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Mauricio, Castañeda-Orjuela, Carlos A., Cegolon, Luca, Cenderadewi, Muthia, Cerin, Ester, Chakraborty, Chiranjib, Chakraborty, Sandip, Chan, Jeffrey Shi Kai, Chandrasekar, Eeshwar K., Chaudhary, Anis Ahmad, Chen, Hana, Chen, Haimei, Chen, Shanquan, Cheng, Esther T. 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Nuruzzaman, Khan, Maseer, Khan, Mohammad Jobair, Khan, Moien AB, Khanal, Vishnu, Khatab, Khaled, Khatatbeh, Moawiah Mohammad, Khidri, Feriha Fatima, Khosravi, Majid, Kim, Kwanghyun, Kim, Yun Jin, Kimokoti, Ruth W., Kinati, Tadele, Kisa, Adnan, Kisa, Sezer, Kivimäki, Mika, Knibbs, Luke D., Kolahi, Ali-Asghar, Kompani, Farzad, Koomson, Isaac, Korshunov, Vladimir Andreevich, Korzh, Oleksii, Kostev, Karel, Kothari, Nikhil, Krishan, Kewal, Kritikos, Neoklis, Kuddus, Mohammed, Kuitunen, Ilari, Kulimbet, Mukhtar, Kumar, Dewesh, Kumar, Jogender, Kumar, Rakesh, Kundu, Satyajit, Kunutsor, Setor K., Kurmanova, Almagul, Kurmi, Om P., Kurniasari, Maria Dyah, Kyei-Arthur, Frank, Kytö, Ville, La

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- 1 Original article
- 2 **Global, regional, and national burden of chronic respiratory diseases and the COVID-19**
- 3 **pandemic-driven estimates, 1990-2021: a Global Burden of Disease Study**
- 4 **Running title:** Global burden of chronic respiratory diseases
- 5
- 6 **GBD 2021 Chronic Respiratory Disease Collaborators**
- 7

8 **Abstract**

9 Chronic respiratory diseases (CRD) are one of the leading causes of mortality and morbidity
10 globally. While the COVID-19 pandemic may have substantially influenced acute respiratory
11 health trends, its impact on chronic respiratory conditions remains unclear. We provide updated
12 estimates of the global, regional, and national burden of CRD from 1990 to 2021, identify its
13 risk factors, and evaluate how the burdens have shifted during the COVID-19 pandemic period.
14 To evaluate the burden of CRD, including chronic obstructive pulmonary disease (COPD),
15 asthma, pneumoconiosis, and interstitial lung disease (ILD) and pulmonary sarcoidosis, we
16 analyzed estimates from the Global Burden of Disease, Injuries, and Risk Factors Study 2021.
17 We extracted age-standardized prevalence, disability-adjusted life years, mortality estimates,
18 and burden attributable to 13 risk factors. As a secondary analysis, we assessed the potential
19 influence of the COVID-19 pandemic (2019–2021) on incidence and mortality from CRD by
20 comparing the expected deaths in the absence of the pandemic based on estimates between
21 2010 and 2019. In 2021, CRD accounted for an estimated 468.3 million (95% uncertainty
22 interval [UI], 428.9–513.1) cases and 4.4 million (95% UI, 4.0–4.9) deaths globally. The age-
23 standardized CRD death rate has decreased by 36.7% worldwide from 1990 to 2021, despite
24 an increase of 15.1% in high-income North America and a 50.3% increase in ILD and
25 pulmonary sarcoidosis. The CRD deaths declined most significantly in individuals aged <15
26 years, whereas older adults had the least decline, or even an increase, particularly for ILD and
27 pulmonary sarcoidosis. The COPD burden was primarily attributed to smoking, whereas high
28 body mass index and occupational silica exposure were the major contributors to asthma and
29 pneumoconiosis, respectively. During the COVID-19 pandemic era, age-standardized
30 incidence rates for CRD increased, but age-standardized CRD mortality rates remained
31 relatively stable. Although the overall burden of CRD has decreased, the number of people
32 affected by CRD still remains substantial, with variations depending on CRD etiology and

33 region. These findings highlight the critical need for targeted interventions addressing region-
34 and context-specific risk factors, such as tobacco control, clean cooking fuel promotion, and
35 obesity reduction, to effectively lower the disease burden.

36

37 **Keywords:** Global burden of disease, chronic respiratory disease, COPD, asthma,
38 pneumoconiosis, interstitial lung disease, pulmonary sarcoidosis

39

40

41 **INTRODUCTION**

42 The lungs are continually exposed to numerous irritants, including pollutants, tobacco smoke,
43 and infections, throughout a lifespan. In addition to environmental and behavioral triggers,
44 genetic factors play an important role in developing or exacerbating chronic respiratory
45 diseases (CRDs).¹ Despite substantial efforts to understand the pathophysiology of CRDs and
46 to reduce their burden over the past decades, CRDs,^{2,3} encompassing chronic obstructive
47 pulmonary disease (COPD), asthma, pneumoconiosis, and interstitial lung disease (ILD) and
48 pulmonary sarcoidosis, together remain a leading cause of deaths among non-communicable
49 diseases (NCDs).⁴

50 Sustainable Development Goal (SDG) target 3.4, adopted by the United Nations,
51 advocates for a one-third reduction in premature mortality due to NCDs by 2030 compared to
52 the rates observed in 2015.⁵ It is imperative to reduce the prevalence and disability-adjusted
53 life years (DALYs) of CRDs to achieve this goal by minimizing exposure to modifiable risk
54 factors, such as smoking, air pollution, occupational dust, and chemicals.

55 The COVID-19 pandemic underscored the vulnerability of the lungs and the
56 importance of respiratory health on a global scale. Beyond the direct effects of SARS-CoV-2,
57 there has been increased attention to CRDs, as well as a greater emphasis on prevention, early
58 diagnosis, and treatment in clinical settings.⁶ Two previous studies have also reported a notable
59 decrease in the incidence of non-COVID lower respiratory infections and tuberculosis during
60 the COVID-19 pandemic.^{7,8} Since airway infections are major triggers for COPD exacerbations,
61 they might similarly account for some of the changes observed in CRD burden. Hence, this
62 study examined the trends and levels of the CRD burden in pre-COVID-19 and pandemic eras.
63 We also explored attributable risk factors globally and by region and Socio-demographic Index
64 (SDI) between 1990 and 2021 across 204 countries and territories.

65 This manuscript was produced as part of the GBD Collaborator Network following the
66 GBD Protocol.^{2,9}

67 **METHODS**

68 ***Overview***

69 The Global Burden of Disease Study (GBD) 2021 provides an updated assessment of the
70 burden of 371 diseases and injuries and 88 risk factors in 204 countries and territories between
71 1990 and 2021.⁴ As part of the GBD Collaborative Network, this study evaluates the CRD
72 estimates of GBD 2021 by age, sex, location, year, and SDI and presents the potential policy
73 impact of the estimates. This study followed the guidelines for accurate and transparent health
74 estimate reporting (GATHER) statement (**Supplementary Methods**). Detailed descriptions of
75 the methodology and statistical codes for the GBD estimation can be found elsewhere,^{4,10}
76 below we provide a comprehensive summary of the relevant methods.

