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# The incidence of asthma attributable to temperature variability: An ecological study based on 1990–2019 GBD data

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HIGHLIGHTS

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# GRAPHICAL ABSTRACT



- High-latitude residents face asthma risk from warming.
- It's important to implement stricter mitigation strategies.

# ABSTRACT

*Background:* Asthma, the second leading cause of death from chronic respiratory diseases, is associated with climate change, especially temperature changes. It is currently unclear about the relationship between long-term temperature variability and the incidence of asthma on a global scale.

*Methods*: We used asthma incidence, demographic and socioeconomic data from the Global Burden of Disease (GBD) Results Database, and environmental and geographical statistics from TerraClimate between 1990 and 2019 to determine the association between maximum temperature variability and asthma incidence. We also predicted the incidence of heat-related asthma in the future (2020–2100) under four shared socioeconomic pathways (SSPs: 126, 245, 370, and 585).

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Received 18 June 2023; Received in revised form 22 August 2023; Accepted 29 August 2023 Available online 1 September 2023 0048-9697/© 2023 Elsevier B.V. All rights reserved. *Results*: Between 1990 and 2019, the global median incidence of asthma was 402.0 per 100,000 with a higher incidence (median: 1380.3 per 100,000) in children under 10 years old. We found that every 1 °C increase in maximum temperature variability increased the risk of asthma globally by 5.0 %, and the effect was robust for individuals living in high-latitude areas or aged from 50 to 70 years. By 2100, the average incidence of asthma is estimated to be reduced by 95.55 %, 79.32 %, and 40.02 % under the SSP126, SSP245, and SSP370 scenarios, respectively, compared to the SSP585 at latitudes  $>60^{\circ}$ .

*Conclusion:* Our study provides evidence that maximum temperature variability is associated with asthma incidence. These findings suggest that implementing stricter mitigation and adaptation strategies may be importment in reducing asthma cases caused by climate change.

# 1. Introduction

Asthma is a chronic inflammatory disorder that varies in intensity and duration, characterized by respiratory symptoms such as breathlessness, wheezing, coughing, and chest tightness (Asthma GIf, 2023). Various factors, including exercise, allergens, irritants, climate change, air pollution, and viral respiratory infections, can exacerbate and prolong the condition (Asthma GIf, 2023; Reddel et al., 2022; Chakaya and Ait-Khaled, 2022). Asthma is also accompanied by various comorbidities, such as obesity, allergic rhinitis, gastroesophageal reflux disease, and obstructive sleep apnea, which can significantly affect the quality of life (Althoff et al., 2021). Asthma, the second leading cause of death from chronic respiratory diseases, is a significant global health problem affecting all age groups and causing severe disability and death worldwide, particularly in low and middle-income countries (LMICs) (Chakaya and Ait-Khaled, 2022). Despite a general decrease in incidence and mortality rates from 1900 to 2019, the number of asthma cases continues to rise due to population growth (Cao et al., 2022).

The global climate has undergone significant changes, with the global average surface temperature increasing by 1.09 °C between 1850 and 2020, according to the IPCC's sixth assessment report. As a result, extreme weather events such as heatwaves, droughts, floods, and hurricanes have increased (Masson-Delmotte et al., 2023). Research has found that climatic changes lead to an increase in the monthly high temperature events and temperature variability, especially in poor countries (Bathiany et al., 2018; Wiel and Bintanja, n.d.). For example, for each degree of global warming in Amazonia and southern Africa, temperature variability increased by 15 %, while up to 10 %  $^{\circ}C^{-1}$  in the Sahel, India, and Southeast Asia (Bathiany et al., 2018). Climate change in turn has been shown to trigger and exacerbate asthma attacks (Han et al., 2023). Climate factors affect pollen amount and concentration, causing allergic asthma outbreaks during the pollen season (D'Amato et al., 2020). Climate factors also cause wildfires and prolong wildfire seasons, which produces more air pollutants, such as O3 and PM2.5, and poses a serious threat to human respiratory health (Li et al., 2019; Dominski et al., 2021).

