Global, regional, national burden of asthma from 1990 to 2021, with projections of incidence to 2050: a systematic analysis of the global burden of disease study 2021

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Summary

Background Asthma is the second leading cause of mortality among chronic respiratory illnesses. This study provided a comprehensive analysis of the burden of asthma.

Methods Data on asthma were extracted from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021. We focused on the effects of age, sex, risk factors, and the socio-demographic index (SDI) on the burden of asthma and calculated the average annual percent change (AAPC) via joinpoint regression. Two-sample Mendelian randomization (MR) was adopted to estimate the causal relationships between risk factors and asthma. The Bayesian age-period-cohort (BAPC) model was used to predict incidence patterns of asthma from 2022 to 2050.

Findings In 2021, there was an observed prevalence of asthma, with 3,340 cases per 100,000 people. Males who were below 20 years old had a greater prevalence of asthma. The incidence and prevalence correlated positively with the SDI, whereas mortality and disability-adjusted life years (DALYs) correlated negatively. The contribution of high body mass index (BMI) to asthma DALYs increased by 4.3% worldwide between 1990 and 2021. MR studies have confirmed that high BMI and smoking can increase the risk of asthma. The prediction results indicated that the global age-standardised incidence rate will remain high from 2022 to 2050.

Interpretation The global mortality of patients with asthma is a significant concern. The analysis of the burden of asthma can help formulate public health policies, allocate resources, and prevent asthma.

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Keywords: Asthma; GBD 2021; Risk factors; Mendelian randomization; Prediction

Introduction

Asthma is a common respiratory disease characterized by wheezing, shortness of breath, chest tightness, and coughing.[1] It affects between 1% and 29% of the population across various countries.[2] The Global Asthma Report indicates that the global prevalence of asthma is 9.1% among children, 11.0% among adolescents, and 6.6% among adults.[3] For asthma patients and families around the world, asthma seriously affects the quality of life and brings a lot of burdens, including psychological burdens, medical burdens, and financial burdens.[4,5]

In recent years, the disease burden of asthma has been studied extensively. In low-income and low-middle-income areas, the burden of asthma is

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Research in context

Evidence before this study

Analyzing the global burden of asthma can guide resource allocation and health policy decision-making. The ability to predict the incidence of asthma is very important for guiding health system planning and providing information for funding decisions. We searched PubMed on November 15, 2024, using the search term 'asthma trends' and filtered the results to include studies published between 2023 and 2024; a total of 366 studies were obtained. Among them, 30 articles examined the burden of asthma in specific regions, 33 articles investigated the burden of asthma in children, and five articles addressed the disease burden in adolescents. Additionally, 36 studies investigated asthma risk factors, whereas 20 studies discussed treatments and interventions for asthma. We also searched PubMed on the same date using the search term 'GBD and asthma'. Among the 34 studies obtained, 17 used data from the GBD 2019. Six studies analyzed the burden of chronic respiratory diseases, which are the broad category of asthma. In other studies, the burden of asthma has either been analyzed in specific areas or in children or adolescents. However, there are no studies on ashma gobal burden using GBD 2021 for all age groups.

Added value of this study

The GBD 2021 was used to assess the incidence, prevalence, mortality, and disability-adjusted life years of asthma at the global, regional, and national levels, as well as at different ages, sexes, and SDI levels. Additionally, the linear relationships between ASRs and the SDI were analyzed to understand the effect of the SDI on disease burden. Simultaneously, MR was used to assess the possibly causal relationship between risk factors and asthma, which indicated that smoking and high body mass index (BMI) can increase the risk of asthma. The ASIR of asthma was predicted using the Bayesian age-cohort model, and the results suggested that 520 people per 100,000 individuals would be affected by asthma in 2050.

Implications of all the available evidence

Policymakers and public health officials around the world are deeply concerned about the increase in the number of asthma patients and deaths as well as their effect on the healthcare system and society. By 2050, the number of asthma patients will be 520 per 100,000 people. Coping with the health challenges of asthma and controlling disease-related deaths in different regions may become an essential part of healthcare services. The harmful trend of deaths caused by asthma risk factors, especially high BMI, needs to be addressed. If no correspondingly effective measures are taken, asthma will continue to have a growing negative effect on personal quality of life, population health, and the global economy in the future.

significant, characterized by elevated mortality and disability-adjusted life years (DALY) rates associated with the disease.[6,7] The DALYs of childhood asthma in Nigeria account for approximately 1.6% of the global burden among children and adolescents.[8] Nowadays, the burden trends, management, and treatment of asthma in children have garnered significant attention from researchers.[9–13] But the mortality and DALYs rates associated with asthma among the elderly are also quite important. Therefore, a systematic analysis of global asthma burden is necessary. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) data is an excellent database to facilitate this analysis.[14] Cao et al. focused on incidence and mortality rates,[15] whereas Zhang et al. investigated childhood asthma cases from 1990 to 2019.[16] Another study only assessed the burden of asthma in China and the United States.[17] Shin et al. conducted a comparison of the global disease burden between asthma and atopic dermatitis, revealing that the prevalence of asthma is higher.[18] Wang et al. analyzed the global burden of asthma using GBD 2019 data, but did not discuss causality between risk factors and disease.[19] However, these studies were based on data prior to GBD 2021 and focused on the disease burden in specific age groups and regions or countries. With the increasing availability of global asthma health data and the update of the GBD database, a comprehensive analysis of the global burden of asthma is needed.

