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

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1 **Global, regional, and national burden of allergic disorders and its risk**  
2 **factors in 204 countries and territories, 1990–2019: a systematic analysis**  
3 **for the Global Burden of Disease Study 2019**

4 **Running head:** Global disease burden of asthma and atopic dermatitis, 1990–2019

5

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32 **Summary**

33 **Background:** Asthma and atopic dermatitis (AD) are chronic allergic conditions that  
34 constitute the “atopic march” and cause significant morbidity both to children and adults.  
35 This study aimed to describe the global, regional, national and temporal trends of the burden  
36 of asthma and AD from 1990 to 2019 and analyze their associations with geographic,  
37 demographic, social, and clinical factors.

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

45 **Results:** In 2019, there were a total of 262 million [224–309] cases of asthma and 171  
46 million total cases of AD globally; age-standardized prevalence rates were 3,416 and 2,277  
47 [2.192–2.369] per 100,000 population for asthma and AD, respectively, a 24.1% [27.2–20.8]  
48 decrease for asthma and 4.3% [4.8–3.8] decrease for AD. Both asthma and AD had similar  
49 trends according to age, with age-specific prevalence rates peaking at age 5-9 and rising  
50 again in adulthood. The prevalence and incidence of asthma and AD were both higher for  
51 individuals with higher SDI; however mortality and DALYs rates of individuals with asthma  
52 had a reverse trend, with higher mortality and DALYs rates in those in the lower SDI  
53 quintiles. Of the three risk factors, high body mass index contributed to the highest DALYs  
54 and deaths due to asthma, accounting for a total of 3.65 million [2.14–5.60] asthma DALYs

55 and 75,377 [40,615–122,841] asthma deaths.

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

63 **Funding:** Bill & Melinda Gates Foundation, Australian National Health and Medical  
64 Research Council, Queensland Department of Health, Australia.

65

#### 66 **Key words**

67 Asthma; atopic dermatitis; epidemiology; mortality; disability-adjusted-life-years; global  
68 burden.

69

#### 70 **Abbreviations**

71 AD, Atopic dermatitis; DALYs, disability-adjusted-life-years; GBD, Global Burden of  
72 Disease; ICD, International Classification of Disease; SDI, socio-demographic index; 95% UI,  
73 95% uncertainty interval; YLD, Years of healthy life lost due to disability; YLLs, Years of  
74 life lost.

75

76 **Word count: 4178**

77

78 **INTRODUCTION**

79 Although frequently dismissed as diseases of childhood, allergic disorders such as asthma  
80 and atopic dermatitis (AD) are chronic diseases that can cause significant morbidity having  
81 long-term effects even into adulthood<sup>1</sup>. The prevalence of these physician-diagnosed allergic  
82 diseases has increased drastically over the years as reported in multiple studies<sup>2,3</sup>, now  
83 affecting approximately 10% to 30% of the population worldwide<sup>2,3</sup>. Not only do asthma and  
84 AD incur great healthcare-related economic costs, they also cause significant indirect costs  
85 due to decreases in quality of life and missed work, school, and productivity<sup>4</sup>.

86         Asthma and AD were once characterized as diseases being frequent in high-income  
87 countries, with affluent countries reporting higher prevalence rates and the “hygiene  
88 hypothesis” suggesting that maternal and childhood exposure to pathogens in low-resource  
89 settings could sensitize individuals to allergens<sup>4</sup>. However, the hypothesis that unhygienic  
90 conditions protect individuals against allergic illness has been criticized and expanded to  
91 encompass a complex interplay between genetic predisposition and the range of  
92 environmental exposures<sup>5</sup>. Further, on an individual level, lower socioeconomic status has  
93 been associated with higher disease burden – increased severity and poorer control of asthma  
94 and AD<sup>6</sup>; racial and ethnic disparities also exist<sup>6,7</sup>. Health equity regarding these diseases  
95 have been further accentuated recently, as novel and targeted treatment options, such as the  
96 use of biologics, has been gaining evidence and popularity, and numerous reports have called  
97 attention to disparities in access and efficacy of these emerging options<sup>8</sup>. As both asthma and  
98 AD are now recognized as major public health problems that greatly impact developing  
99 countries as well as developed countries<sup>6,7</sup>, it is important to provide evidence integrating  
100 data from around the world and across sociodemographic levels.

101           Against this backdrop, it is critical at this time to comprehensively analyze data to  
102 paint a global picture regarding the disease burden and time trends of allergic diseases  
103 (asthma and AD). There have been isolated studies detailing the global prevalence and  
104 disease burden of asthma and AD using the Global Burden of Disease (GBD) 2017<sup>9,10</sup>, but  
105 there has not yet been an up-to-date study encompassing both asthma and AD utilizing  
106 recently released dataset, both ends of the atopic march. Moving forward from scattered  
107 systematic reviews regarding the global distribution of these allergic diseases<sup>11</sup>, the present  
108 study aimed to provide a bird's eye view of the global distribution of asthma and AD by  
109 analyzing data from the GBD study from 1990 to 2019 and discussing temporospatial trends  
110 in association with country-level socioeconomic development to aid future public health  
111 interventions.

112

113

114



## 115 **METHODS**

### 116 *Overview*

117 Data utilized in this paper were obtained from the GBD 2019 Results Database, provides data  
118 in 204 countries and territories from 1990 to 2019. Our analysis was performed as part of the  
119 GBD Collaborator Network and complied with the Guidelines for Accurate and Transparent  
120 Health Estimates Reporting (Supplementary Method). Comprehensive methodology for the  
121 estimation models have been published elsewhere<sup>12</sup>. R software version 3.6.2 (R Foundation,  
122 Vienna, Austria) was used to generate all tables.

123

### 124 *Case Definition*

125 In the GBD 2019 list of causes, asthma corresponds to the International Classification of  
126 Disease 10th revision (ICD-10) codes J45 and J56 and ICD-9 code 493.<sup>10,13,14</sup> Asthma was  
127 defined as a chronic lung disease involving bronchospasms and shortness of breath due to  
128 allergic reactions or hypersensitivity, adjudicated by physician diagnosis and wheezing in the  
129 past year. AD, consistent with ICD-10 code L20, was defined as relapsing dermatitis, either  
130 localized or widespread, associated with pruritus, elevated serum immunoglobulin E, and  
131 immune dysregulation.<sup>1,9</sup> Cases were selected through literature review with physical exam  
132 and claims data, then further stratified into three severity levels with different disability  
133 weights according to physical deformity and pain/itch.