77

78 ***Case definition and input data***

79 For CRDs, GBD 2021 produced estimates for four categories: COPD, asthma, pneumoconiosis,
80 and ILD and pulmonary sarcoidosis.^{2,9} COPD is defined in accordance with the Global
81 Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.^{11,12} Asthma is a chronic
82 respiratory condition induced by allergic reactions or hypersensitivity that results in bronchial
83 spasms and breathing difficulties. Pneumoconiosis is a chronic lung disease that results from
84 lung scarring and interstitial damage caused by prolonged exposure to dust and other
85 contaminants; GBD 2021 estimated pneumoconiosis by incorporating diagnoses of specific
86 conditions such as silicosis and asbestosis. ILD and pulmonary sarcoidosis encompass various
87 chronic respiratory conditions that affect lung function and oxygen absorption owing to
88 scarring and/or inflammation. The definition provided by the American Thoracic Society for
89 ILD is the gold standard. In addition to the CRD discussed earlier, there are other CRDs and

90 their associated complications. Further details, including International Classification of
91 Diseases (ICD) codes for each disease, are provided in the **Supplementary Methods**.⁴

92

93 ***Prevalence estimates***

94 GBD 2021 used population-representative surveys, small-scale prevalence studies identified
95 through systematic literature reviews, and hospital claims data to estimate the prevalence of
96 CRDs.¹³ Particularly, hospital claims data constituted the primary data sources for estimating
97 the prevalence of pneumoconiosis, ILD, and pulmonary sarcoidosis. To integrate these diverse
98 data sources and ensure consistency across sex, location, year, and age group, prevalence was
99 modeled using DisMod-MR 2.1 (Disease Modeling Meta-regression version 2.1). DisMod-MR
100 2.1 is a Bayesian disease modeling meta-regression tool that generates consistent estimates by
101 sex, location, year, and age group.¹³ The modeling process for GBD 2021 incorporated
102 adjustments for severity distributions, disability weights, and the complications of sequelae,
103 enabling more refined and comprehensive prevalence estimates for CRDs.^{2,9} This tool
104 estimates prevalence across five levels of the GBD geographic hierarchy and produces
105 estimates for locations lacking raw epidemiological data, enabling more accurate and reliable
106 estimates across different populations and time frames. More details for each disease are
107 provided in the **Supplementary Methods**.

108

109 ***Mortality estimates***

110 The modeling framework for mortality estimation is described briefly below with further detail
111 provided in the summary cause of death publication for GBD 2021.¹² The cause-of-death
112 ensemble model (CODEm) was used to simulate the majority of cause-of-death estimates for

113 illnesses and injuries. CODEm tests covariate combinations based on the out-of-sample
114 predictive validity using an ensemble of statistical models. The results were then combined to
115 estimate deaths by cause, location, age, sex, and year.¹⁴ CODEm was run separately for each
116 sex and region with and without comprehensive vital registration data to reduce the potential
117 increase in uncertainty due to heterogeneous data.¹³ The estimation of mortality due to CRDs
118 relied on various sources, including vital registration and verbal autopsy, with outlier data
119 points excluded based on criteria such as implausible values, inconsistent age or time trends,
120 and significant discrepancies with other sources.¹² Models with the smallest mean squared error
121 were weighted more heavily to create the final ensemble model. The GBD 2021 methodology
122 adheres to ICD-9 and 10, attributing each death to the underlying cause and initiating the chain
123 of events leading to death.^{2,9} CRD mortality estimates were scaled using a procedure known as
124 CoDCorrect to ensure consistency between the sum of cause-specific mortality and the total
125 envelope of all-cause mortality.¹²

126

127 ***DALY estimates***

128 DALYs are the primary measures of total health loss due to fatal and non-fatal disease burdens,
129 allowing comparisons across diseases and injuries.¹³ To estimate DALYs for GBD 2021, years
130 of life lost (YLLs) were combined with years lived with disability (YLDs) across age-sex-
131 location groups for each year considered.¹¹ YLLs were calculated by multiplying the global
132 standard life expectancy at the time of death by the number of deaths per 100,000 people. To
133 estimate YLDs, the combined frequency and duration of an illness or injury are weighted by a
134 disability weight, a measure of disease severity that ranges from 0 (full health) to 1 (fatal
135 severity). Consequently, DALYs, calculated as the total of YLLs and YLDs, quantify the
136 equivalent of one lost year of healthy life per DALY for a population.¹⁵

137

138 ***Risk factor analysis***

139 The GBD Comparative Risk Assessment framework was used to quantify the attributable
140 burden of CRDs.^{8,10,14} GBD risk factors are categorized into a four-level hierarchy, from broad
141 categories (behavioral, environmental/occupational, and metabolic) at level 1 to specific
142 categories (e.g., ambient particulate matter pollution) at level 4.^{4,10}

143 Theoretical minimum risk exposure level (TMREL) is defined in the GBD Study as the ideal
144 population exposure level with the lowest risk, served as the benchmark for calculating
145 attributable burden. The modeling process included the following steps: (1) estimating the
146 relative risk (RR) for potential risk-outcome pairs through a comprehensive analysis of
147 previously published studies, (2) estimating exposure levels using population-based datasets
148 and modeled estimates for missing data, (3) defining TMREL based on epidemiological
149 evidence, (4) calculating the population attributable fraction (PAF) using exposure data and
150 RR, considering latency periods for risk factors with delayed effects on health outcomes, (5)
151 adjusting disease prevalence or mortality data by incorporating RR, and applying the PAF to
152 estimate the attributable burden, and (6) combining multiple risk factors using a multiplicative
153 PAF approach while incorporating mediation analysis to account for overlapping pathways and
154 interactions. To address data heterogeneity and uncertainty, the MR-BRT model was applied,
155 providing refined estimates for risk-outcome relationships.¹⁰

156 The selection of risk-outcome pairs was established based on the presence of strong or
157 probable evidence, evaluated according to the methods and criteria set by the World Cancer
158 Research Fund¹⁶, availability of exposure data, feasibility of behavioral changes, and public
159 health relevance.

160 For each disease, risk factors for CRDs were estimated differently. For COPD, eight
161 factors were identified: ambient ozone pollution; ambient particulate matter pollution; smoking;
162 secondhand smoke; occupational exposure to particulate matter, gases, fumes; household air
163 pollution from solid fuels; and high and low temperatures. Four factors were identified for
164 asthma: high body mass index (BMI), smoking, occupational asthma, and nitrogen dioxide
165 pollution, with the inclusion of nitrogen dioxide pollution as a contributing factor being
166 updated in the GBD 2021 framework. Pneumoconiosis is associated with three factors:
167 occupational exposure to asbestos, silica, and particulate matter, gases, and fumes. No risk
168 factors for ILD or pulmonary sarcoidosis were identified. Further details on each risk factor
169 are available in **Supplementary Methods** ^{4,10,16}

170

171 ***Burden of CRD in pre-COVID-19 and pandemic periods***

172 To investigate temporal trends before (2010–2019) and during (2019–2021) the pandemic, we
173 calculated the average annual percentage change (AAPC) for each disease (**Supplementary**
174 **Methods**).¹⁷ AAPC is a summary measure derived from the APC, which reflects the year-over-
175 year rate of change in incidence or mortality, averaged over a specified time period. The APC
176 was estimated using a log-linear regression model, and AAPC was calculated as the weighted
177 average of APCs over the specified time intervals, with weights proportional to the number of
178 years in each interval.