To have an up-to-date and comprehensive understanding of the asthma disease burden, we used the latest data from the GBD to analyze the burden of asthma in different locations, ages, sexes and socio-demographic index (SDI) levels from 1990 to 2021. In this study, age-standardised rates (ASRs) across 204 countries or 21 regions and the average annual percent change (AAPC) were analyzed systematically. Furthermore, we utilized Mendelian randomization (MR) to provide supplementary insights into the risk factors contributing to the burden of asthma. The study may contribute to a better understanding of the global epidemic trends of the asthma.

Methods

Data source

The GBD 2021 (https://vizhub.healthdata.org/gbd-results/) is a comprehensive and extensive analysis that brings together a diverse array of data from various sources, such as surveys, censuses, vital statistics, and health-related information.[20] This data are used to assess various health indicators, including incidence, prevalence, mortality, and DALYs. The GBD relies on the

International Classification of Diseases (ICD) system for coding and categorizing diseases, making it easier to understand and compare health trends globally. The Global Health Data Exchange (GHDx, https://www.healthdata.org/) provides interactive access to this wealth of data, allowing researchers and policymakers to explore and analyze the findings. The data regarding asthma incidence, prevalence, mortality, and DALYs, along with the corresponding 95% uncertainty intervals (UIs), were obtained from the GBD 2021. This dataset encompasses all age groups from 5 to 95 years and older, spanning the period from 1990 to 2021.[21–25] Other information can be found in the Appendix (p 2).

Average annual percent change

To assess the AAPC (%), the Joinpoint Regression Program (version 5.1.0.0) was used to calculate the AAPC of the age-standardised incidence rate (ASIR), age-standardised prevalence rate (ASPR), age-standardised mortality rate (ASMR), and age-standardised DALY rate (ASDR), with corresponding 95% confidence intervals (CIs) (Appendix p 3). Joinpoint is a statistical software for the analyzing of trends using joinpoint models, which takes trend data and fits the simplest joinpoint model that the data allows. The minimum and maximum number of connection points are provided by the users.[26,27]

Socio-demographic index

The SDI is a combined measure that reflects the social and economic conditions affecting health outcomes in different areas. It is the geometric mean of three indices: the total fertility rate (TFR) for individuals under 25 years old (TFU25), the average education level for individuals who are 15 years old or older (EDU15+), and the per capita lag-distributed income (LDI).[28] For the GBD 2021 study, the SDI values were multiplied by 100 to create a scale ranging from 0 to 100 (https://ghdx.healthdata.org/record/global-burden-disease-study-2021-gbd-2021-socio-demographic-index-sdi-1950%E2%80%932021).[21]

Mendelian randomization analysis

The GBD 2021 reported that high BMI and smoking were risk factors for asthma. Here, the causal relationships between risk factors and asthma were further examined by MR.[29] Genome-wide association study summary data for asthma (ebi-a-GCST90018795) were obtained from the Integrative Epidemiology Unit open GWAS project (Open GWAS project), featuring 38,369 cases and 411,131 controls of European descent (Appendix p 3).[30]

Bayesian age-period-cohort (BAPC) analysis

The BAPC model is a method applied in epidemiology and biostatistics to analyze the relationship between incidence rate and time. It uses sample information and prior information to obtain unique parameter estimates, and the obtained results are robust and reliable.[31–33] The BAPC package (R version 4.3.2) was used to predict the incidence trend from 2022 to 2050, which can help formulate public health policies and prevent for asthma.

Role of funding source

The funding sources played no role in the study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Results

Global burden analysis from 1990 to 2021

The global burden of asthma declined from 1990 to 2021. The AAPC for ASIR, ASPR, ASMR, and ASDR were −1.147, −1.619, −1.932, and −1.872, respectively. Specifically, the prevalence decreased from 5,568 cases per 100,000 individuals in 1990 to 3,340 cases per 100,000 individuals in 2021. Similarly, the DALY rate decreased from 476 per 100,000 individuals to 265 per 100,000 individuals over the same period (Table S1).

At the regional level, the highest ASPR was observed in high-income North America in 2021 (Table 1). The highest ASMR and ASDR were in Oceania (ASMR: 34 per 100,000, ASDR: 848 per 100,000), whereas the Eastern Europe was relatively low ASMR and ASDR (ASMR: 0.5 per 100,000, ASDR: 117 per 100,000). Although Southern Sub-Saharan Africa presented the lowest ASIR (340 per 100,000) and ASPR (1875 per 100,000), the ASMR (14 per 100,000) remained relatively high (Table 1 and Table S1).

In 2021, the 204 countries and territories with the highest ASIRs were Haiti (1,617 per 100,000), Poland (1,468), and Puerto Rico (1,464) (Table S2), whereas the highest ASPRs were recorded in Haiti (11,504), the United States of America (10,150), and the United Kingdom (10,030) (Fig. 1A and Table S3). The highest ASMRs were reported in Papua New Guinea (40 per 100,000), Fiji (40), and Kiribati (30), and the highest ASDRs were found in Papua New Guinea (966), Fiji (902), and Haiti (849) (Tables S4 and S5). Among these nations, Poland and the United States of America need special attention because of the increasing burden of asthma observed from 1990 to 2021 (Table 2 and Fig. 1B).

Differences in asthma burden across age and sex

The asthma prevalence was the highest in children aged 5–9 years, with 21.231 million males and 16.057 million females. Among patients who were below 20 years old, the number of male patients was greater than the number of female patients, but the opposite pattern was found for patients who were above 20 years old. The same pattern of sex differences was found for the ASPR (Figure S1).