134

### 135 *Data acquisition and processing*

136 Main data inputs for assessing the prevalence of asthma and AD were population  
137 representative surveys, limited prevalence investigations in the literature described by a

138 systematic review of the literature, health service visits, surveillance data, survey data, and  
139 medical claims information. Estimates for prevalence, incidence, and disease burden were  
140 modeled through three main standardized tools, namely, (1) Cause of Death Ensemble model  
141 (CODEm), an optimized tool for analyzing cause of death by collecting an ensemble of  
142 different modeling methods with varying choices of covariates for high predictive validity; (2)  
143 Spatiotemporal Gaussian Process Regression (ST-GPR), a model for analyzing and  
144 comparing temporal and regional estimates between different groups; and (3) DisMod-MR  
145 2.1, a Bayesian meta-regression tool, utilized to provide consistency between epidemiological  
146 parameters including prevalence, incidence, remission, and mortality by adjusting variations  
147 of heterogeneous datasets from various modeling methods<sup>12</sup>.

148

#### 149 *Estimators of disease burden*

150 For this study, we obtained the publication estimates of incidence, prevalence, mortality,  
151 years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years  
152 (DALYs) for asthma and AD, respectively, for each 5-year age group, sex, year, and location  
153 from GBD 2019. Briefly, age-standardized rates per 100,000 population were computed by  
154 the direct method to the GBD population standard. YLLs were defined as the product of the  
155 number of deaths and the remaining life expectancy per age group, as per the GBD standard  
156 life table; YLDs were calculated as the product of the prevalence estimate and disability  
157 weights for that specific condition, in this case asthma and AD. DALYs were computed by  
158 the summation of YLL and YLD, representing the health loss due to a specific cause; in this  
159 case, asthma and AD. Estimates for disease burden were reported with 95% uncertainty  
160 intervals (UIs), defined as the 25<sup>th</sup> and 975<sup>th</sup> values of 1,000 samples drawn for each variable.

161 A detailed description of the methods can be found in the literature<sup>15</sup>.

162

### 163 ***Socio-demographic index***

164 The development status of each country was graded based on the socio-demographic index  
165 (SDI) as defined in the GBD study since 2017, which is a composite score from 0 to 1 based  
166 on the total fertility under age 25, average education in those over age 15, and lag-distributed  
167 income per person<sup>12,15</sup>. In our analysis, we classified countries into quintiles of ranked SDI  
168 values as low, low-middle, middle, high-middle, and high SDI as obtained from the GBD  
169 2019 data.

170

### 171 ***Risk factors***

172 DALYs and deaths for asthma attributable for three risk factors: namely, high body mass  
173 index (BMI), occupational asthmagens, and smoking, as classified in GBD 2019<sup>31</sup>, were  
174 obtained and further stratified by region and sex. Attributable risk factors for AD could not be  
175 evaluated from the current GBD database at this time.

176

### 177 ***Role of the funding source***

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

## 180 **RESULTS**

### 181 *Global and regional burden of asthma*

182 The age-standardized prevalence rates of asthma are mapped at the country level on Figure 1.  
183 Globally, the total number of patients with asthma increased slightly from 227 million [95%  
184 UI 195–270] in 1990 to 262 million [224–309] in 2019 (Figure 2 and Table S1). However,  
185 age-standardized prevalence rates had a 24.1% [20.8–27.2] decrease, from 4,497 [3,914–  
186 5,224] per 100,000 population in 1990 to 3,416 [2,899–4,066] per 100,000 population in  
187 2019. Incidence rates of asthma showed similar trends, with total incident cases having  
188 increased from 32.2 million [25.8–40.5] to 37.0 million [29.6–45.9], whereas age-  
189 standardized incidence rates having decreased from 580.1 per 100,000 population [474.7–  
190 715.0] to 504.3 per 100,000 population [400.6–633.3] in 1990 and 2019, respectively (Table  
191 S2).

192 Asthma accounted for a total of 0.461 million [0.367–0.559] deaths in 2019, resulting  
193 in an age-standardized mortality rate of 5.8 per 100,000 population; this was a 51.3%  
194 decrease since 11.9 in 1990. Both the total number of DALYs and age-standardized DALYs  
195 rates due to asthma decreased from 1990 to 2019 (Figure 2 and Table S3 and S4). In  
196 particular, age-standardized DALYs rates underwent a steep dive of 42.5% [48.5–36.6] from  
197 1990 and 2019, with DALYs rates of 476.3 per 100,000 population [378.5–579.6] in 1990 to  
198 273.6 [216.7–343.4] per 100,000 population in 2019.

199 High-income North America and Australasia regions had the highest and second-  
200 highest age-standardized prevalence of asthma at 9,848 [8,624–11,312] and 8,393 [6,909–  
201 10,347] per 100,000 population, respectively, in 2019. Notably, the high-income North  
202 America region had a 9.6% [1.2–19.2] increase from 1990, with the United States

203 contributing most of the increase at 10.9% [2.0–21.4] from 1990 to 2019; Australasia,  
204 consistent with most regions and the global trend, had a 30.6% [40.6 –18.5] decrease from its  
205 prevalence rate in 1990.

206 East, Central, and South Asia were the regions with the lowest age-standardized  
207 prevalence of asthma, at 2,026 [1,577–2,631], 2,277 [1,883–2,788], and 2,443 [2,030–2,910]  
208 per 100,000 population, respectively, in 2019. The lowest age-standardized prevalence rates  
209 of asthma were reported in Nepal and Bangladesh, at 1,073 [932–1,215] and 1,391 [1,217–  
210 1,574] per 100,000 population.

211 DALYs rates showed a somewhat different regional trend, with Oceania reporting  
212 the highest DALYs rates of 1,102 [864–1431] per 100,000 population, and East Asia  
213 reporting the lowest DALYs rates of 106.4 [75.3–152.1] per 100,000 population.

214 In most countries, age-standardized DALYs rates had a precipitous decrease over time, the  
215 drop in DALYs rates being as large as 72.3% [60.8–79.2] in the Republic of Korea; the only  
216 exceptions were Montenegro, the United States, and Paraguay, with 6.7% [-1.3–15.9], 4.4%  
217 [-3.4–12.9], and 3.1% [7.8–13.7] increase in DALYs from 1990 to 2019.