The relationship between temperature and asthma incidence has been studied, but these studies have largely focused on average and extreme temperature (Han et al., 2023; Konstantinoudis et al., 2023), overlooking the potential impact of maximum temperature variability as a powerful indicator of evaluating the severity and frequency of impending extreme weather events and climate change (Ebi et al., 2021). In this paper, we use the absolute difference between the "ideal" annual maximum temperature (at which the incidence of asthma is the lowest) and the average annual maximum temperature to express the maximum temperature variability. Moreover, these studies have been limited to a single region and a relatively short period of time, failing to explore the global and long-term relationship between maximum temperature variability and asthma (Chen et al., 2022; Kang et al., 2022). Moreover, we were unable to locate any research that examined future trends of asthma incidence under varying greenhouse gas emissions and climate policies on a global scale, represented by the Shared Socioeconomic Pathways (SSPs: 126, 245, 370, and 585). To address these gaps, we planned to examine the correlation between maximum temperature variability and asthma incidence in 203 countries/regions from 1990 to 2019. We also predicted changes in maximum temperature variability and asthma incidence rates for the future (2020–2100) under these SSPs. We hypothesized that elevated maximum temperature variation would be positively associated with an increased risk of asthma incidence.

# 2. Methods

#### 2.1. Data sources

The data for this study was obtained from the publicly available Global Burden of Disease (GBD) results database, which systematically estimated disease incidence, prevalence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs) for 369 diseases and injuries in 204 countries and regions from 1990 to 2019. In GBD 2019, asthma diagnosis relied on self-reported wheezing and physician diagnosis over the past 12 months (International Classification of Diseases 9th edition code 493, 10th edition codes J45 and J46).

TerraClimate is a global gridded dataset providing high-spatial resolution  $(1/24^\circ, ~4\text{-km})$  monthly meteorological and water balance variables for global terrestrial surfaces from 1958 to the present (Abatzoglou et al., 2018). For this study, monthly climatic data (from 1990 to 2019) was extracted from TerraClimate based on the shapefile of the first level administrative areas of GBD countries/locations, including maximum temperature, wind speed, soil moisture, and precipitation accumulation. The maximum temperature in each year was determined by averaging the top 4 highest monthly temperatures (Sultan et al., 2005; Ma et al., 2021), while soil moisture, precipitation accumulation, and wind speed measurements were averaged over the course of twelve months to represent their annual value.

We utilized the Coupled Model Intercomparison Project Phase 6 (CMIP6) dataset to access to the past, present, and future climate data (Thrasher et al., 2022). To collect maximum temperature and precipitation data for all GBD countries/locations from CMIP6, we created a 20  $km \times 20$  km fishnet to identify 474,975 locations. Locations that were unavailable were excluded, while another nine locations were added to ensure our data covered all regions. These locations included American Samoa, Bermuda, Cook Islands, Maldives, Marshall Islands, Monaco, Nauru, Niue, San Marino, Tokelau, and Tuvalu. We extracted monthly maximum temperature values under four Shared Socioeconomic Pathways (SSPs: 126, 245, 370, and 585). These pathways represent projected scenarios of global socioeconomic change up to 2100 (O'Neill et al., 2017). SSP126 represents a scenario where humans choose sustainable, low-carbon lifestyles, resulting in a decrease in global warming by 2100. Conversely, the SSP585 scenario paints a bleak picture, characterized by escalating greenhouse gas emissions, burgeoning population growth, increased fossil fuel consumption, and worsening air pollution. This scenario leads to a relentless rise in greenhouse gas emissions and a consequential high level of global warming. SSP245 and SSP370 are considered moderately between SSP126 and SSP585. We calculated the new maximum temperature variability value based on these temperature values. We averaged the maximum temperature variability value at 20-year intervals (2021-2040, 2041-2060,



**Fig. 1.** Changes in global mean maximum temperature variability and the incidence rate of asthma from 1990 to 2019. Global map of the average value of maximum temperature variability (ranging from 0.01 to 3.36 °C) of each country over the past 30 years and color-scaled dots showing the severity of the local mean asthma incidence rate (ranging from 182.7 to 1276.2 new cases per 100 k population) of each country over 1990–2019. The association between asthma incidence rate and maximum temperature variability in different latitudes from 1999 to 2019 is expressed on the right side with ORs and 95 % confidence intervals. The change in unit for maximum temperature variability is represented as a 1 °C increase.

2061-2080, and 2081-2100).

#### 2.2. Maximum temperature variability

Temperature variability was predominantly defined as the frequency of extreme temperatures, the absolute difference in temperature between two adjacent years, or the standard deviation of temperature. Nonetheless, most studies were conducted in a single region (Xiao Ying Chen et al., 2013; Guo et al., 2021). We have employed the standard deviation of the top quartile of monthly temperatures as a measure of yearly maximum temperature variability. However, we observed it substantially exaggerated the estimates of maximum temperature variability, which has been mentioned in other study (Sippel et al., 2016).