Males aged 70–74 years and females aged 80–84 years had the highest number of asthma-related deaths

Indicator	Location	ASR (95% Uncertain interval)	AAPC (95% Confidence interval)
Incidence	High-income North America	1403.64 (1137.64–1766.66)	−0.017 (−0.221 to 0.187)
	Caribbean	1193.84 (1000.88–1445.97)	−0.282 (−0.309 to −0.256)*
	Central Europe	898.73 (725.29–1136.93)	0.034 (−0.076 to 0.144)
Prevalence	High-income North America	9717.74 (8485.1–11,226.93)	0.088 (−0.014 to 0.191)
	Australasia	7747.21 (6479.30–9107.51)	−1.652 (−1.784 to −1.519)*
	Caribbean	7638.48 (6722.22–8563.44)	−0.624 (−0.688 to −0.559)*
Deaths	Oceania	33.98 (24.05–51.08)	−1.027 (−1.075 to −0.979)*
	South Asia	17.68 (12.55–26.32)	−1.352 (−1.880 to −0.822)*
	Central Sub-Saharan Africa	15.79 (8.99–37.27)	−1.210 (−1.306 to −1.114)*
DALYs	Oceania	847.59 (626.75–1212.54)	−1.157 (−1.224 to −1.089)*
	Central Sub-Saharan Africa	491.68 (337.41–909.34)	−1.484 (−1.588 to −1.380)*
	Caribbean	468.60 (349.60–628.75)	−1.038 (−1.145 to −0.930)*

ASR, age-stadardised rate per 100,000 people; AAPC, average annual percent change; The data marked with an asterisk (*) in the AAPC column indicates that the *P*-value for this AAPC is less than 0.05.

Table 1: **The regions ranked among the top three in age-standardised rates (ASRs) in 2021 across 21 areas, along with the corresponding average annual percent change (AAPC).**

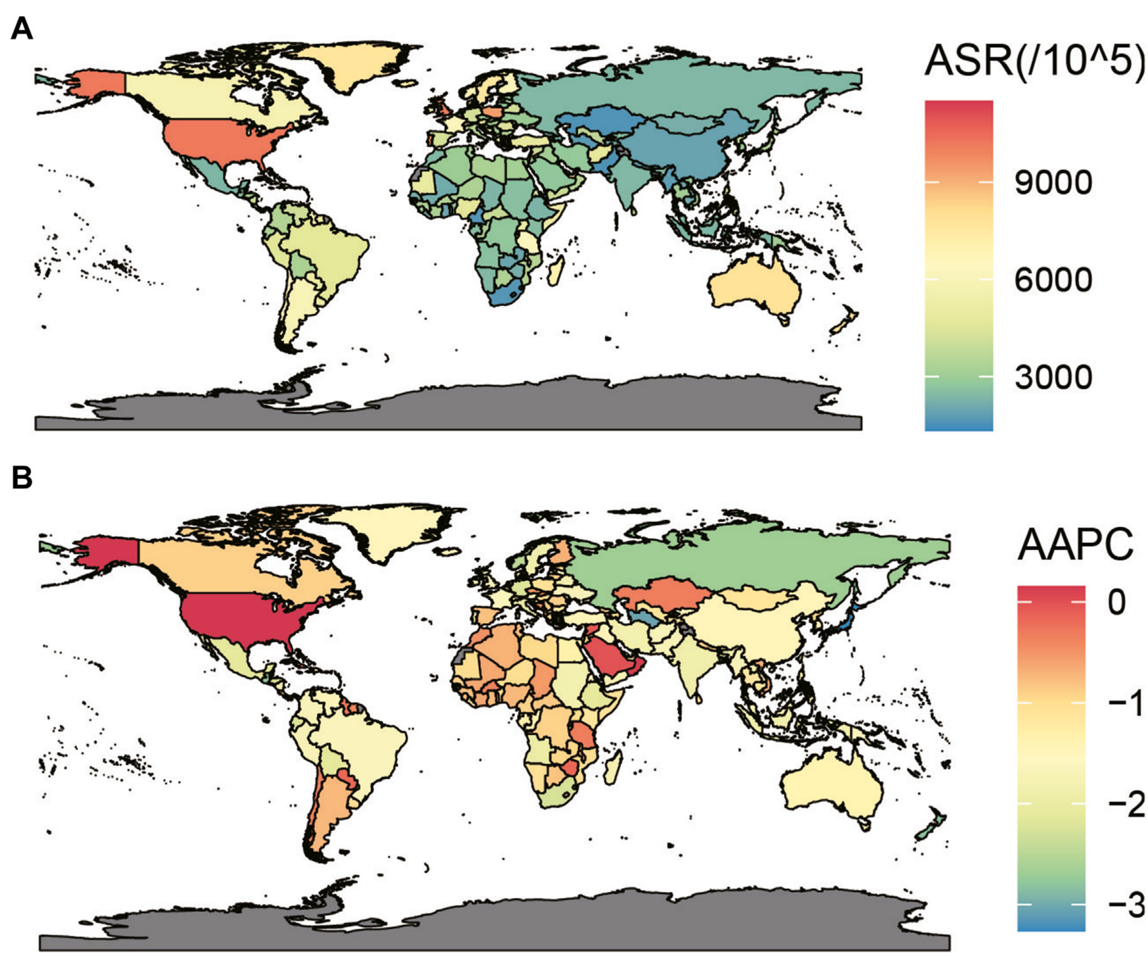

Fig. 1: **The age-standardised prevalence rates of asthma and the AAPC of age-standardised prevalence rates from 204 countries and territories. Notes:** (A) Age-standardised prevalence rate in 2021. (B) AAPC of age-standardised prevalence rate from 1990 to 2021. AAPC, average annual percent change.