179 As a secondary analysis, we used GBD estimates to assess the expected number of
180 deaths from CRDs for 2020—2021, based on estimates from 2015 to 2019 and a quasi-Poisson
181 regression model.^{8,18} Although the Poisson distribution is appropriate for modeling the number
182 of events occurring within a specified time frame or geographic area, the inherent variability
183 in event frequency observed in real-world data can result in overdispersion.¹⁷ Accordingly, a

184 quasi-Poisson regression model was selected to address this overdispersion and to accurately
185 model the variability in count data.⁸ Through this analysis, we compared the predicted mortality
186 numbers with the observed figures for CRDs by age group and calculated the differences and
187 ratios between the observed and expected deaths.⁸

188

189 ***SDI***

190 SDI is a composite measure that includes a country's lag-distributed income per capita, average
191 years of educational attainments, and the total fertility rate in females <25 years, and it varies
192 from 0.0 to 1.0.¹⁹ Further details can be found in **Supplementary Methods**.

193

194 ***Data presentation***

195 The GBD world population age standard was applied to calculate age-standardized rates for
196 prevalence, death, and DALY of CRD. To assess changes over time, we calculated the
197 percentage change in the rates between the start and end of the time period, with the change
198 expressed as the difference between the new and old rates divided by the old rate. All rates
199 presented are age-standardized unless specifically indicated as age-specific rates. All modeling
200 was conducted for 500 draws^{10,11}, and the uncertainty intervals (UI) were calculated using the
201 2.5th and 97.5th percentiles of the draws. Analyses were performed using Python (version 3.10.4;
202 Python Software Foundation, Wilmington, DE, USA) and R (version 4.2.1; R Foundation,
203 Vienna, Austria).

204

205 ***Role of funding source***

206 The funder had no role in the study design, data collection, data analysis, data interpretation,
207 report writing, or decision to submit the manuscript for publication.

208 **RESULTS**

209 ***Overview***

210 In 2021, there were 468.3 million (95% UI, 428.9 to 513.1) individuals with CRD worldwide,
211 representing an age-standardized rate of 5,785.4 per 100,000 (**Figure S1**). The global age-
212 standardized prevalence rate decreased by 27.2% from 7,936.4 in 1990, and 20 of the 21 GBD
213 regions showed significant declines. The most significant reduction in the age-standardized
214 prevalence rate was observed in the high-income Asia Pacific (−50.3% [−46.9 to −53.3]),
215 followed by Eastern Europe (−38.4% [−35.0 to −41.4]; **Table S1**). However, high-income
216 North America revealed a stable trend (2.8% [−1.4 to 7.4]; **Figure 1A**) and had the highest
217 age-standardized prevalence rate (14,879.6 [13,883.8 to 16054.1]). At the national level, the
218 age-standardized prevalence rate ranged from 3,207.8 in Cabo Verde to 13,316.0 in the United
219 States in 2021.

220 Among the four major CRDs, asthma accounted for more than half of CRD cases in
221 2021, with 260.5 million (227.2 to 298.0) cases and the age-standardized rate of 3,340.1
222 (2,905.2 to 3,832.2) per 100,000 (**Figure 2**). COPD ranked second, with 213.3 million (194.9
223 to 234.0) cases and an age-standardized rate of 2,512.9 (2,293.9 to 2,748.5). In 2021, the global
224 age-standardized prevalence rate was 50.0 (44.2 to 56.8) for ILD and pulmonary sarcoidosis
225 and 4.6 (3.9 to 5.5) for pneumoconiosis. Except for ILD and pulmonary sarcoidosis, which
226 experienced an 8.7% (4.1 to 14.0) increase, the age-standardized prevalence of CRDs
227 decreased from 1990 to 2021.

228 CRDs were the fourth leading cause of death in 2021, accounting for 4.4 million (4.0
229 to 4.9) mortalities. The global age-standardized death rate decreased from 84.6 in 1990 to 53.6
230 in 2021 (−36.7% [−42.6 to −27.1]). However, this trend was not universal; high-income
231 North America showed a 15% increase in age-standardized death rates (9.1 to 18.4; **Figure 1B**).

232 COPD remained the leading contributor to the mortality burden, accounting for 84.3%
233 of the deaths due to all CRD cases (**Table 1** and **Figure 3**). Asthma ranked second, accounting
234 for 9.9% of the mortality cases. Notably, from 1990 to 2021, pneumoconiosis showed the most
235 substantial decline in age-standardized mortality rates, with a reduction of -52.8% (-59.9 to
236 -44.4). In contrast, the age-standardized mortality rates for ILD and pulmonary sarcoidosis
237 increased by 50.3% (31.7 to 74.3), marking them as the only CRD with rising mortality trends
238 during this period. Further details on the age-standardized estimates by region can be found in
239 **Figures S1-S5** and **Table 1**.

240

241 *Trends in age-sex-specific CRD burden*

242 **Figure 4** presents the trends in age-sex-specific death rates for four CRDs from 1990 to 2021.
243 For COPD, age-specific death rates were higher in males across all age groups and showed
244 substantial declines across all age-sex groups from 1990 to 2021. Females aged 15-44 years
245 had the greatest reduction of 55.2%, from 1.8 per 100,000 in 1990 to 0.8 per 100,000 in 2021,
246 among all age-sex groups. For asthma, we observed a significant reduction in the age-sex-
247 specific death rates across all groups, most pronounced in males aged <15 years (1.5 per
248 100,000 population in 1990; 0.4 per 100,000 population in 2021; -73.3% percentage change).
249 As a result, in 2021, death rates were higher among females in most age groups, with rates
250 increasing progressively with advanced age. Pneumoconiosis also showed a declining trend in
251 all age-sex groups, and males had a greater mortality burden of pneumoconiosis than females
252 of all ages. Last, age-sex-specific death rates for ILD and pulmonary sarcoidosis increased in
253 most groups, most pronounced in those aged ≥ 75 years, with an increase of 105.9% in females
254 and 84.1% in males from 1990 to 2021. Conversely, individuals aged <15 years had a marked
255 reduction in death rates (-45.9% in females; -48.3% in males). More details on the global age

256 and sex distributions of COPD, asthma, pneumoconiosis, and ILD and pulmonary sarcoidosis
257 prevalence and death are shown in **Figures S6-S8**.

258

259 ***Risk factors attributable to COPD, asthma, and pneumoconiosis***

260 In GBD 2021, risk factor estimation is available for COPD, asthma, and pneumoconiosis
261 (**Figure 5**). For COPD, smoking remained the leading global risk factor for males, accounting
262 for over half of the global age-standardized DALY rates in males (595.3 [478.2 to 703.9] per
263 100,000 population). In contrast, household air pollution from solid fuels was the leading risk
264 factor for females globally (161.7 [98.1 to 261.8]) and in regions such as Central Sub-Saharan
265 Africa, Eastern Sub-Saharan Africa, Western Sub-Saharan Africa, Oceania, South Asia, and
266 Southeast Asia. Ambient particulate matter pollution was a significant contributor for both
267 sexes, consistently ranking high across multiple regions.