In our study, we calculated the absolute difference between the annual maximum temperature in the year with the lowest asthma incidence rate (considered as the "ideal" temperature) and the average annual maximum temperature. This absolute difference as a measure of maximum temperature variability can avoid the overestimation caused by the normalized measures. Using this method, we calculated the maximum temperature variability for each GBD country and region in each year.

# 2.3. Covariates

The Sociodemographic Index (SDI) was used as a comprehensive indicator of a region's economic development level, where a higher index represents a more developed economy. SDI is a time-varying index based on the geometric mean of total fertility rate under the age of 25 (TFU25), mean education for individuals aged 15 and older (EDU15+), and lag distributed income (LDI) per capita. The SDI in 2019 was used in this study to ensure its representativeness. Countries and regions were further divided into five SDI categories: low (0–0.455), medium-low (0.456–0.608), medium (0.609–0.690), medium-high (0.691–0.805), and high (0.806–1) (Diseases GBD, Injuries C, 2020).

All age groups were divided into ten subgroups. GBD provided data

on O<sub>3</sub> and PM<sub>2.5</sub> for 1990, 1995, 2000, 2005, and between 2010 and 2019. We used the mean value of the closest available data for unavailable data. PM<sub>2.5</sub> (5–10; 10–15; 15–25; 25–35; >35  $\mu$ g/m<sup>3</sup>) and O<sub>3</sub> (0–28.4; 28.4–33.1; 33.1–47.3; >47.3 ppb) were classified according to the World Health Organization's recommended annual AQG levels and mid-term goals (WHO, 2021). Unlike most GBD studies that categorized countries into 21 geographic regions, we categorized 203 countries by 10-degree latitude to better explore the correlation between asthma and climate factors.

## 2.4. Statistical method

We used a two-step approach to investigate the link between climate variation and asthma incidence. First, we used a generalized linear mixed model to explore the association between asthma incidence and each climate variable. Variables with significant differences were then included in further analysis using a generalized additive regression model. For the second step, we used a generalized additive regression model to further investigate the association between asthma incidence and maximum temperature variability. We employed a forward stepwise selection technique and likelihood ratio tests to compare models. Unadjusted and adjusted odds ratios (OR) and a corresponding 95 % confidence intervals (Cls) were estimated for odds of asthma associated with each 1 °C increase in maximum temperature variability. The fully model adjusted for latitude, sex, age, year, SDI, O<sub>3</sub>, PM<sub>2.5</sub> and meteorological factors (maximum temperature, soil moisture, precipitation, wind speed). We performed subgroup analysis by sex, age, SDI, latitude,  $O_3$ , and PM<sub>2.5</sub>.

In the prediction step, we assumed that the "ideal" baseline temperature and the effect of maximum temperature variability on asthma incidence would remain constant in the future with little change in the study population's demographic composition. We extracted future meteorological data from CMIP6 to calculate new maximum temperature variability, which were input into our final model. We randomly selected 10,000 points (5000 points if the number of points is <10,000)

#### Table 1

The distribution of Asthma incidence from 1990 to 2019.

Variables	Incidence	P value
Global	402.0(255.6, 672.3)	
Sex		0.03
Male	366.6(222.0, 636.4)	
Female	429.9(289.6, 704.0)	
SDI <sup>a</sup>		0.25
Low	430.2(279.2, 675.2)	
Low-middle	392.2(243.8, 671.4)	
Middle	390.2(244.9, 683.8)	
High-middle	396.1(255.7, 670.0)	
High	365.9(245.7, 642.9)	
Latitude (°)		< 0.001
0–10	426.0(262.2, 694.8)	
10-20	383.5(253.0, 646.5)	
20–30	422.6(252.8, 689.8)	
30–40	428.5(260.3, 705.5)	
40–50	375.6(252.1, 612.9)	
50-60	332.0(225.3, 615.3)	
>60	470.2(321.6, 805.6)	
O <sub>3</sub> (ppb)		0.43
0–28.4	435.6(271.6, 744.6)	
28.4-33.1	409.6(255.6, 700.0)	
33.1-47.3	388.0(249.0, 651.3)	
>47.3	411.7(260.1, 674.3)	
PM <sub>2.5</sub> <sup>b</sup> (μg/m <sup>3</sup> )		0.17
5–10	425.1(263.4, 758.1)	
10–15	393.0(261.0, 688.3)	
15–25	367.8(239.7, 634.6)	
25–35	413.1(248.0, 666.8)	
>35	430.0(275.5, 676.4)	
Age		< 0.001
1 to 9	1380.3 (1046.5, 1897.9)	
10 to 19	603.4 (475.2, 771.2)	
20 to 29	300.5 (220.5, 400.3)	
30 to 39	221.2 (162.1, 292.6)	
40 to 49	238.9 (177.1, 311.6)	
50 to 59	330.2 (242.1, 441.9)	
60 to 69	442.4 (317.5, 605.7)	
70 to 79	399.4 (267.6, 555.8)	
80 to 89	462.4 (288.0, 662.1)	
90 plus	658.8 (418.1, 957.8)	

<sup>a</sup> SDI: Sociodemographic index.