218

### 219 *Global and regional burden of AD*

220 In 2019, the number of prevalent cases of AD worldwide was 171 million [165–178], an  
221 increase from 133 million [128–138] cases in 1990; in contrast, global age-standardized rates  
222 of AD had a slight decrease of -4.3% [-4.8 to -3.8] to 2,277 [2.192–2.369] per 100,000  
223 population in 2019 (Figure 1 and Table S5). Similarly, total incident cases rose from 19.2  
224 million [18.3–20.2] in 1990 to 24.4 million [23.3–25.6] in 2019, but age-standardized  
225 incidence rates dropped slightly (-4.2% [-4.8 to -3.6] change; Table S6).

226 As there were no deaths directly attributable to AD, DALYs for AD was the same as  
227 the YLDs. DALYs rates due to AD showed the same trend as prevalence and incidence; the  
228 total number of DALYs rose steeply from 5.827 million [3.090–9.784] in 1990 to 7.480  
229 million [3.987–12.58] in 2019, age-standardized rates had a slight drop of 4.1% [3.5–4.8] to  
230 99.7 per 100,000 population (Table S7 and S8).

231 The prevalence rates of AD did not vary as drastically between regions as those of  
232 asthma, but there were still some regional trends. The highest prevalence rates of AD were  
233 reported in the High-income Asia Pacific region at 4,876 [4,639–5,113] per 100,000  
234 population and Central Asia at 4,678 [4,210–5,192] per 100,000 population; the lowest  
235 prevalence rates of AD were reported in African countries, including Central, Eastern,  
236 Southern, and Western Sub-Saharan Africa, with 1,081 [1,009–1,162], 1,082 [1,035–1,132],  
237 1,083 [1,027–1,140], and 1,102 [1,054–1,149] per 100,000 population. In most regions,  
238 prevalence rates of AD remained stable over 1990–2019; the steepest increase was seen in  
239 Kenya at merely 5.3% [2.0–8.2], and the largest drop was seen in the Maldives at a similar  
240 percentage of 6.6% [6.0–7.2]. DALYs rates of AD had a similar regional distribution with  
241 prevalence rates of AD, with highest DALYs rates in the High-income Asia Pacific region  
242 and lowest DALYs rates in the Sub-Saharan Africas.

243

#### 244 ***Trends according to demographic factors***

245 Consistently throughout 1990–2019, the total number of incident cases and age-standardized  
246 incidence rates of asthma were similar between females and males, whereas those of AD  
247 were substantially higher in females than males (Figure 3). Both total incidence and incidence  
248 rates of asthma down-trended slightly from 1990 to 2005, then increased from 2005 to 2019,

249 drawing a slight V-shape over time. In contrast, the total incidence of AD increased steadily  
250 from 1990 to 2019, while age-standardized rates decreased slightly over the same period.  
251 Time trends were similar in both sexes.

252         Stratified by age, in 2019, the total number of prevalent cases peaked at age 5-9,  
253 down-trended to reach a plateau at age 25-69, then decreased in the older age groups (Figure  
254 4). In contrast, the age-specific prevalence rate of asthma had an N-shaped distribution, with  
255 prevalence rates peaking in age 5-9, reaching a lowest point at age 25-29, then subsequently  
256 rising well into the oldest age group ( $\geq 95$  years). Total age-specific prevalent cases and  
257 prevalence rates of asthma were higher for males up to the 15-19 age group; afterwards, the  
258 trend reversed with higher prevalence in females.

259         Total prevalent cases of AD according to age groups showed similar trends as that of  
260 asthma, having a distribution heavily skewed in infancy and early childhood with a high peak  
261 in the 5-9 age group and a steep decrease thereafter (Figure 4). Age-specific prevalence of  
262 AD was characterized by an earlier peak in age groups 1-4 and 5-9 and a later trough at age  
263 35-44. For AD, both age-specific prevalence rates and total number of prevalent cases were  
264 higher for females in all age groups, with the difference almost twofold in young adulthood  
265 (ages 25-45).

266

### 267 ***Burden of asthma and AD in accordance with SDI***

268 Age-standardized DALYs rates of asthma decreased steadily from 1990 to 2005 over all SDI  
269 quintiles, with the exception of the High SDI quintile, for which the DALYs rates increased  
270 slightly since 2005 (Figure 5). Higher SDI levels tended to have lower DALYs rates, with  
271 High, High-middle, and Middle SDI quintiles having substantially lower DALYs rates than

272 Low and Low-middle quintiles consistently over the study period, and with the Low SDI  
273 quintile having the highest, and the High-middle quintile having the lowest DALYs rates  
274 throughout 1990 to 2019 (553.9 [434.7–726.8] and 158.3 [114.0–220.2] per 100,000  
275 population, respectively, in 2019). On the other hand, the High SDI quintile had the highest  
276 age-standardized prevalence, incidence, and YLDs rates of asthma across the study period,  
277 compared to lower SDI quintiles (Figure S4–S6). The highest SDI quintile had a prevalence  
278 rate of 6,855 [5,877–8,058] per 100,000 population; at the same time, the High and High-  
279 middle SDI quintiles experienced the largest decrease in asthma prevalence of 17.7% [14.2–  
280 20.9] and 26.8% [22.2–32.1], respectively, over the study period. The discrepancy in  
281 associations with SDI could be explained by the mortality rate; although the mortality rate  
282 decreased for all SDI quintiles over the study period, lower SDI was associated with higher  
283 mortality in all timeframes (Figure S3).

284 Age-standardized DALYs rates of AD were stagnant across time in all SDI levels,  
285 and the association between DALYs and SDI was reversed in AD. Higher SDI levels had  
286 higher DALYs rates of AD throughout 1990–2019, with the High SDI quintile having more  
287 than double the DALYs rates of the Low SDI quintile (155.5 [83.5–262.0] and 59.7 [32.0–  
288 100.1] per 100,000 population, respectively, in 2019). This trend was replicated in prevalence  
289 and incidence rates of AD; the High SDI quintile had the highest prevalence rate of 3,540  
290 [3,376–3,685] per 100,000 population, whereas the Low SDI quintile had the lowest  
291 prevalence rate of 1,359 [1,301–1,424] per 100,000 population in 2019 (Figures S1 and S2).