Indicator	Location	AAPC (95% Confidence interval)
ASIR	Oman	0.317 (0.245–0.388)
	Poland	0.284 (0.187–0.381)
	Barbados	0.256 (0.164–0.347)
	Saudi Arabia	0.111 (0.043–0.180)
	Bermuda	0.084 (0.054–0.114)
ASPR	Oman	0.138 (0.061–0.216)
	United States of America	0.155 (0.069–0.241)
ASMR	Zimbabwe	0.396 (0.033–0.760)
ASDR	Zimbabwe	0.567 (0.309–0.825)
	Lesotho	0.351 (0.146–0.557)

***Table 2:* Countries and regions with an increase in the average annual percent change (AAPC) from 1990 to 2021.**

(27,947 cases vs. 31,884 cases) (Figure S2). The DALYs exhibited a bimodal distribution. The number of DALYs for males was the highest at the ages of 5–9, reaching 924,212, whereas the number of disabled females was the highest at the ages of 55–59, with 856,216 individuals (Fig. 2).

Differences in asthma burden across SDI levels

From 1990 to 2021, the global burden of asthma was significantly influenced by the SDI. High-SDI regions had the highest ASIRs and ASPRs, but they had lower ASMRs and ASDRs than the global average. In low-SDI regions, the ASDR and ASMR were always the highest, with an ASDR of 527.4 cases per 100,000 people and an ASMR of 16.5 per 100,000 people in 2021. In this 30-year trend in burden, the ASMR decreased most significantly in high-SDI regions, from 4.8 (95% UI: 4.5–5.3) deaths per 100,000 people in 1990 to 0.9 (95% UI: 0.8–1.0) deaths per 100,000 people in 2021. The greatest decrease in ASIR was recorded in low-middle-SDI regions. Specifically, the ASIR of asthma decreased from 730.7 cases per 100,000 people in 1990 to 443.6 cases per 100,000 people in 2021 (Table S1 and Fig. 3).

The results of the correlation analysis between disease burden and SDI revealed that a higher the SDI was associated with a greater ASIR (Fig. 4A), whereas the ASDR (Fig. 4C) and ASMR (Fig. 4D) both decreased as the SDI increased. The AAPC in the ASIR (Fig. 4F) first decreased and then increased as the SDI increased, resulting in a nonlinear U-shaped curve, which also indicated that the lowest incidence rate occurred in the low-middle-SDI regions. In contrast, the AAPC in the ASMR (Fig. 4H) was strongly negatively correlated with the SDI.

Influence of risk factors on the asthma burden of asthma

Factors such as high body mass index (BMI), occupational asthmagens, and smoking affected asthma at the global level, accounting for 14.9%, 7.9% and 6.1% of asthma DALYs in 2021, respectively. The leading risk factors in terms of risk-attributable DALYs globally were

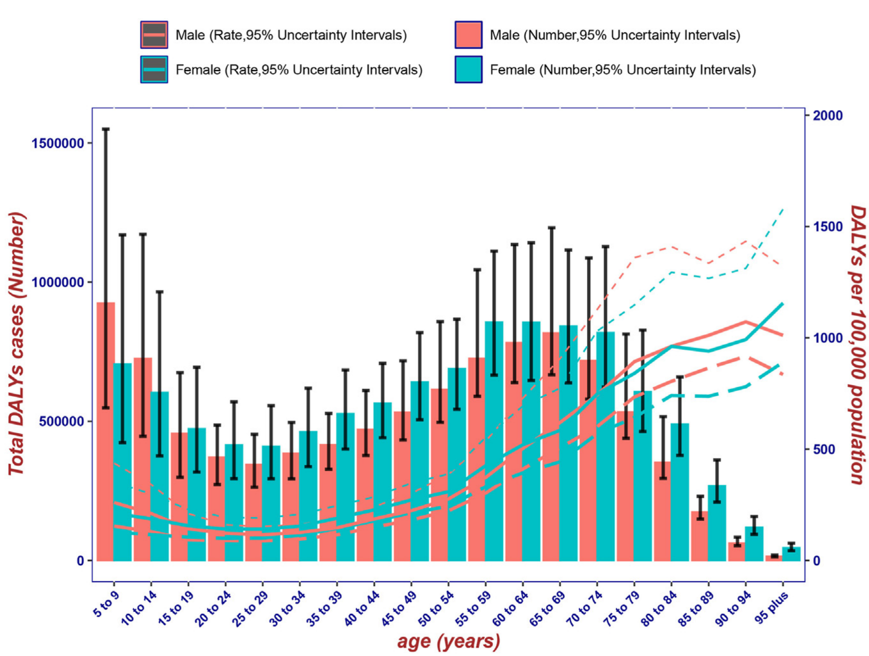

***Fig. 2:* The number of DALYs and age-standardized DALY rates of asthma in 2021 by sex. Notes:** DALYs, disability-adjusted life years. Dotted lines indicate 95% upper and lower uncertainty intervals, respectively.