 $^{b}$  PM\_{2.5}: Particulate matter with aerodynamic diameter  ${<}2.5~\mu\text{m}.$ 

from different latitude groups  $(0-10^\circ: 42,624 \text{ points}, 10-20^\circ: 59,590 \text{ points}, 20-30^\circ: 72,389 \text{ points}, 30-40^\circ: 61,871 \text{ points}, 40-50^\circ: 61,568 \text{ points}, 50-60^\circ: 6168 \text{ points}, >60^\circ: 170,666 \text{ points})$  and repeated the process 10,000 times under the four SSPs (126, 245, 370, and 585) to estimate the range of changes in asthma incidence.

# 3. Results

The global median incidence rate of asthma was 402.0 (255.6, 672.3) per 100,000 population from 1990 to 2019, with high SDI having a lower incidence rate of 365.9 (245.7, 642.9) than low SDI with 430.2 (279.2, 675.2) (Table 1). Incidence rates of asthma were higher in populations living above 60° latitude than in other areas. Children (1-9 years old) had a significantly higher median incidence rate than other age subgroups, with a proportion of >2:1. Over the past 30 years, the global average maximum temperature was 29.4 °C (Table 2). The regions between 0 and 20° latitude had significantly higher average soil moisture (0-10°: 100.2 mm, 10-20°: 83.8 mm) and precipitation (0-10°: 166.0 mm, 10-20°: 129.3 mm) than other regions, while the wind speed was opposite. Besides wind speed (1.01, 95 % CI: 1.00-1.01, P = 0.005), maximum temperature variability, soil moisture (1.00, 95 % CI: 1.00–1.00, *P* < 0.001) and precipitation (1.00, 95 % CI: 1.00–1.00, *P* < 0.001) had statistical differences with the incidence rate of asthma in the preliminary association screening. Among them, the maximum temperature variability had the most significant impact (1.03, 95 % CI: 1.02–1.04, P < 0.001) on the incidence rate of asthma (Table S1).

According to the average maximum temperature variability from 1990 to 2019, we observed that the highest maximum temperature variability in some countries and regions were >3 °C (Fig. 1). The incidence rate in the Americas may be slightly higher. Incidence rates do not always correspond to the average maximum temperature variability across countries.

In the fully adjusted model, we found that each 1 °C increment in maximum temperature variability increased the global risk of asthma by 5.0 % (OR: 1.05, 95 % CI: 1.05–1.06), the effects increased in relatively high-latitude areas ( $50^{\circ}-60^{\circ}$ , OR: 1.17, 95 % CI: 1.15–1.19; > $60^{\circ}$ , OR: 1.23, 95 % CI: 1.20–1.26) (Table 3, Fig. 1). In subgroup analysis, we noticed that middle SDI was more susceptible to heat-related asthma. For stratified age groups, we found that the risk of maximum temperature variability on asthma gradually increases as age increases, but this effect decreases in elderly adults (80-89, OR: 0.98, 95 % CI: 0.97–1.00; 90 plus, OR: 0.91, 95 % CI: 0.89–0.92) (Table 4). It showed that PM<sub>2.5</sub> have a high risk of maximum temperature variability on asthma at the lowest and higher pollutant concentrations<sub>5</sub>.O<sub>3</sub> have a high risk of maximum temperature variability on asthma at the high pollutant concentrations<sub>5</sub>.

In our predictive model, there is a significant rise in asthma incidence moving from the SSP126 scenario to the SSP585 scenario, particularly in latitudes above 60 degrees (Fig. 2). The SSP126 scenario resulting in low asthma incidence rates across all latitudes from 2040 to 2100. In contrast, the SSP585 scenario causing a sharp increase in asthma incidence rates in latitudes  $>60^{\circ}$ , which may accelerate after the 2050s due to worsening greenhouse gas emissions. By 2100, the asthma incidence rate in latitudes above  $60^{\circ}$  may increase by over 5 times compared to other scenarios. The average incidence rate of asthma is estimated to be reduced by 95.55 %, 79.32 %, and 40.02 % under the SSP126, SSP245, and SSP370 scenarios compared to the SSP585 scenario by 2100. Under the SSP245 and SSP370 scenarios, the incidence rate of asthma increases moderately, but begins to decline in latitudes above  $60^{\circ}$  in the 2080s under the SSP370 scenario.