292

### 293 ***Burden of asthma attributable to risk factors***

294 We also analyzed the DALYs of asthma attributable to three different risk factors, namely



295 BMI, occupational asthmagens, and smoking (Figure 6).

296 Globally, high BMI contributed to the most DALYs and deaths due to asthma in  
297 2019, followed by smoking and occupational asthmagens, with a total of 3.65 million [2.14–  
298 5.60], 2.12 million [1.13–3.01], and 1.90 million [1.51–2.33] asthma DALYs, and total  
299 75,377 [40,615–122,841], 54,849 [29,149–78,006] and 34,395 [27,828–42,614] deaths  
300 attributable to each risk factor, respectively (Figure S25 and S27). In both men and women,  
301 South Asia had the highest number of asthma DALYs attributable to all three risk factors  
302 (0.910 million [0.447–1.587] for high BMI, 0.622 million [0.475–0.818] for occupational  
303 asthmagens, and 0.689 million [0.333–1.044] for smoking), mirroring the number of total  
304 DALYs due to asthma. South Asia was followed by North Africa and Middle East, High-  
305 income North America, and Southeast Asia, for highest asthma DALYs due to high BMI; the  
306 trend was slightly different for occupational asthmagens and smoking, for which the second  
307 and third-highest asthma DALYs occurred in Southeast Asia and Eastern Sub-Saharan Africa  
308 for occupational asthmagens, and Southeast Asia and East Asia for smoking, respectively  
309 (Figure S25).

310 Consistent with the high absolute numbers of attributable DALYs, high BMI  
311 accounted for nearly 30% of asthma DALYs in the North Africa and Middle East (27.9%  
312 [18.3–38.8]) and Southern Sub-Saharan Africa (27.7% [18.3–38.0]), but only 9.6% [5.0–6.6]  
313 in the High-income Asia Pacific. In most regions, females had a higher proportion of asthma  
314 DALYs attributable to high BMI, with the exception of the high-income Asia Pacific and East  
315 Asia regions. These two regions also had the lowest percentages of DALYs due to high BMI.

316 Eastern, Western, and Central Sub-Saharan Africa had a substantially higher  
317 percentage of asthma DALYs due to occupational asthmagens compared to other regions,

318 which were 13.3% [11.8–14.8], 11.9% [10.5–13.3], and 10.8% [9.0–12.4], respectively.  
319 Further, the percentage of asthma DALYs attributable to occupational asthmagens were  
320 higher in males than in females in all regions.

321           The highest asthma DALYs attributable to smoking occurred in Central Europe (12.7%  
322 [7.2–17.8]) and Western Europe (12.2% [6.7–17.0]), and lowest in Andean Latin America  
323 (1.3% [0.5–2.1]). Notably, the percentage of DALYs attributable to smoking was  
324 substantially higher in males in most regions with the exception of High-income North  
325 America, Southern Latin America, and Australasia; these countries had some of the highest  
326 proportions of DALYs due to smoking in females nearing 10%.

327

328 **DISCUSSION**

329 Asthma and AD increased in total prevalent and incident cases worldwide, but have  
330 decreased in age-standardized prevalence rates from 1990 to 2019. Both have strong  
331 associations with age, being most prevalent at age 5-9 but the prevalence increasing in later  
332 adulthood. These diseases tend to have higher prevalence in countries with higher SDI, but  
333 for asthma, lower SDI was associated with higher mortality and DALYs rates; further, disease  
334 burden varied substantially across geographic region. Further epidemiologic studies of  
335 asthma and AD spanning the globe are warranted to mitigate the high disease burden due to  
336 these allergic diseases and achieve equity in prevention, diagnosis and treatment.

337 Asthma and AD are atopic diseases that can affect individuals throughout the life  
338 course, having major repercussions both in population health and in the global economy.  
339 However, reflecting heightened awareness from early in life, improved diagnostic resources,  
340 and perceptions that affluent populations are prone to allergic diseases, many studies have  
341 been focused on high-income countries, such as the United Kingdom, the European Union,  
342 and the United States<sup>16,17</sup>. Furthermore, as these diseases have been considered as pediatric  
343 conditions, most studies have leaned towards children<sup>3</sup>. To provide a global bird's eye view  
344 regarding the true public health impact of these diseases across the lifespan, we investigated  
345 the most up-to-date data from the GBD 2019 study to describe the global prevalence,  
346 incidence, and disease burden of asthma and AD and analyzed their associations with  
347 geographic region, demographic characteristics, SDI, and risk factors.

348 In 2019, there were 262 million total cases (2.4%) of asthma globally across all ages,  
349 the percentage lower than other studies from the World Health Survey (4.3% in adults),  
350 Global Asthma Network (10.4% in adolescents and 9.9% in children), and the International

351 Study of Asthma and Allergies in Childhood (13.7% in age 13–14 and 11.6% in age 6–  
352 7)<sup>2,18,19</sup>. This discrepancy could be explained by the difference in included countries and age  
353 groups, especially considering the significant variation in asthma prevalence between  
354 countries and along the life course evident in the GBD data and in the other worldwide  
355 studies. While the total number of patients with asthma increased, age-standardized  
356 prevalence rates had a large decrease of 24.1% globally, with incident cases and incidence  
357 rates mirroring the same trend, which suggests that the increase in number was in part due to  
358 population expansion. Likewise, the prevalence rate of asthma decreased in most regions.  
359 However, few regions, such as the United States, had a rise in asthma prevalence; this  
360 increase could be attributed to increased awareness and diagnostic availability of asthma due  
361 to public health campaigns such as the National Asthma Education and Prevention Program  
362 and, in part, overdiagnosis<sup>20</sup>.

363         The disease burden of asthma represented by age-standardized DALYs rates and  
364 mortality rates also underwent a steep decrease of 42.5% and 51.3% from 1990 to 2019,  
365 respectively. This could reflect the establishment of cornerstone guidelines (e.g., the National  
366 Heart, Lung, and Blood Institute guidelines, first issued in 1991, and the Global Initiative for  
367 Asthma guidelines, first published in 1995), heightened awareness and better management of  
368 asthma globally, and the development and popularization of different treatment options<sup>21,22</sup>.  
369 For example, the decrease in asthma DALYs were especially precipitous in some countries,  
370 reaching 72.3% in the Republic of Korea; this could reflect various initiatives and cohorts  
371 that took place since the early 2000s, such as the Cohort for Reality and Evolution of Adult  
372 Asthma, the Korea Asthma Allergy Foundation, and the Seoul Atopy-Asthma-friendly  
373 School Project<sup>23</sup>. However, as there still exist wide variations in DALYs and mortality rates

374 around the globe and within regions, it is critical to continue efforts for better prevention and  
375 control of asthma, especially in under-resourced settings<sup>6</sup>.