268 Regional disparities were observed in the rankings of other COPD risk factors. For
269 instance, although low temperature ranked 6th out of 8 globally for males and 7th for females,
270 it was a prominent risk factor in Australasia, Eastern Europe, Western Europe, and high-income
271 North America. Similarly, occupational particulate matter, gases, and fumes had a higher
272 impact in industrialized or resource-driven regions. The age-standardized DALY rates for
273 COPD due to household air pollution were relatively low in high-income regions, where they
274 ranked 8th for females.

275 For asthma, high BMI was the leading global risk factor for age-standardized DALY
276 rates globally (34.5 [17.8 to 52.7] in males; 44.1 [21.4 to 68.3] in females) and in most regions
277 for both sexes. Although the rankings of asthma risk factors were consistent across regions, the
278 proportion of DALYs attributable to high BMI was higher in regions such as North America,

279 the Middle East, and high-income North America compared to the global average.
280 Occupational asthmagens ranked second globally and across most regions for both males and
281 females.

282 For pneumoconiosis, occupational exposure to silica was the top global risk factor for
283 males (59.7 [51.8 to 63.8]), while it ranked second for females (38.6 [31.9 to 43.5]).
284 Occupational particulate matter, gasses, and fumes was the second leading global risk factor
285 for males (24.4 [20.8 to 32.5]) but ranked the first for females (43.2 [38.7 to 50.0]).

286

287 ***Burden of CRD in pre-COVID-19 and pandemic periods***

288 We examined the AAPC of age-standardized incidence and death rates before (2010-2019) and
289 during the COVID-19 pandemic (2019-2021). Globally, age-standardized incidence rates of
290 CRD shifted from a declining trend before the pandemic (AAPC, -0.85) to a slight increase
291 during the pandemic (AAPC, 0.42). In contrast, AAPC of age-standardized death rates of CRD
292 continued to decrease, although at a slower rate (before the pandemic: AAPC, -1.35; during the
293 pandemic: AAPC, -0.71; **Figure S9**). This overall trend was also observed for COPD and
294 asthma, which experienced increasing or plateaued incidence rates with slower declines in
295 death rates during the pandemic. Pneumoconiosis exhibited minimal changes in its age-
296 standardized incidence rate, with the AAPC remaining relatively stable during the pandemic
297 (before: -1.22; during: -0.01). However, the decline in age-standardized death rates slowed
298 significantly (before: -2.57; during: -0.95). In contrast, ILD and pulmonary sarcoidosis showed
299 distinct patterns: age-standardized incidence rates continued to decline consistently (before:
300 AAPC, -0.17; during: AAPC, -0.18), whereas mortality rates reversed from an increase before
301 the pandemic (AAPC, 0.84) to a marked decline during the pandemic (AAPC, -1.14; **Figure**
302 **6**).

303 **Figure S10** shows the expected versus observed number of deaths due to CRDs during
304 the pandemic. We estimated that 4,376,560 and 4,464,911 deaths are expected worldwide in
305 2020 and 2021, respectively, which are slightly higher than GBD estimates (4,349,391 in 2020;
306 4,414,182 in 2021), indicating minimal changes in overall mortality during this period.
307 Mortality trends also varied by disease type (**Figures S10 and Table S2**); COPD had the largest
308 gap between GBD estimates (3,654,945 in 2020 and 3,719,937 in 2021) and expected deaths
309 (3,668,460 in 2020 [$p<0.0001$]; 3,745,838 in 2021 [$p<0.0001$]).

310

311 **DISCUSSION**

312 ***Key findings of this study***

313 We provided estimates of CRD burden at the global, regional, and national levels from 1990 to
314 2021. Although global age-standardized incidence rates for CRD increased during the COVID-
315 19 pandemic, age-standardized CRD mortality rates remained relatively stable. Despite notable
316 progress in reducing the global age-standardized death rate, high-income North America has
317 shown a considerable increase of 15% from 1990 to 2021, particularly in ILD and pulmonary
318 sarcoidosis. We further observed that this progress substantially varied by age; individuals aged
319 < 15 years had the greatest reductions, primarily in deaths due to asthma, while older adults
320 had the most minor declines or even increases in some diseases, such as ILD and pulmonary
321 sarcoidosis. Smoking, high BMI, and occupational exposure to silica were leading risk factors
322 for COPD, asthma, and pneumoconiosis, respectively. Disparities in key risk factors according
323 to SDI levels were observed; for instance, household air pollution from solid fuels was a key
324 risk factor for COPD among females and in low SDI settings, highlighting that region- and
325 demography-specific public health measures are warranted to effectively mitigate CRD burden.

326

327 ***Plausible mechanisms***

328 Globally, substantial progress has been made in reducing the burden of asthma, COPD, and
329 pneumoconiosis. This achievement is partly attributed to various efforts to improve prevention
330 and therapeutics through targeted strategies and actions.²⁰ For instance, adopting the World
331 Health Organization Framework Convention on Tobacco Control in 2005, which includes
332 raising taxes on tobacco and enforcing a ban on advertising, marking a significant turning point
333 for enhancing global tobacco control efforts and preventing CRDs.²¹ Considering that some

334 resource-limited countries have shown slow implementation of policies²¹, there is potential for
335 further reduction in the disease burden, with overall advances in healthcare access and patient
336 education. In recent decades, innovations in targeted therapies have contributed to a better
337 prognosis for patients with chronic respiratory conditions. Novel targeted treatments, such as
338 anti-IgE or anti-IL-5 monoclonal antibodies, represent a substantial advancement for patients
339 with asthma refractory to conventional treatments, which could further contribute to
340 a reduction in premature deaths.²² For severe COPD, triple therapy, a combination of a long-
341 acting muscarinic antagonist, a long-acting beta-agonist, and an inhaled corticosteroid in a
342 single inhaler, has shown improved outcomes.²³

343 Nevertheless, global age-standardized death rates from ILD and pulmonary sarcoidosis
344 have significantly increased from 1990 to 2021. This may be due to the relatively recent
345 recognition of the disease compared to asthma and COPD.²⁴ Advances in radiology and
346 pathology might have increased recognition and more accurate diagnosis of ILD and
347 pulmonary sarcoidosis.²⁵ Moreover, the broader use of antimetabolites and cytotoxic agents—
348 known to contribute to lung tissue scarring—has likely influenced this rise in ILD burden,
349 especially among the older population.²⁶

350 Notably, high-income North America had the highest age-standardized prevalence rate
351 of CRDs. This is primarily due to asthma, which accounts for more than half of CRD cases,
352 driving the overall trend of the prevalence rate (**Figure 2**). Asthma has been historically more
353 common in Western countries due to a complex interplay of genetic and environmental
354 factors.²⁷ In addition, high-income North America exhibited an increase in age-standardized
355 mortality rates for CRD from 1990 to 2021. Specifically, the age-standardized mortality rates
356 for ILD and pulmonary sarcoidosis showed a marked rise, while those for asthma and
357 pneumoconiosis experienced declines. This trend is also evident in other high-income regions,

such as Australasia and Western Europe (**Figure 3**), suggesting heightened recognition and clinical awareness of these diseases in these countries, where advances in diagnostic technologies and improved healthcare infrastructure have led to better identification of previously underdiagnosed conditions.²⁴ Additionally, genetic and ethnic factors may also contribute to the rising mortality of pulmonary sarcoidosis.²⁸ Furthermore, high-income North America had the highest age-standardized rate of CRDs in 2021 but ranked lower in age-standardized mortality rates (**Figure 3**), likely due to advances in diagnostic measures and improvements in disease management and comorbidity care. In contrast, East Asia, despite having a lower age-standardized incidence rate, ranked higher in age-standardized mortality rates, which may be attributed to limited access to early diagnosis and timely treatment.