#### 4. Discussion

To our knowledge, this is the first study to assess and quantify asthma incidence with climate change-induced maximum temperature variability on a global scale, and then predict the future tendency of the incidence of heat-related asthma. Our findings suggest that global asthma incidence is closely linked to changes in temperature. For each 1 °C increase in maximum temperature variability, the risk of asthma increases by 5.0 %. Furthermore, our results show that individuals living in middle SDI, high-latitude areas or aged 50 to 70 are at a higher risk of developing asthma. Adopting SSP126 is the best approach to minimize the effect caused by climate change.

A great number of studies have found that ambient temperature was associated with hospital admissions for asthma in the United States, China, and South Africa (Lin et al., 2009; Lam et al., 2016; Kapwata et al., 2021). The mechanism by which exposure to environmental maximum temperature variability trigger asthma involves three aspects. Firstly, high temperature may have a direct impact on inflammatory pathways or airway hyper-responsiveness leading to asthma attacks. An animal study shows that high temperatures can aggravate airway inflammation of asthma by activating the transient receptor potential (TRP) (Deng et al., 2020). Moreover, high temperature can elicit reflex bronchoconstriction by activating vagal bronchopulmonary C-fiber sensory nerves (Hayes et al., 2012). Secondly, high temperature may have an indirect impact on airborne allergens. High temperature can enhance the growth of and exposure to aeroallergens, such as mold spores, cockroaches, house dust mites (HDMs) (Murrison et al., 2019). Pollen and mold allergens are able to trigger the release of proinflammatory and immunomodulatory mediators that accelerate the onset the IgE-mediated sensitization and of allergy (D'Amato et al., 2020). Thirdly, hot days was associated with the level of air pollutants. Table 2

The characteristics of meteorological elements and O<sub>3</sub> and PM<sub>2.5</sub> from 1990 to 2019.

Variables	Maximum Temperature Variability (°C)	Maximum temperature <sup>a</sup> (°C)	Precipitation (mm)	Soil moisture (mm)	Wind speed (m/ s)	O <sub>3</sub> (ppb)	РМ <sub>2.5</sub> <sup>с</sup> (µg/ m <sup>3</sup> )
Global	0.70 (0.61)	29.4 (6.5)	103.3 (75.3)	66.7 (62.4)	2.9 (1.1)	39.6 (10.2)	27.2 (16.9)
SDI <sup>b</sup>							
Low	0.64 (0.52)	32.6 (4.4)	104.6 (73.2)	84.7 (75.9)	2.8 (1.2)	38.2 (9.7)	38.9 (16.8)
Low-middle	0.62 (0.54)	20.6 (4.4)	117.4 (84.2)	71.8 (69.6)	2.9 (1.0)	38.8 (11.1)	26.3 (14.0)
Middle	0.76 (0.71)	29.1 (6.4)	108.2 (82.7)	57.5 (55.2)	2.9 (1.0)	39.9 (9.9)	23.2 (13.7)
High- middle	0.76 (0.68)	27.0 (7.1)	89.0 (68.3)	48.7 (33.5)	2.9 (1.1)	40.9 (10.4)	20.0 (14.3)
High	0.83 (0.69)	22.5 (7.4)	83.7 (44.0)	50.6 (25.6)	3.2 (1.2)	42.8 (7.8)	15.4 (12.7)
Latitude (°)							
0-10	0.53 (0.44)	31.0 (2.9)	166.0 (78.8)	100.2 (73.6)	2.8 (0.9)	32.0 (8.5)	28.5 (16.1)
10-20	0.56 (0.47)	32.1 (3.3)	129.3 (72.5)	83.8 (72.5)	2.8 (1.0)	34.4 (6.9)	26.7 (16.9)
20–30	0.69 (0.54)	33.7 (6.4)	48.3 (46.9)	29.0 (41.5)	3.1 (1.2)	47.2 (10.0)	41.2 (21.6)
30–40	0.73 (0.59)	29.8 (5.6)	52.9 (37.2)	33.9 (27.0)	3.0 (1.1)	49.6 (7.4)	27.9 (14.1)
40–50	1.09 (0.81)	25.0 (4.2)	70.4 (33.4)	50.5 (29.1)	3.2 (1.2)	46.9 (5.2)	21.9 (8.8)
50-60	0.94 (0.77)	20.7 (1.7)	67.3 (18.3)	62.1 (15.3)	2.6 (1.0)	38.5 (3.3)	15.8 (5.5)
>60	0.80 (0.69)	11.6 (6.8)	56.9 (19.1)	42.4 (17.3)	3.5 (1.3)	38.6 (2.6)	8.6 (3.0)

All results are presented as mean (SD).