376 For AD, there were 171 million total cases globally, approximately 2.23% of the  
377 population. Although the absolute number of prevalent and incident cases rose from 1990 to  
378 2019, age-standardized prevalence and incidence rates stayed relatively stable over time,  
379 undergoing only a slight drop of 4.3% and 4.2%, respectively. Between regions, the  
380 prevalence and DALYs rates of AD did not vary as drastically between countries and regions  
381 as those of asthma; however, the highest prevalence and DALYs rates were reported in the  
382 High-income Pacific region, and the lowest rates were reported in the Sub-Saharan Africa  
383 regions. The low reported disease burden in African countries may be partly ascribed to  
384 differences in diet and environment, but may also be a result of under-reporting, especially as  
385 AD prevalence has recently been increasing in these developing countries<sup>24</sup>. Therefore,  
386 additional epidemiologic studies should take place to delineate complex factors associated  
387 with the changes in different parts of the world and efforts to boost awareness and diagnostic  
388 capability in under-resourced settings should be continued.

389 Consistent with the literature and common perceptions, this study found that both  
390 asthma and AD peaked in the younger ages, typically ages 5-9<sup>18,21</sup>; however, we also found  
391 that age-standardized rates increased past adulthood well into older ages. As asthma and AD  
392 in older populations may be difficult to diagnose and treat due to their traditional  
393 misconceptions as “pediatric diseases”, different clinical presentations (i.e., phenotypes)and  
394 functional characteristics, and multiple comorbidities associated with aging, physicians  
395 should be vigilant in the recognition and multi-dimensional management of these conditions  
396 in older adults<sup>25</sup>.

397 Higher SDI levels tended to have higher prevalence of asthma and AD, as reported in  
398 numerous international studies previously<sup>3,18,26</sup>. Notably, however, mortality and DALYs  
399 rates had the reverse trend, with lower SDI quintiles having substantially higher DALYs and  
400 higher mortality. Low-resource settings have been associated with worse outcomes of asthma,  
401 mediated by socioeconomic factors such as income and education, environmental allergens or  
402 pollutants, psychosocial stressors, and lack of access to healthcare<sup>6,27</sup>. Likewise, many inner-  
403 city populations in low- and middle-income countries have very high prevalence of asthma  
404 but limited access and affordability for essential medications for persistent asthma<sup>28</sup>; under-  
405 treatment in these countries causes significant morbidity and mortality<sup>29</sup>. Further, the high  
406 incidence of acute respiratory infections in low- and middle-income countries can lead to  
407 asthma exacerbations as well as under-diagnosis and thus under-treatment of asthma, leading  
408 to a relatively lower reported prevalence and higher morbidity<sup>30</sup>. These trends suggest a large  
409 potential for global and community initiatives to improve asthma outcomes in low-resource  
410 populations<sup>27,31</sup>.

411 The present study was the first to systematically assess the disease burden of asthma  
412 and AD across regions and throughout the lifespan using the most recent GBD data. However,  
413 there are some limitations to our study. First, the definition of asthma and AD were made  
414 mainly through physician diagnosis and symptom data, the stringency of which could have  
415 been heterogeneous across regions – for example, different countries using different terms to  
416 describe symptoms of asthma or AD – and thus resulted in a discrepancy of prevalence  
417 statistics. Second, as this study was driven by data from the GBD study, it includes the  
418 limitations of the GBD dataset, mainly, that some regions had low availability and quality of  
419 data, for which statistics had to rely on predictive covariates. Furthermore, as we compared

420 country-level aggregate data, the trends and associations we found are subject to ecological  
421 bias. Lastly, we could only assess the attributable risk for asthma on three risk factors (high  
422 BMI, occupational asthmagens, and smoking); more research is necessary to investigate  
423 associations with different demographic and clinical factors, and also for AD.

424 In summary, asthma and AD are both allergic diseases that have increased in total burden  
425 worldwide but have decreased in age-standardized prevalence rates from 1990 to 2019.  
426 Although both are more frequent in the younger ages and prevalent in high-SDI countries,  
427 each condition has distinct temporal and regional trends. This study will help assess regional  
428 and temporal trends regarding the distribution and disease burden of asthma and AD, and  
429 guide interventions to better manage these diseases worldwide as well as to attain equity in  
430 prevention, diagnosis and treatment.

431

432

433 **Contributors**

434 Please see the appendix for detailed information about individual author contributions to the  
435 research, divided into the following categories: managing the estimation or publication  
436 process; writing the first draft of the manuscript; primary responsibility for applying  
437 analytical methods to produce estimates; primary responsibility for seeking, cataloguing,  
438 extracting, or cleaning data; designing or coding figures and tables; providing data or critical  
439 feedback on data sources; development of methods or computational machinery; providing  
440 critical feedback on methods or results; drafting the manuscript or revising it critically for  
441 important intellectual content; and managing the overall research enterprise. Youn Ho Shin,  
442 Jimin Hwang, Seung Won Lee, Jae Il Shin, and Dong Keon Yon had full access to the data in  
443 the study and final responsibility for the decision to submit for publication.

444

445 **Data sharing**

446 Citations for the data used in the study can be accessed from the Global Health Data  
447 Exchange (<http://internal-ghdx.healthdata.org/>). Access to the data is also provided as a data  
448 use agreements permit.