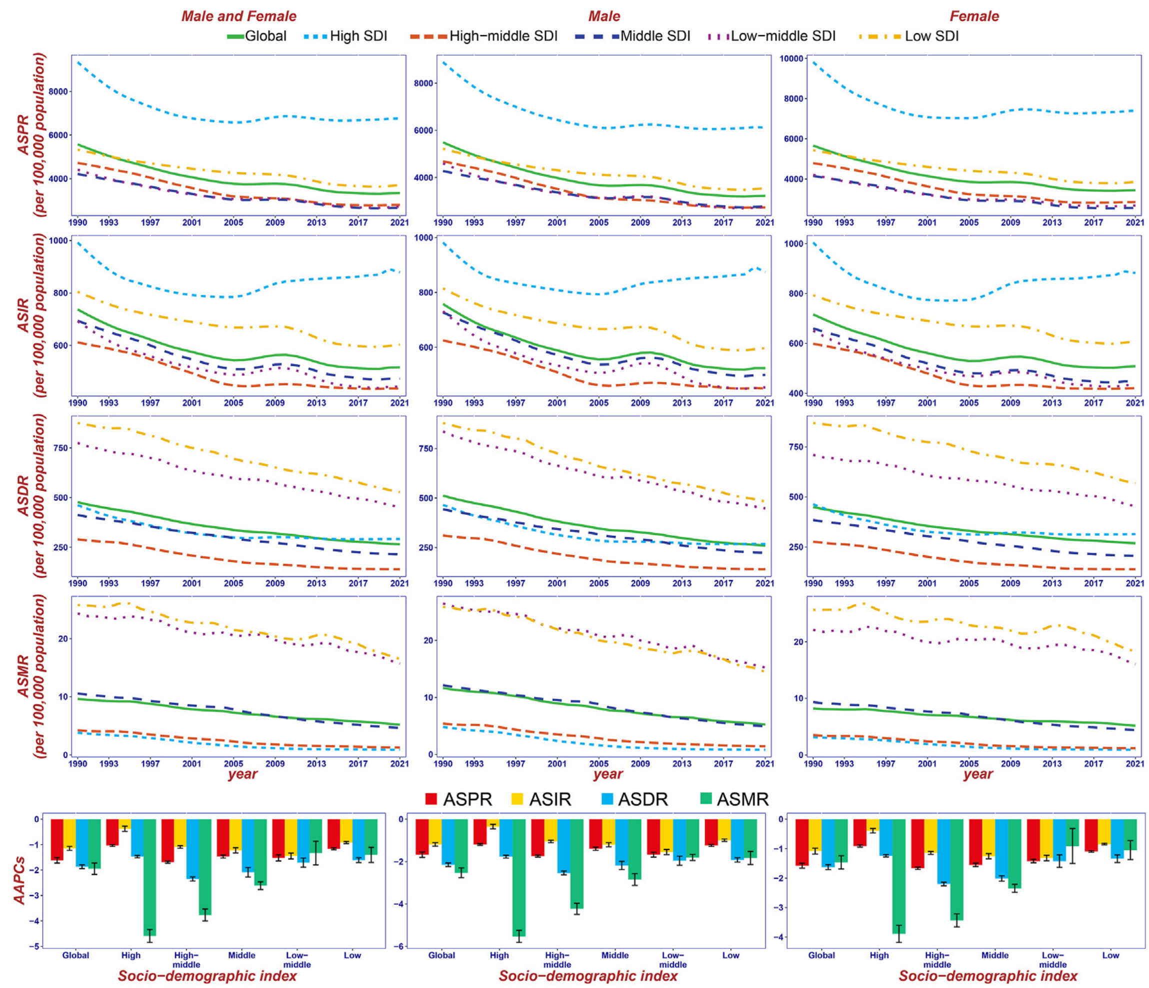

Fig. 3: **Temporal trend of age-standardised prevalence rates, age-standardised incidence rates, age-standardised disability-adjusted life years rates and age-standardised mortality rates for the burden of asthma, globally and by socio-demographic index from 1990 to 2021. The average annual percent change, globally and by socio-demographic levels, from 1990 to 2021. Notes:** Five levels of socio-demographic index, high, high-middle, middle, low-middle, or low. ASPR, age-stadardised prevalence rate per 100,000 people. ASIR, age-stadardised incidence rate per 100,000 people. ASDR, age-stadardised DALY rate per 100,000 people. ASMR, age-stadardised mortality rate per 100,000 people.

high BMI in females (risk-attributable DALYs = 16.4%) (Fig. 5) and occupational asthmagens in males (risk-attributable DALYs = 10.1%) (Figure S3). At the regional level, the contribution of high BMI to asthma DALYs ranged from 10.8% to 26.5% (Fig. 5), that of occupational asthma ranged from 4.2% to 11.9% (Figure S3), and that of smoking ranged from 1.3% to 8.4% (Figure S4). The global proportion of asthma DALYs caused by high BMI increased in 2021 compared to that in 1990. The most significant increase in percentage increase (by 9.2%) was recorded in North Africa and the Middle East.

We also conducted an MR analysis to assess the relationships between risk factors and asthma. The inverse variance weighted (IVW) method was used as the standard for the results of the MR, which revealed that a higher BMI (OR = 1.15, 95% CI: 1.07–1.24) (Fig. 6A and Table S6) and longer smoking duration (OR = 1.28, 95% CI: 1.13–1.43) (Fig. 6B and Table S7) were associated with an increased risk of asthma. The analysis of both pairs of results is included in the Supplementary Material (Figures S5 and S6).

BAPC prediction of the ASIR

From 2022 to 2050, the ASIR of asthma is predicted to slightly increase among individuals aged 20–80 years (Fig. 7). Around 520 cases of asthma per 100,000 people are estimated by 2050, representing a serious burden in terms of the ASIR (Figure S5).