<sup>a</sup> Max temperature: the average temperature of the hottest 4 months of a year.

<sup>b</sup> SDI: Sociodemographic index.

 $^{c}$  PM<sub>2.5</sub>: particulate matter with aerodynamic diameter <2.5  $\mu$ m.

## Table 3

The association between asthma incidence and maximum temperature variability from 1999 to 2019.

	Model 1	Model 2
Global	1.05 (1.04, 1.06)	1.05 (1.05, 1.06)
Latitude (°)		
0–10	1.00 (0.97, 1.02)	0.99 (0.97, 1.00)
10-20	1.02 (1.00, 1.04)	1.07 (1.06, 1.08)
20-30	1.10 (1.07, 1.13)	1.07 (1.05, 1.08)
30–40	1.02 (0.99, 1.04)	1.00 (0.99, 1.02)
40–50	1.04 (1.02, 1.06)	1.02 (1.01, 1.03)
50–60	1.16 (1.13, 1.20)	1.17 (1.15, 1.19)
>60	1.21 (1.17, 1.26)	1.23 (1.20, 1.26)

Model1 was only adjusted for latitude. Model2 was further adjusted for sex, age, SDI, O<sub>3</sub>, PM<sub>2.5</sub>, year and climate factors (maximum temperature, soil moisture, precipitation and wind speed) based on Model1.

In our study, high levels of  $O_3$  and  $PM_{2.5}$  are a risk factor for asthma, and many studies also have shown that  $O_3$  and  $PM_{2.5}$  pollution would increase the incidence of asthma (Li et al., 2019; Zhou et al., 2022; Shen et al., 2023; Huang et al., 2022). Even a short-term elevation of low-level ozone (<70 ppb) were also associated with lung function decrements in adolescents with asthma (Hernandez et al., 2018).  $O_3$  and  $PM_{2.5}$  exposure can significantly increase the level of oxidative stress, which in turn quickly activates the release of alarmins, leading to a series of proinflammatory changes in structural and immune cells in the respiratory mucosal tissue (Enweasor et al., 2021). High levels of ROS can lead to airway smooth muscle hypertrophy, airway hyperresponsiveness, and lung histopathological changes, which increase the sensitivity of the airway to high temperature. We also found that high temperatures have a higher risk of asthma at the lowest pollutant concentrations of  $PM_{2.5}$ . But the underlying mechanism is not clear.

It is important to note that individuals living in high latitude areas  $(>50^\circ)$  are more vulnerable to maximum temperature variability compared to those living in other areas. Research using a mouse model of asthma has shown that extreme cold can activate transient receptor

potential proteins (TRPs) in the respiratory tract, leading to airway inflammation and hyper-responsiveness (Deng et al., 2020). This suggests that individuals in high latitude areas with extreme cold events may be more susceptible to asthma and other respiratory illnesses. Moreover, high latitude areas also have less exposure to sunlight, which is the primary source of vitamin D. Vitamin D has been found to reduce airway reactivity by modulating the expression of chemokines from airway smooth muscle cells and inhibiting dendritic cell maturation and Th1 cell development in experimental models (Salmanpour et al., 2022). Several studies have also shown that vitamin D deficiency increases the risk of asthma development, and maternal vitamin D insufficiency is associated with an increase in asthma events in early life of their infants (Jolliffe et al., 2017; Wolsk et al., 2017). Hence, maintaining optimal vitamin D levels may be important for preventing asthma and managing symptoms.

Our study has found that there is no significant correlation between maximum temperature variability and asthma incidence rate in children aged 0-9 years. However, in the 10-69 age group, the correlation between maximum temperature variability and asthma incidence rate increases with age. Interestingly, maximum temperature variability has been found to decrease the risk of asthma in elderly adults, particularly those aged 80 years and above. Studies have also shown that the risk of hospitalization for asthma related to temperature is more prominent in the population aged 19-64 (Chen et al., 2022; Zhao et al., 2019; Zafirah et al., 2021). One possible explanation for the lack of correlation in children aged 0-9 years is that they spend more time indoors and are often restricted in their activities, which reduces their exposure to outdoor temperature changes and other risk factors. On the other hand, the elderly may have reduced mobility and the past life experiences, which reduces their exposure to adverse temperature conditions and other risk factors. As a result, they may be less affected by maximum temperature variability. For most other age groups, individuals are more likely to go outdoors and be exposed to high temperatures. Therefore, when the maximum temperature deviates from the "ideal" temperature, the incidence rate of asthma in this population increases significantly.