449

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453



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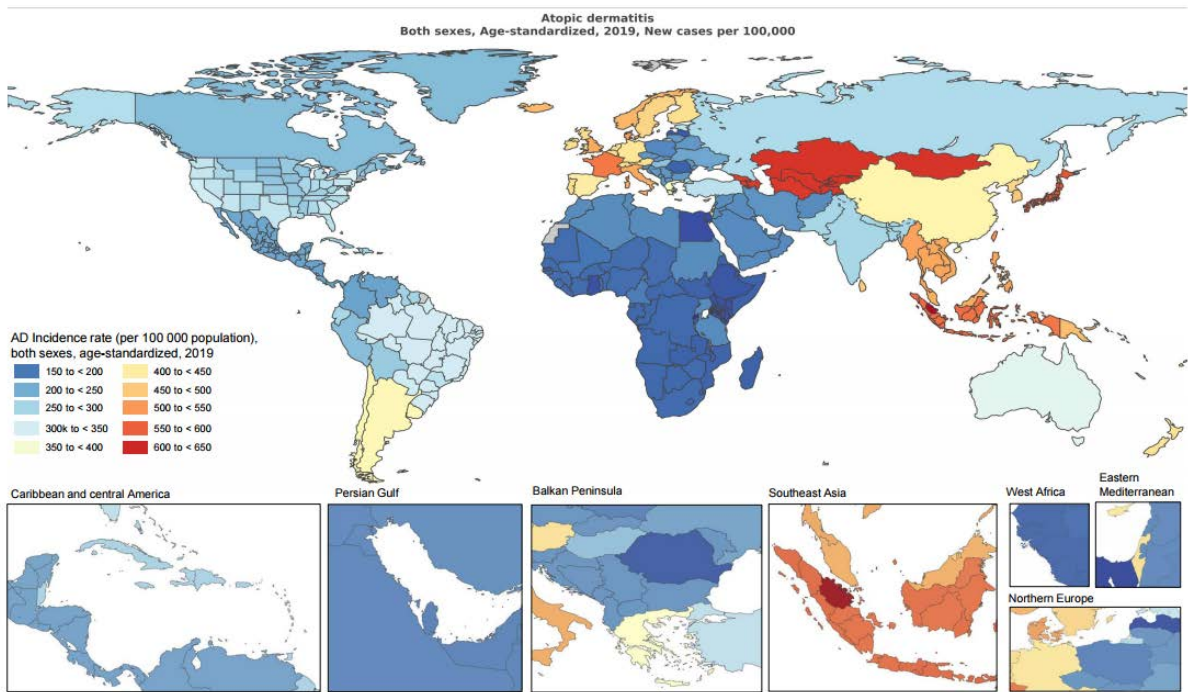
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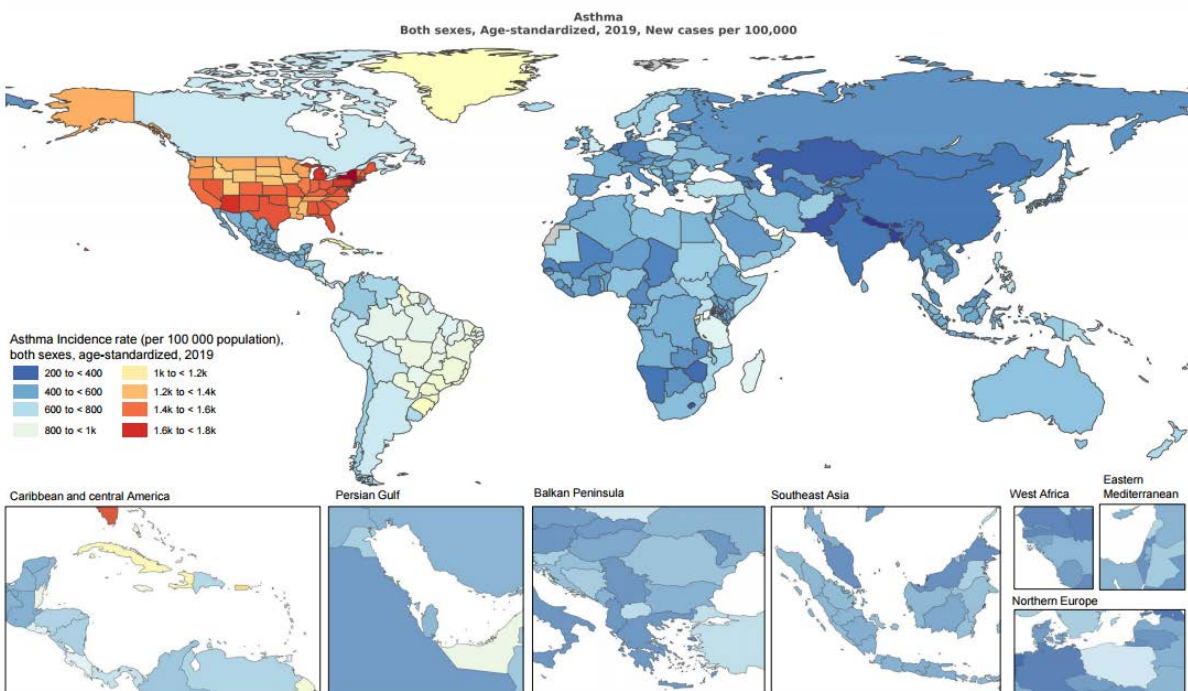
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547 **Figure 1.** Global distribution of the age-standardized prevalence rates of asthma (A) and AD  
 548 (B). AD, atopic dermatitis.



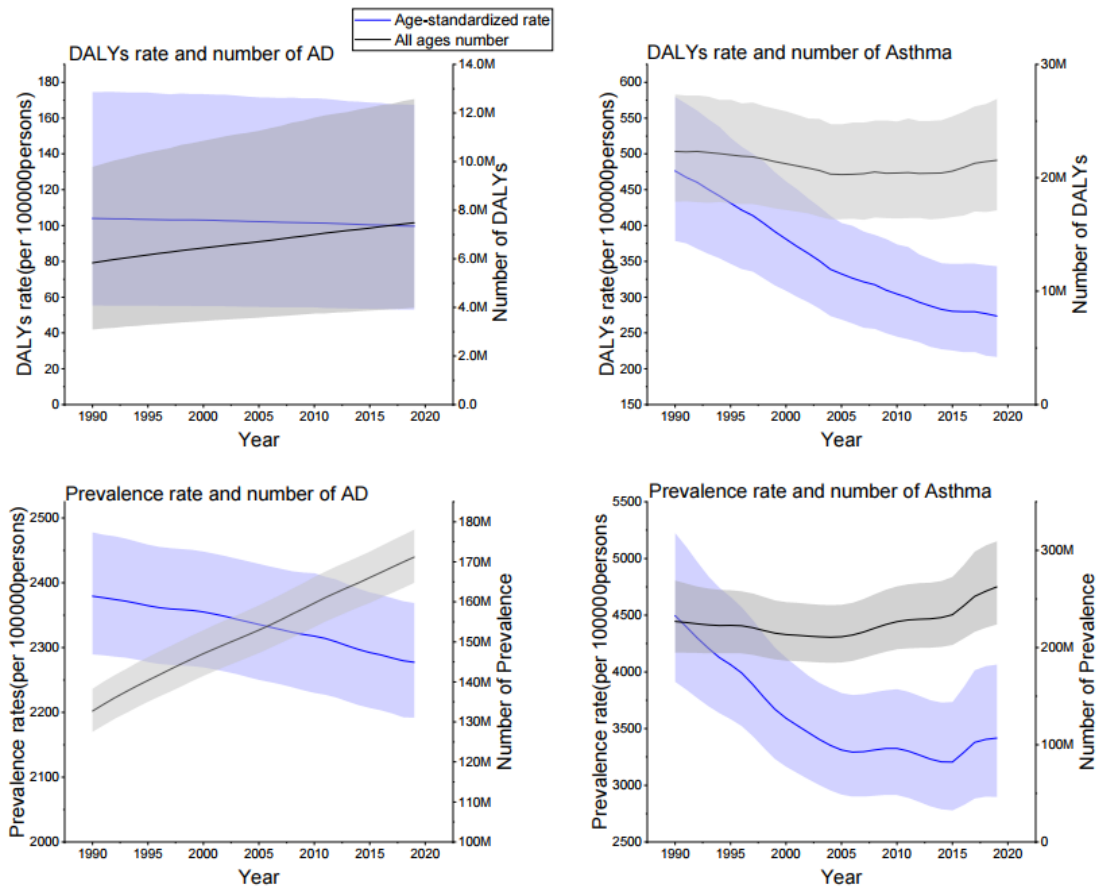
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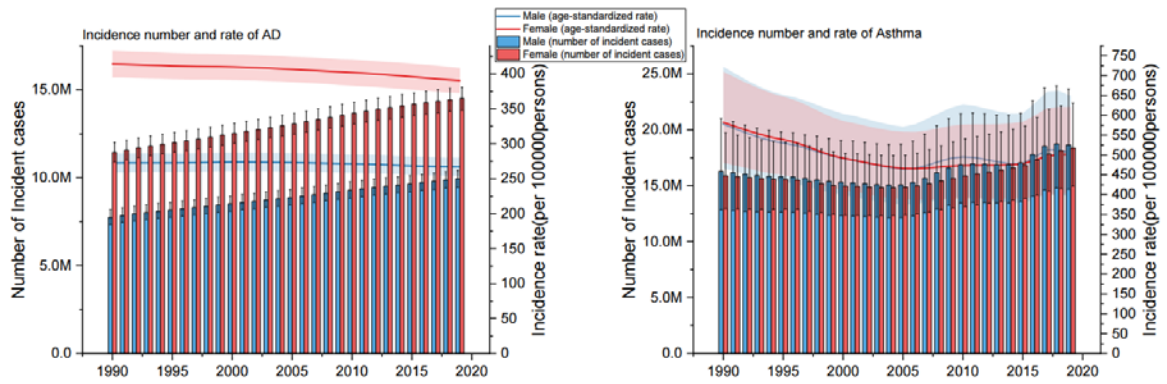
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552 **Figure 2.** Global prevalence and DALYs of asthma (A and B) and AD (C and D), 1990–2019.  
 553 AD, atopic dermatitis; DALY, disability-adjusted life-years.