The higher death rates of COPD, pneumoconiosis, ILD, and pulmonary sarcoidosis in males than females, which are especially pronounced in advanced age, can be attributed to several mechanisms, including more significant physiological lung function impairment with aging, historically higher smoking rates, and greater occupational exposure to potential irritants in males. However, the prevalence and mortality rates of asthma were both higher in female adults, resulting from the transition of sex discordance in prevalence, which reverses with puberty. This may be due to the influence of sex hormones. Androgens can improve bronchodilation and attenuate airway inflammation²⁹, while hormonal fluctuations during menstruation, pregnancy, and menopause can increase the risk in women.³⁰

Last, during the COVID-19 pandemic, we observed a rise in the age-standardized incidence rates of CRDs, likely driven by enhanced healthcare engagement and high priority placed on respiratory health in clinical settings.⁶ Individuals affected by COVID-19 or CRD risk factors³¹ may have prompted more frequent hospital visits, along with the increased number of CT scans performed³², during the pandemic and led to incidental diagnoses of

382 underlying conditions, such as asthma or COPD.³³ This increased healthcare engagement and
383 heightened awareness and monitoring of pulmonary health during the pandemic might have
384 contributed to better detection of previously undiagnosed cases.

385 While the age-standardized incidence rates increased, the age-standardized death rates
386 for CRDs stabilized or declined more slowly compared to pre-pandemic trends. This slower
387 decline could suggest that pandemic-related factors, such as exacerbations triggered by
388 respiratory infections, offset some of the progress made in reducing CRD-related deaths. This
389 is particularly evident for asthma and COPD, where the pandemic may have increased the
390 frequency of exacerbations while still reducing mortality overall due to heightened healthcare
391 focus.^{6,34,35} It is important to note the distinct patterns seen in ILD and pulmonary sarcoidosis.
392 For these conditions, age-standardized incidence rates continued their pre-pandemic decline,
393 and mortality rates reversed from an upward trajectory to a decline during the pandemic. This
394 could be due to reduced exposure to environmental toxins (e.g., dust and asbestos) resulting
395 from mask-wearing during the COVID-19 pandemic.^{36,37}

396 Overall, the impact of the COVID-19 pandemic on CRDs is less pronounced than in
397 tuberculosis and non-COVID-19 lower respiratory infections.^{7,8} Unlike these acute conditions,
398 the nature of chronic diseases may have made them less immediately affected by the pandemic.
399 In addition, the interactions between COVID-19 and CRDs are complex and bidirectional.
400 Individuals with a history of COVID-19 are more likely to develop a range of pulmonary
401 sequelae^{38,39}, while those with pre-existing chronic respiratory conditions are more susceptible
402 to severe COVID-19 outcomes when infected.^{40,41} These factors may lead to an
403 underestimation of the true extent of excess mortality related to CRDs, as some of these cases
404 may be recorded as COVID-19-related fatalities.⁴² Therefore, further studies are needed to

405 better understand the full impact of the COVID-19 pandemic on CRDs and to clarify the factors
406 contributing to variations in disease outcomes across different CRDs.

407

408 ***Policy and clinical implications***

409 Although the burden of CRD remains large, it is important to note that CRDs have received
410 less attention compared to other major NCDs, such as cancer and cardiovascular diseases, in
411 the research field and literature.⁴³ Decreasing respiratory function is a natural part of the aging
412 process; however, it can be delayed by dietary, behavioral, and environmental approaches,
413 which prevent additional exposure to risk factors.⁴⁴ Furthermore, as most CRDs are not fully
414 curable, it is important to focus on prevention to mitigate the burden of CRDs. This study
415 provides estimates of modifiable risk factors contributing to CRD globally and by SDI level.
416 These insights highlight the potential impact of health interventions in reducing disease burden
417 and provide a strategic roadmap for targeting the most significant risk factors in each region.

418 For instance, we noted that household air pollution from solid fuels, rather than
419 smoking, primarily contributed to the COPD burden among females in low SDI settings.
420 Therefore, using cleaner fuel or technology for domestic work is required to reduce solid fuel
421 exposure in these countries⁴⁵, which aligns with the Clean Cooking Alliance, a leading global
422 initiative to make clean cooking more accessible.⁴⁶ Enhancing access to modern energy for
423 cooking is crucial to meet the UN's SDG by 2030, and this shift can reduce the disease burden,
424 contribute to climate change mitigation, and protect terrestrial ecosystems. High DALY rates
425 for asthma, COPD, and pneumoconiosis in low-SDI regions, despite lower prevalence, suggest
426 that poor healthcare access, suboptimal treatment, and unhealthy environments amplify the
427 burden.⁴⁷ Therefore, prevention, diagnostic, and therapeutic approaches in limited-source
428 settings should be addressed at a global level.

429

430 ***Limitations and strengths***

431 This is the first study to examine the global, regional, and national burden of CRDs during the
432 COVID-19 pandemic across 204 countries and territories. In addition to providing updated
433 comprehensive estimates of the disease, we analyzed the potential impact of the pandemic on
434 the mortality of CRD. However, this study has several limitations, primarily due to the limited
435 amount and high input data variability. First, despite the massive use of international vital
436 registration and insurance claims data to construct the GBD model, numerous locations and
437 years lack primary data, particularly in low- and middle-income countries (LMICs). This led
438 to lower certainty and generalizability of our findings, highlighting the importance of improved
439 data collection in LMICs to ensure that the estimates from the modeling process are grounded
440 in more primary data. Second, while there is evidence suggesting an association between air
441 pollution and ILD and between occupational risk and pneumoconiosis, the GBD model has not
442 yet incorporated these risk-outcome pairs.^{12,48} This gap limits our understanding of how
443 environmental factors contribute to these diseases.⁴⁹ Meanwhile, this lag in risk factor
444 integration may reflect the rigorous selection criteria of the GBD framework¹⁰, which requires
445 sufficient evidence of causation for each risk-outcome pair, as determined by the Bradford Hill
446 criteria. These criteria also mandate the availability of risk exposure data and ensure the
447 relevance of the risk for modification and policy implementation.⁵⁰ As such, emerging
448 exposures, such as vaping and cannabis use, remain yet excluded due to the lack of standardized
449 global data or insufficient evidence to satisfy these criteria.⁵¹ Expanding the list of risk factors
450 is strong motivation of GBD, and more risk factors are expected to be included in future GBD
451 iterations.¹⁰ Third, the diagnostic criteria for CRDs and interpretation of spirometry results
452 were heterogeneous across input data sources and regions, which may influence the reliability

453 of the estimates, although GBD 2021 adjusted for input data that did not use the reference
454 definition.