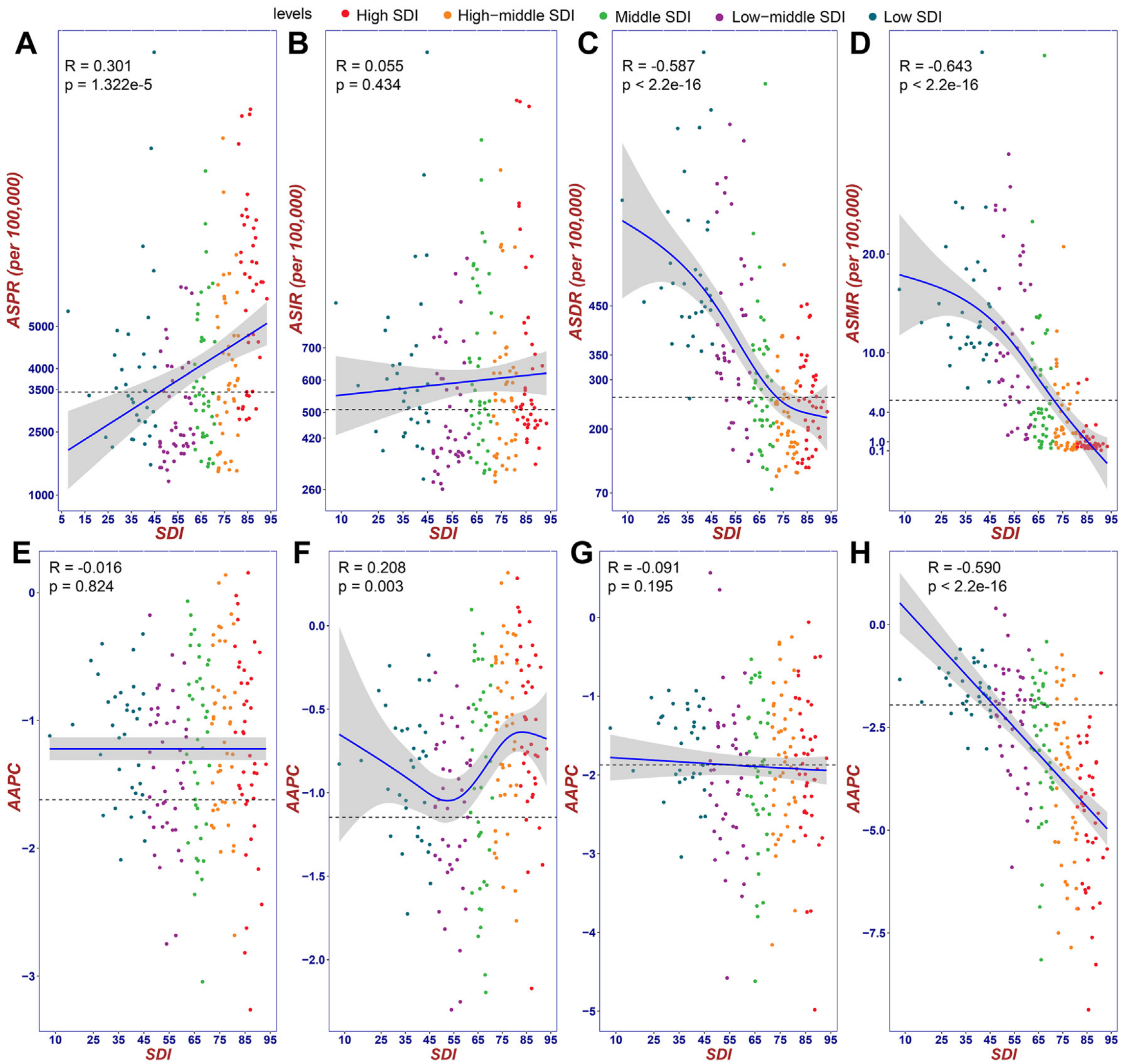

Fig. 4: **Association between SDI and age-standardised prevalence, incidence, DALY and mortality rates of asthma in 2021 and corresponding AAPC from 1990 to 2021. Notes:** (A) ASPR and SDI. (B) ASIR and SDI. (C) ASDR and SDI. (D) ASMR and SDI. (E) AAPC of ASPR and SDI. (F) AAPC of ASIR and SDI. (G) AAPC of ASDR and SDI. (H) AAPC of ASMR and SDI. Dotted lines refer to the global level of rates. SDI, socio-demographic index. AAPC, average annual percent change. ASPR, age-stadardised prevalence rate per 100,000 people. ASIR, age-stadardised incidence rate per 100,000 people. ASDR, age-stadardised DALY rate per 100,000 people. ASMR, age-stadardised mortality rate per 100,000 people.

Discussion

Compared to other studies on the GBD related to asthma, this study revealed that the burden of asthma was more severe in Southern Sub-Saharan Africa in 2021. In this region, although the prevalence of asthma is relatively low, the mortality associated with asthma is notably high. Additionally, Poland and the United States of America need special attention, as the number of asthma patients has increased from 1990 to 2021. This study revealed that the prevalence and incidence of asthma increase with increasing SDI, whereas the mortality and DALY rates decrease with increasing SDI. High BMI and smoking were risk factors for numerous diseases, including asthma. In this study, we further validated that they were able to increase the risk of asthma.