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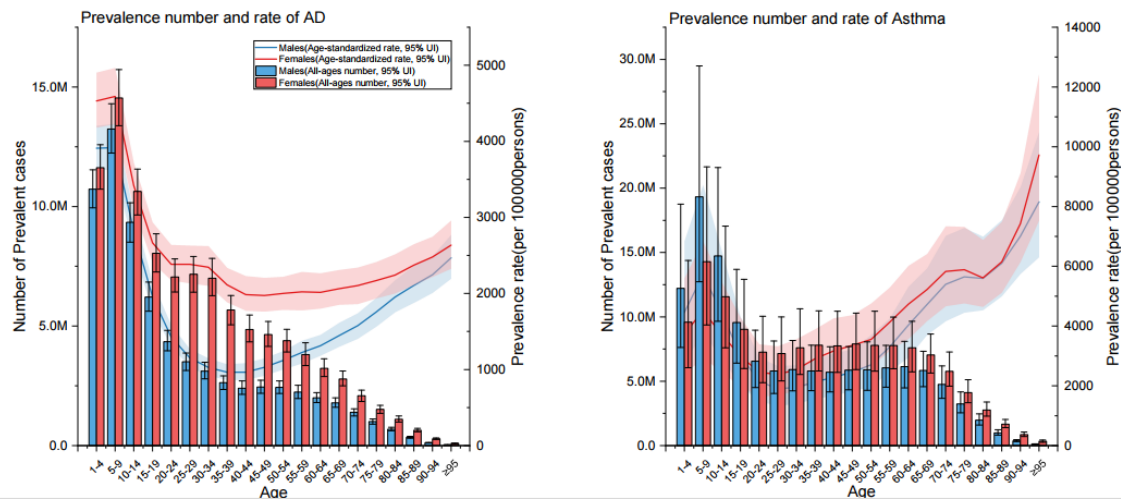
557 **Figure 3.** Total number of incident cases and global incidence rates of asthma (A) and AD (B)  
 558 by sex, 1990–2019.



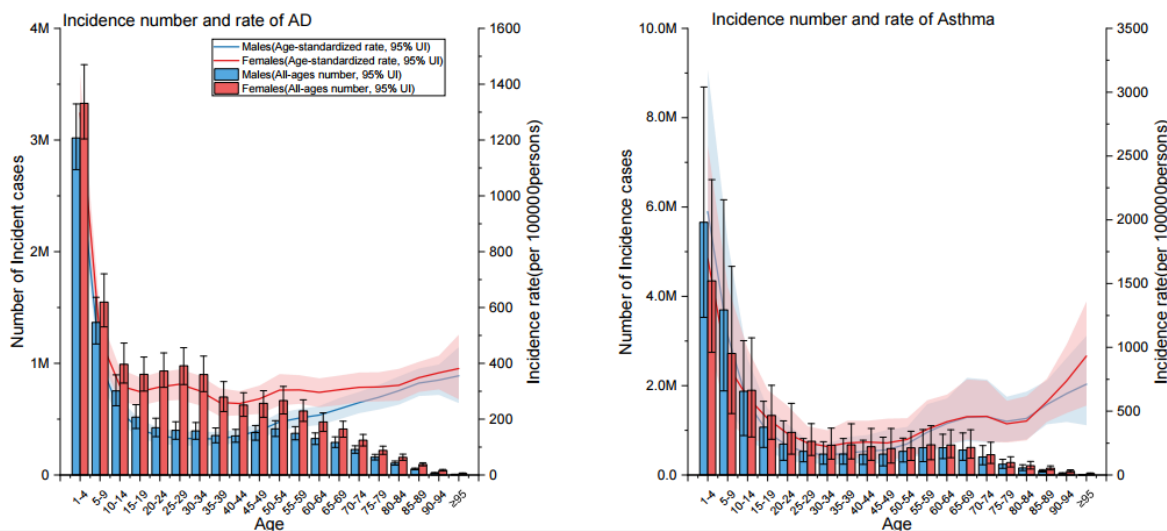
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561 **Figure 4.** Total number of prevalent cases and global prevalence rates of asthma (A) and AD  
 562 (B) by age, 1990–2019.