455 Finally, our findings regarding the impact of the COVID-19 pandemic on CRDs should
456 be interpreted with caution for several reasons. The complex relationship between COVID-19
457 and CRD, such as COVID-19 potentially leading to long-term respiratory complications and
458 increases the risk of severe infection in individuals with preexisting respiratory conditions, may
459 complicate the findings. Additionally, deaths from CRDs may be underreported, as individuals
460 with these conditions who were infected with COVID-19—particularly older adults—might
461 have been classified as COVID-19-related fatalities. Moreover, our analysis extends only to
462 the year 2021 due to the availability of GBD estimates, which restricts our assessment of the
463 COVID-19 pandemic's long-term effects. This suggests the need to consider the impact of the
464 COVID-19 pandemic on disease estimates in the next GBD iteration.

465

466 **CONCLUSION**

467 Although the overall burden of CRD has decreased over time, the number of people affected
468 by CRD still remains significant, with variations depending on CRD etiology and region.
469 Despite the lower prevalence in limited-resource settings, the DALY was relatively high in
470 these regions, suggesting that lower socioeconomic status is influential for CRD prevention
471 and managements. During the COVID-19 pandemic, age-standardized incidence rates for CRD
472 has risen, while age-standardized mortality rates remained relatively stable. The CRD burden
473 estimates across pre-COVID-19 and pandemic periods provided by this study may help guide
474 healthcare policymaking and prioritization to achieve the SDG 3.4 goals.

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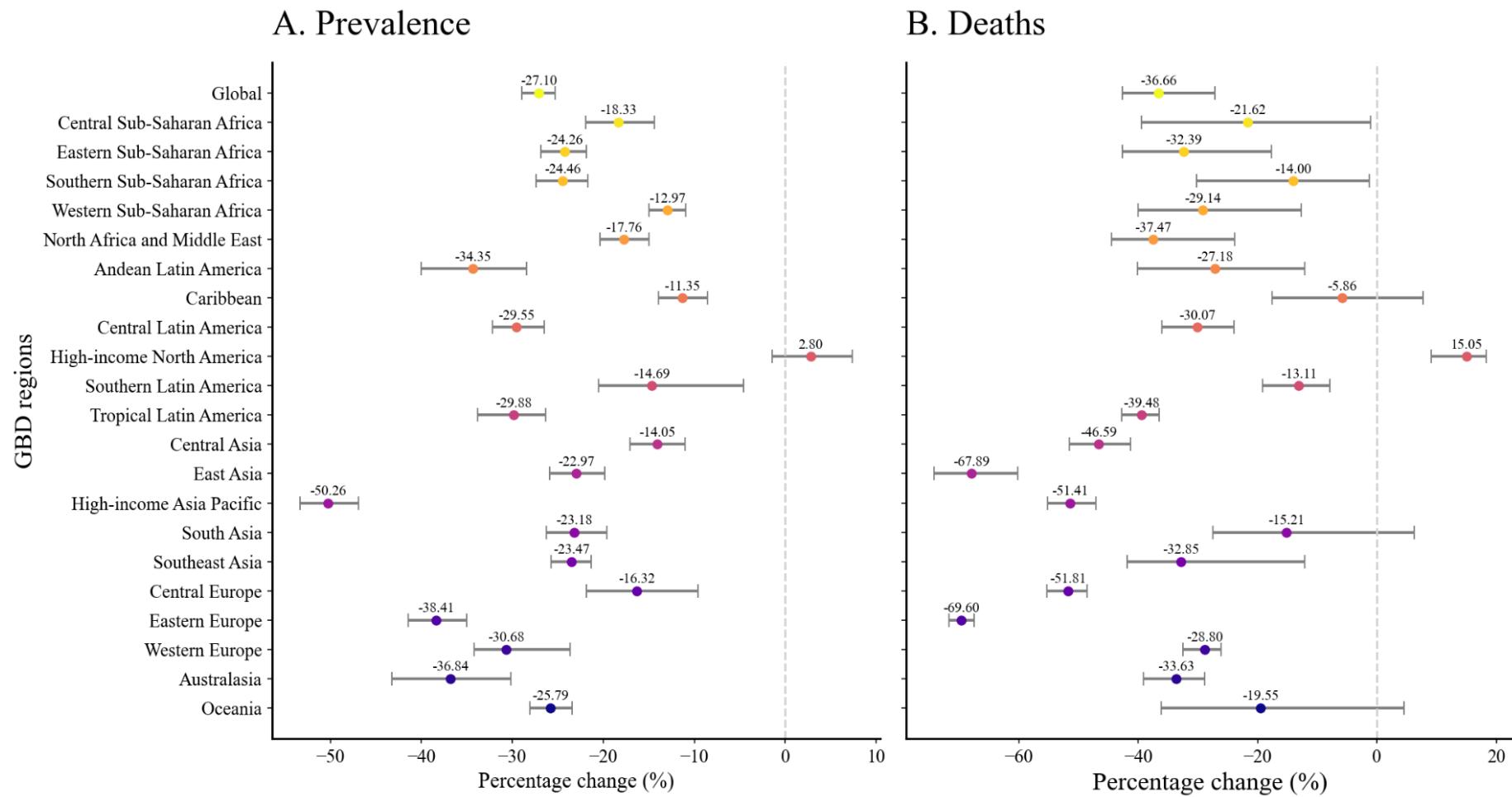
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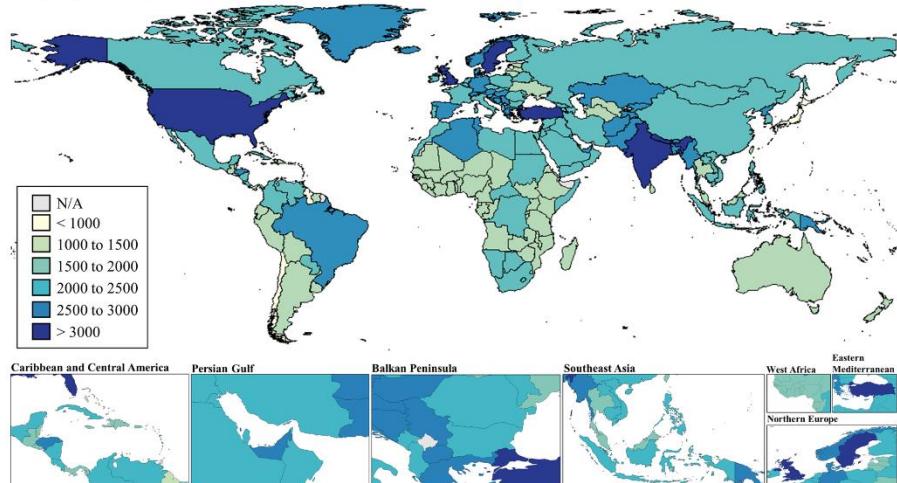
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613 **Figure 1. Percentage change in age-standardized prevalence rates (A) and death rates (B) due to chronic respiratory diseases between**
 614 **1990 and 2021, globally and across 21 GBD regions, for both sexes combined (1990–2021). Abbreviation: GBD, Global Burden of Disease,**
 615 **Injuries, and Risk Factors Study.**