Most asthma cases occur in early life. The main reason for this phenomenon may be attributed to the primary genetic factor of childhood-onset asthma, which is related to a genetic locus on chromosome 17q 12–21.[34] Researchers have also proposed a potential link between the elevated incidence during childhood and the

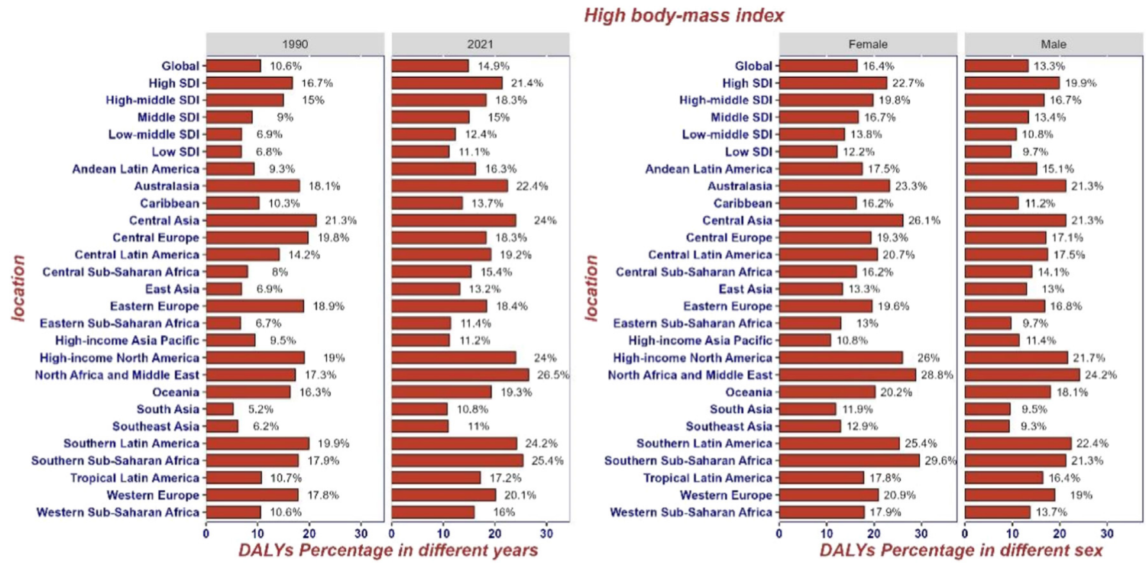

Fig. 5: **Proportion of asthma DALYs caused by high body mass index in 1990 and 2021 from different regions and sex. Notes:** DALYs, disability-adjusted life years.

presence of the respiratory syncytial virus.[35] Additionally, early exposure to pollen was found to be associated with an increased likelihood of developing asthma in childhood.[36] Studies on ways to reduce the burden of childhood asthma need to be conducted urgently for these reasons.

A significant positive correlation was found between the SDI and the occurrence of ASIR and ASPR in this study, whereas a negative correlation was found between SDI and both ASDR and ASMR. This may be attributed to enhanced healthcare management and medication accessibility in countries with a high SDI, which helps reduce mortality risks associated with asthma.[37,38] These findings also showed that the management measures for asthma were effective until 2021. Conversely, although the ASIR and ASPR were relatively low in low-SDI countries, their ASDR and ASMR were elevated, which reflected more serious mortality rates

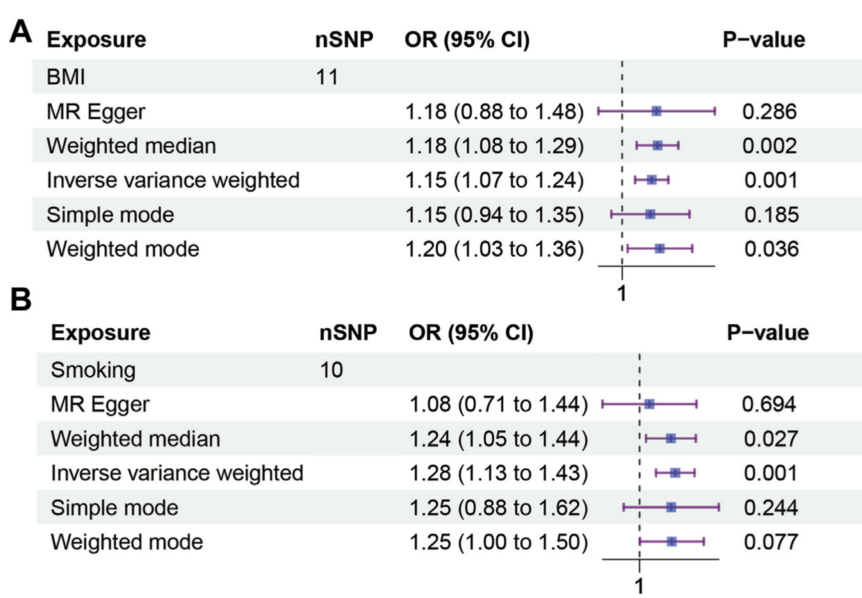

Fig. 6: **Forest plot of Mendelian randomization analysis. Notes:** (A) The associations of body mass index with risk of asthma. (B) The associations of current pack years of smoking with risk of asthma. BMI, body mass index.