Our study shows that the risk of developing asthma is influenced by greenhouse gas emissions, as represented by the four socioeconomic pathways: SSP126, SSP245, SSP370, and SSP585. People living in areas

#### Table 4

Subgroup analysis between covariates and maximum temperature variability.

	OR (95 % CI)	P value
Sex		
Male	1.05 (1.05, 1.06)	Ref.
Female	1.05 (1.04, 1.06)	0.45
SDI <sup>a</sup>		
Low	1.05 (1.04, 1.06)	Ref
Low-middle	1.03 (1.02, 1.04)	0.002
Middle	1.12 (1.10, 1.13)	< 0.001
High-middle	1.05 (1.04, 1.06)	0.82
High	1.00 (0.99, 1.02)	< 0.001
0		
Age		
1 to 9	1.00 (1.00, 1.01)	Ref
10 to 19	1.07 (1.06, 1.09)	< 0.001
20 to 29	1.08 (1.06, 1.11)	< 0.001
30 to 39	1.10 (1.08, 1.13)	< 0.001
40 to 49	1.14 (1.11, 1.16)	< 0.001
50 to 59	1.20 (1.18, 1.22)	< 0.001
60 to 69	1.20 (1.19, 1.22)	< 0.001
70 to 79	1.11 (1.09, 1.13)	< 0.001
80 to 89	0.98 (0.97, 1.00)	0.02
90 plus	0.91 (0.89, 0.92)	< 0.001
O <sub>3</sub> (ppb)		
0-28.4	1.01 (1.00, 1.03)	Ref.
28.4–33.1	1.01 (1.00, 1.02)	0.93
33.1-47.3	1.11 (1.10, 1.12)	< 0.001
>47.3	1.04 (1.03, 1.05)	0.002
$PM_{2.5}^{b}$ (µg/m <sup>3</sup> )		
5–10	1.05 (1.04, 1.06)	Ref.
10–15	1.00 (0.99, 1.02)	< 0.001
15–25	0.98 (0.97, 0.99)	< 0.001
25–35	1.10 (1.09, 1.11)	0.91
>35	1.09 (1.08, 1.10)	0.25

The final model was adjusted for latitude, sex, age, SDI, O<sub>3</sub>, PM<sub>2.5</sub>, year and climate factors (maximum temperature, soil moisture, precipitation and wind speed).

All results were represented with ORs and 95 % confidence interval.

<sup>a</sup> SDI: sociodemographic index.

 $^{b}\,$  PM\_{2.5}: particulate matter with an aerodynamic diameter  $<\!2.5\,\mu\text{m}.$ 

above 50° latitude are at a higher risk of developing asthma. The incidence rate of asthma is significantly higher under SSP585, characterized by high greenhouse gas emissions, while SSP126 represents the lowest emission scenario where strict actions are taken to combat global warming. In this scenario, the incidence rate of asthma remains stable and relatively low, with people living above 60° latitude experiencing greater health benefits. By 2100, the average incidence rate of asthma is estimated to decrease by 95.55 % in SSP126 compared to SSP585. Our findings highlight the importance of implementing stricter mitigation and adaptation strategies to combat global warming and promote targeted preventive measures against abnormal weather to better understand the impact of increased high temperatures on asthma. The implementation of proactive measures to safeguard public health against the effects of temperature variability is of paramount importance. One practical approach could involve establishing an early warning system to anticipate significant temperature variability, thus enabling timely, preventive actions at the individual level. Developing guidelines for personal protection and community-based planning, such as recommendations for staying indoors during severe temperature swings, would greatly assist individuals in understanding the appropriate responses to such climatic changes. On a broader and longer-term scale, initiatives designed to mitigate the impact of climate change should be enacted. These may include the adoption of clean energy sources and the reduction of greenhouse gas emissions as fundamental

steps towards alleviating the escalating trend of global warming. Furthermore, the creation and implementation of more targeted policies are vital to mitigating the negative effects of temperature variability on health, particularly in regions with heightened susceptibility to such climatic fluctuations.