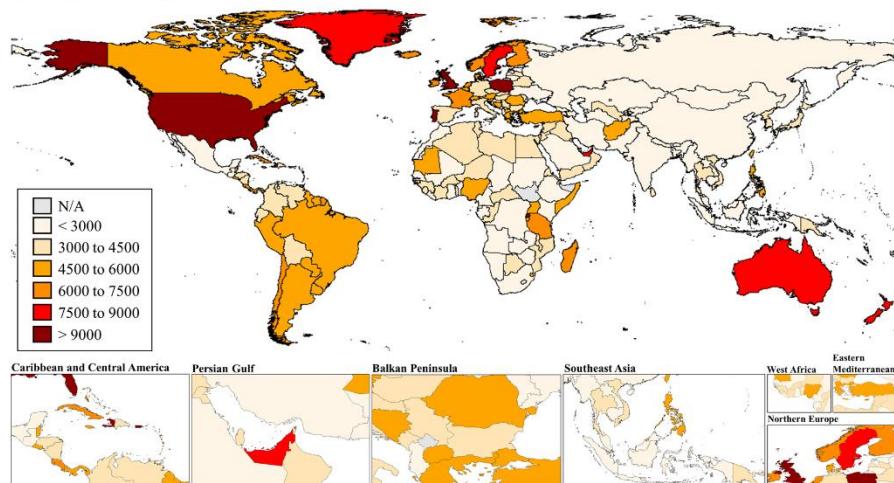


616 **Figure 2. World map of age-standardized prevalence rates for COPD (A), asthma (B), pneumoconiosis (C), and ILD and pulmonary**
 617 **sarcoidosis (D) in 2021.** Abbreviation: COPD, Chronic obstructive pulmonary disease; ILD, interstitial lung disease.

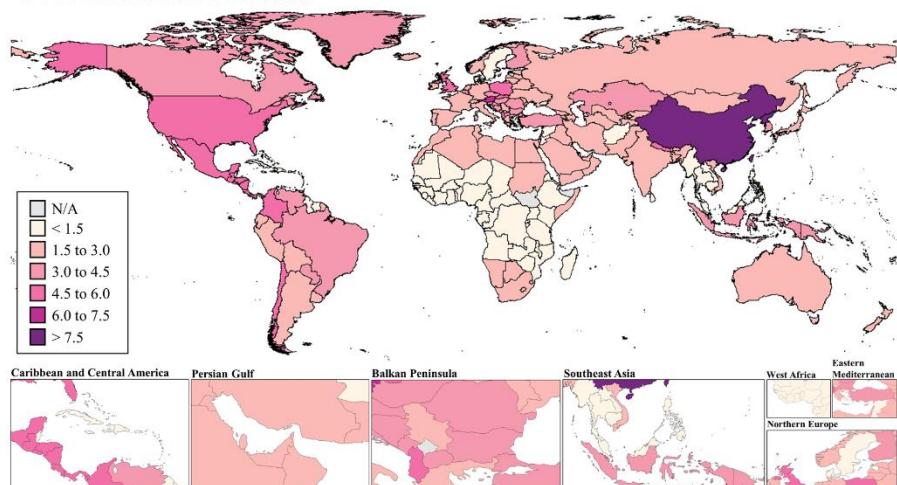
A. COPD



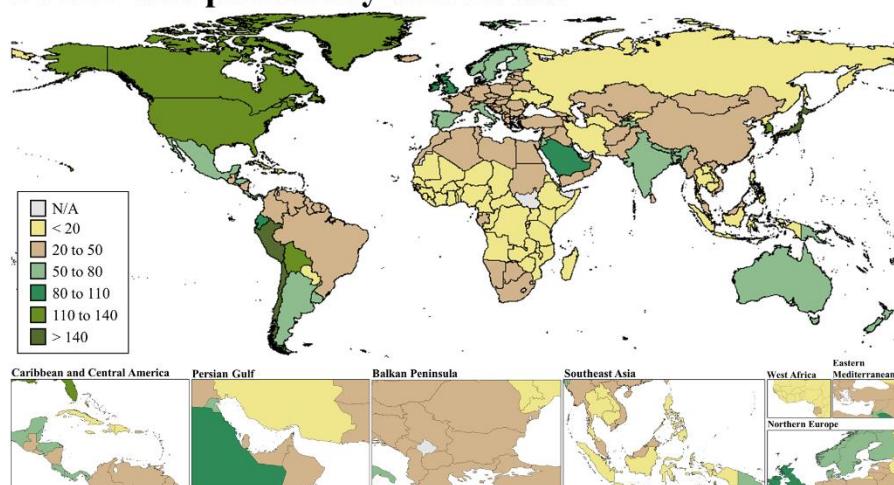
B. Asthma



C. Pneumoconiosis

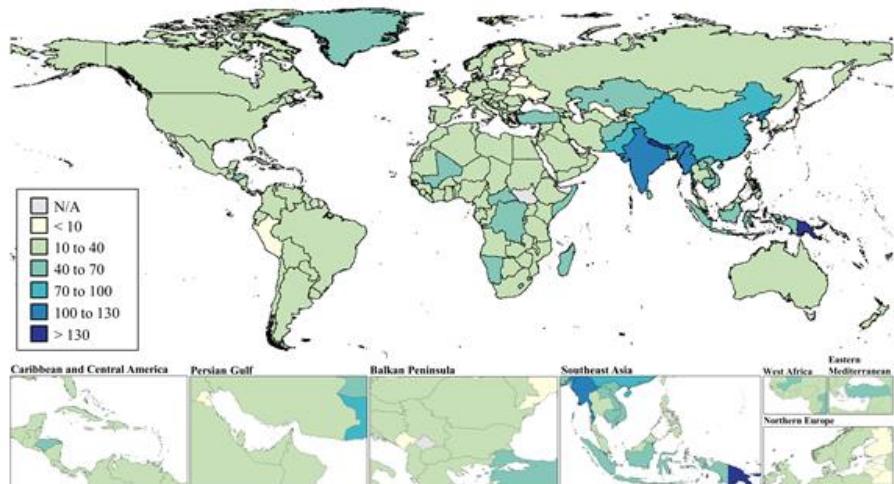


D. ILD and pulmonary sarcoidosis

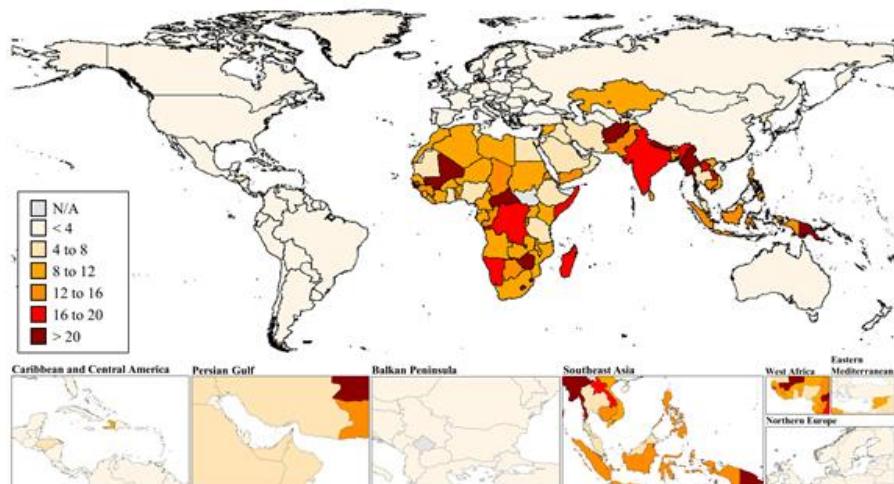


618 **Figure 3. World map of age-standardized death rates for COPD (A), asthma (B), pneumoconiosis (C), and ILD and pulmonary**
619 **sarcoidosis (D) in 2021. Abbreviation: COPD, Chronic obstructive pulmonary disease; ILD, interstitial lung disease.**