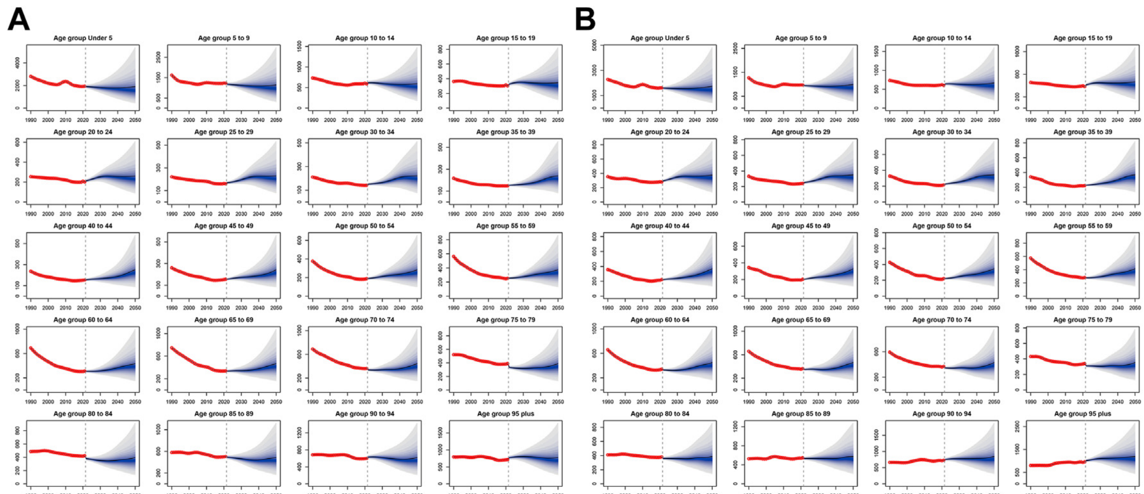

***Fig. 7*: The trends of age-standardized incidence rates for each age group of asthma in worldwide from 2022 to 2050 predicted by Bayesian age-period-cohort model. Notes:** (A) Male. (B) Female. Blue shades are the corresponding confidence intervals.

related to asthma in less-developed countries. The primary challenge faced by these countries or regions is the lack of adequate healthcare facilities and security for asthma, as well as the inability of patients to cope with the economic burden of asthma.[39] Controlling the asthma burden of asthma in low-SDI areas may become more important in the future.

The increase in the effect of high BMI and the decrease in the influence of smoking and occupational asthma on asthma suggest that lifestyle changes and weight loss need more and more attention.[24] A possibly causal risk factor for asthma is high BMI, which indicates overweight or obesity. Some studies have shown that obesity is more prevalent in high-income countries or regions.[40,41] This explains why the disease burden is greater in high-SDI areas as well. This study also revealed that in high-income North America, the highest proportion of deaths occurred due to high BMI, accompanied by relatively high ASPR and ASDR for asthma. Besides the three asthma-related risk factors reported in the GBD database, other risk factors leading to asthma include depression, chronic rhinitis, gastroesophageal reflux disease, anxiety, and temperature changes.[42–44] The direct medical cost of climate change is expected to reach \$2–\$4 billion by 2030.[45] After the COVID-19 pandemic from 2020 to 2021, whether the increased burden of asthma is affected by COVID-19 remains to be studied.[22] To summarize, the identification of these risk factors can help people selectively avoid and reduce the occurrence and deaths related to asthma.

In this study, we provided a thorough overview of the most recent trends in the global burden of asthma, analyzed by age and sex. Considering the effect of development in different countries or regions on disease outcomes, we assessed the linear relationship between the ASRs and SDI. The ASIR and ASPR were positively correlated with the SDI, whereas the ASMR and ASDR were negatively correlated with the SDI. A linear relationship was also found between AAPC and the SDI. This study established that smoking and high BMI are associated with an increase in the risk of developing asthma, demonstrating a possibly causal relationship that has not been described in other studies; we further evaluated this association. These findings not only enhance our understanding of the complexity of the disease but also provide a strong foundation for developing more effective public health measures, optimizing resource allocation, fostering international cooperation, and advancing scientific research. These efforts aim to improve the quality of life of patients with asthma and reduce the overall burden of the disease.

This study had several limitations. First, the GBD data were derived from modeling, which may intduce biases in data sources due to the variability in raw data quality across different regions and countries. Such biases result in inaccuracies related to the true burden of asthma. For example, the incidence of asthma may be underreported in low-income and middle-income countries, due to inadequate infrastructure and policy mechanisms in certain areas. Conversely, in other countries, the incidence of asthma may be overestimated, as the data are predominantly collected from major urban centers. Second, in the linear analysis of the SDI and AAPC, we categorized countries based on the SDI from 2021. Although the SDI levels of most countries did not change during this these 31 years, there were still a few countries with slight fluctuations in SDI levels, which may have slightly affected our results. Third, owing to the predominance of data on

European populations in the GWAS database, the assessment of regions with undeveloped regions and countries was limited. Fourth, the BAPC model indicated that as the forecast time horizon extends, the confidence intervals for future disease burden will expand, potentially resulting in less reliable predictions. Human interventions and preventive measures for asthma can influence incidence of the disease, which may affect the results generated by the BAPC model.

Asthma is a significant global health burden, particularly among children aged 5–9 years, who require focused early prevention and intervention efforts. Additionally, high BMI is a critical risk factor for the prevalence of asthma in high-income regions or countries. Although the prevalence rate of asthma is relatively low in low SDI regions, the mortality rate is relatively high, particularly in Southern Sub-Saharan Africa. The results of this study may serve as an important reference for formulating corresponding public health policies and preventive measures for different regions, and help alleviate the global burden of asthma.

Contributors

Yongshuai Jiang, Mingming Zhang and Hongchao Lv designed this study. Linna Yuan, Junxian Tao, Jiacheng Wang, Wei She, Yuping Zou and Ruilin Li prepared the initial draft and finalised the manuscript with comments from all other authors. Yingnan Ma, Chen Sun, Shuo Bi and Siyu Wei collected and analysed the data. Haiyan Chen, Xuying Guo and Hongsheng Tian validated the data. Jing Xu, Yu Dong and Ye Ma made important revisions to the manuscript. Hongmei Sun, Wenhua Lv and Zhenwei Shang participated in the interpretation of the data and provided important comments on the manuscript. All authors had full access to all the data in the study and were responsible for the integrity of the data and the accuracy of the data analysis. All authors reviewed the draft for criticality and approved the final version.

Data sharing statement

The data used for the analyses is available by email request to the corresponding author.

Editor note

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Declaration of interests

We declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.103051.

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