and (E) high body-mass index attributable to DALYs-SDI (2019). (C) Occupational asthmagens attributable to deaths-SDI (2019) and (F) occupational asthmagens attributable to DALYs-SDI (2019). The size of the circle represents the quantity of asthmatic patients in a single country or territory.

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