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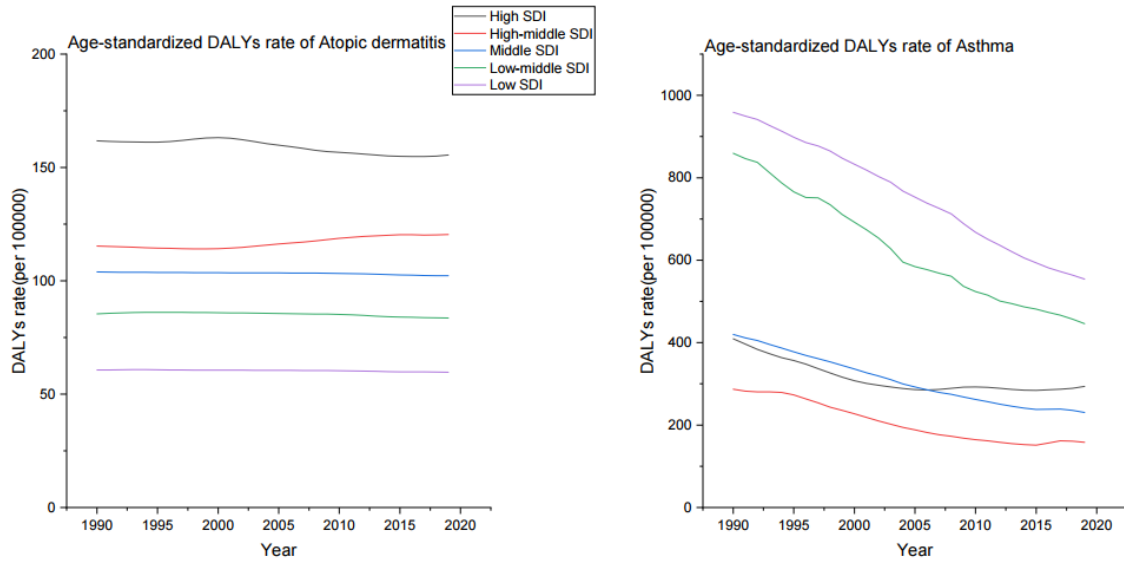


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567 **Figure 5.** Age-standardized DALYs rates of asthma (A) and AD (B) according to SDI, 1990–  
568 2019. AD, atopic dermatitis; DALY, disability-adjusted life-years; SDI, socio-demographic  
569 index.

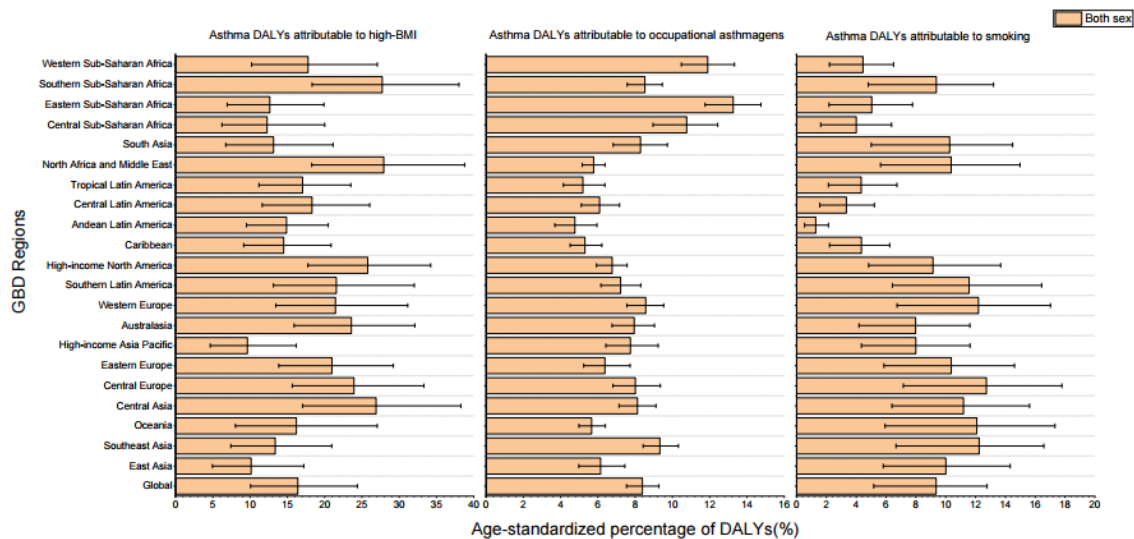


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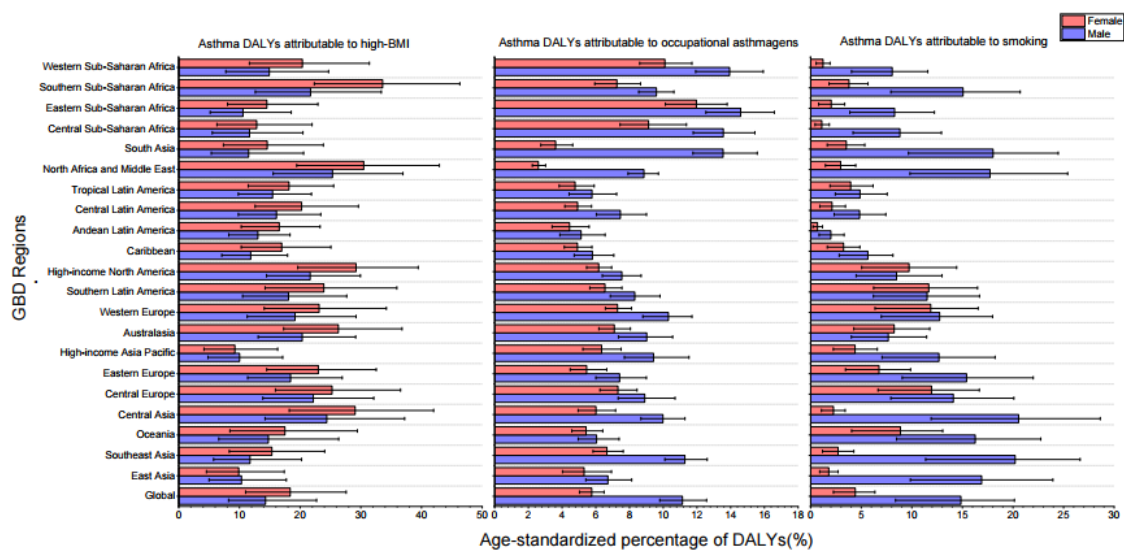
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573 **Figure 6.** Percentage of age-standardized DALYs rates of asthma attributable to high BMI,  
 574 occupational asthmagens, and smoking by geographic region, total (A) and sex-stratified (B).  
 575 BMI, body mass index; DALY, disability-adjusted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



576



577