Our research is subject to several limitations due to its reliance on GBD disease data and future prediction data. One significant challenge is the lack of a unified diagnostic standard across all GBD countries and regions, as well as differences in compliance with asthma guidelines across different levels of medical institutions (Chima et al., 2017). One significant challenge is the lack of a unified diagnostic standard across all GBD countries and regions, as well as differences in compliance with asthma guidelines across different levels of medical institutions. No reliable and universal definition exists for asthma, and a number of international guidelines on asthma diagnosis exist including Global Initiative for Asthma (GINA), National Asthma Education Prevention Programme/Expert Panel Report (NAEPP/EPR) and National Institute for Care Excellence (NICE) (Magwenzi et al., 2022). For example, in Central and Eastern European countries, bronchitis, and in particular asthmatic, spastic or obstructive bronchitis, may be used for diagnosis, when in Western Europe asthma would have been diagnosed. Many doctors at primary and secondary care facilities do not have access to equipment for lung function tests, which can impact the accuracy of diagnoses (Leonardi et al., 2002). Many doctors at primary and secondary care facilities do not have access to equipment for lung function tests, which can impact the accuracy of diagnoses. Moreover, the GBD dataset may provide highly administrative data for many countries, lacking detailed data from provinces, states, and counties. For example, although China has a large number of provinces and the world's largest population, the country only reports one incidence rate value each year, which may introduce uncertainty into our estimates of asthma incidence. Another limitation of the GBD analysis is the availability of primary data (Diseases GBD, Injuries C, 2020). GBD data is estimated using standardized Bayesian regression tools, but some countries, particularly those in Africa, may have wider confidence intervals due to limited disease data. In such cases, the estimation of asthma incidence rates may involve modeling results from neighboring countries, which may introduce uncertainty into our results. While data processing and modeling can improve the accuracy of estimates, the collection of more and better primary data is ultimately the best way to address these limitations. Additionally, annual data may not fully reflect the annual incidence rate and climate change and may not make full use of the high temporal resolution of TerraClimate monthly data. TerraClimate provides key climate variables, monthly reference evapotranspiration, and water balance components. In relation to our research focus and the data offered by TerraClimate, our model incorporates soil moisture, precipitation, and wind speed. However, it lacks other pertinent climatic factors, such as relative humidity. Finally, the lagged impact of environmental exposure on the occurrence of asthma among the population cannot be fully accounted for in our models due to a lack of good temporal epidemiological data (Sun et al., 2016). In addition, our analysis doesn't include information on possible behavioral changes that may occur under extreme temperatures and lifestyle habits, such as smoking, staying indoors, closing windows, and using air conditioning, which may reduce exposure to environmental temperature and air pollutants. Due to the wide range of countries and regions involved, our model cannot directly reflect the impact of pollen and wildfires, but instead refers to previous studies using PM2.5 to indirectly reflect the impact of wildfires (Noah et al., 2023). Our prediction model assumes that other factors remain constant from 2020 to 2100. However, it's important to note that as maximum temperature variability escalates, it's likely that some variables within the model will also undergo changes. Consequently, the observed effects in these regions could potentially be influenced by factors other than maximum temperature variability.



**Fig. 2.** The prediction of asthma incidence changes from 2020 to 2100 under SSP126, SSP245, SSP370, and SSP 585. **A**, the prediction of  $0-10^{\circ}$  latitude; **B**, the prediction of  $10-20^{\circ}$  latitude; **C**, the prediction of  $20-30^{\circ}$  latitude; **D**, the prediction of  $30-40^{\circ}$  latitude; **E**, the prediction of  $40-50^{\circ}$  latitude; **F**, the prediction of  $50-60^{\circ}$  latitude; **G**, the prediction of  $>60^{\circ}$  latitude.

#### 5. Conclusion

Our study provides evidence that maximum temperature variability is associated with the incidence rate of asthma. We also found that different shared socioeconomic pathways may lead to significantly different consequences for the future incidence rate of asthma, especially in high latitudes, which highlight the importance of implementing stricter mitigation and adaptation strategies to protect individuals against heat-related asthma.

Supplementary data to this article can be found online at https://doi. org/10.1016/j.scitotenv.2023.166726.

#### CRediT authorship contribution statement

Q.X.: Conceptualization, Methodology, Formal analysis, Data Curation, Writing-original draft preparation, Writing-review & editing, Visualization. Q.Z.: Methodology, Formal analysis, Writing-review and editing. J.C.: Conceptualization. T.L., J.M., R.D., M.S.: Writing-review and editing. J.L., M.X., S.S., J.M., M.R.: Supervision. Z.Z.: Conceptualization, Methodology, Supervision.

# **Ethics** approval

Not applicable.

# Role of the funding source

This research received no specific funding.

#### **Consent for publication**

All the authors have reviewed and approved the manuscript for publication.

# Declaration of competing interest

The authors have no possible conflicts of interest to declare.

#### Data availability

Please get in touch with the corresponding author for more information.

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