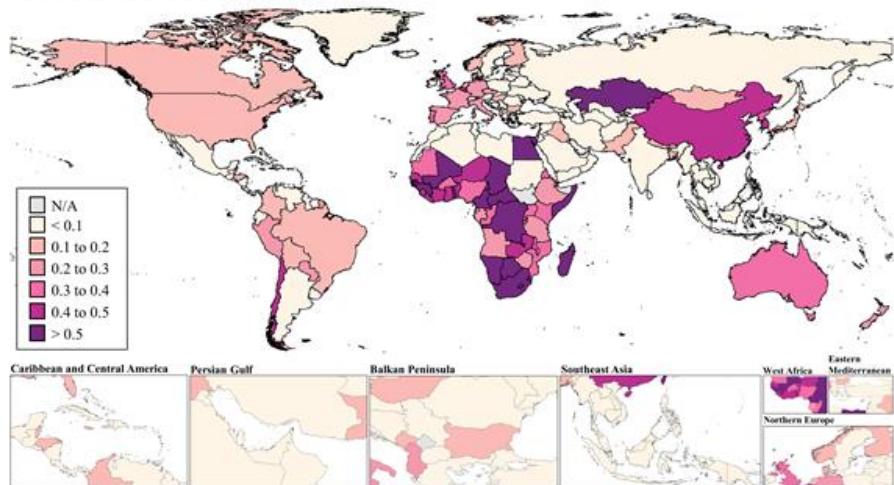
A. COPD



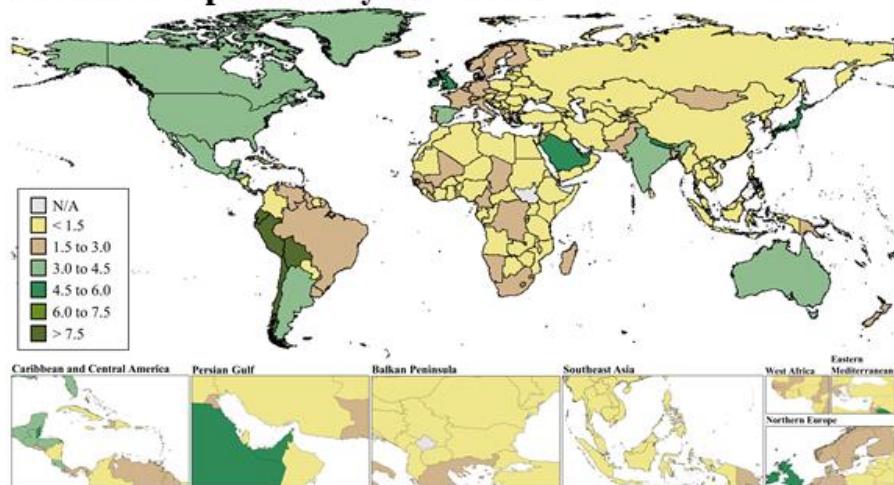
B. Asthma



C. Pneumoconiosis

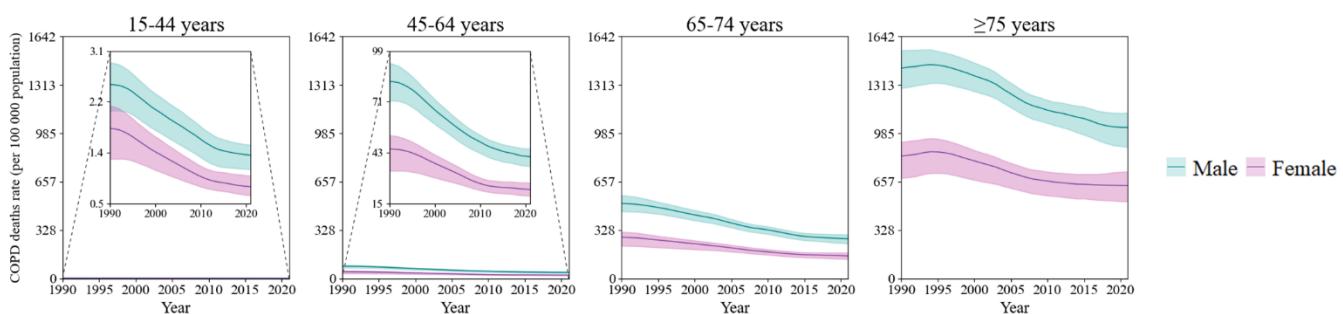


D. ILD and pulmonary sarcoidosis

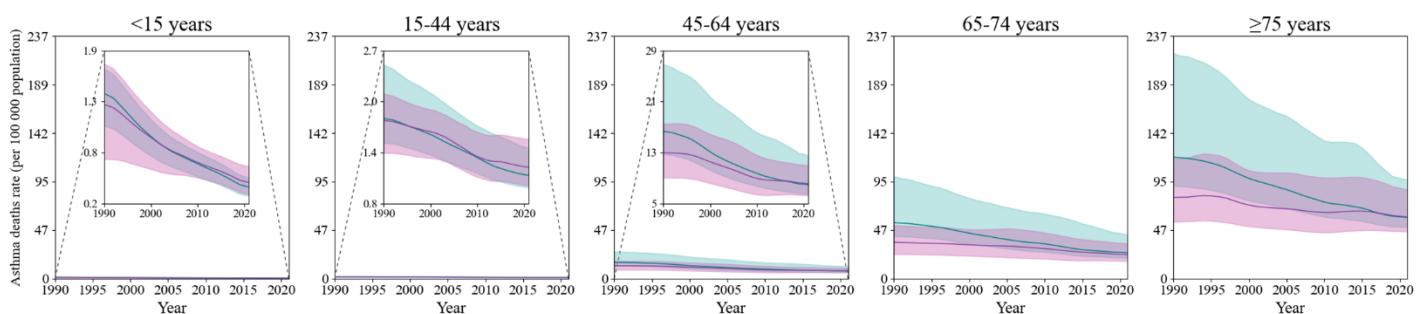


620 **Figure 4. Global age-sex-specific COPD (A), asthma (B), pneumoconiosis (C), ILD and**
 621 **pulmonary sarcoidosis (D) death rates, 1990–2021.** Abbreviation: COPD, Chronic
 622 obstructive pulmonary disease; ILD, interstitial lung disease.

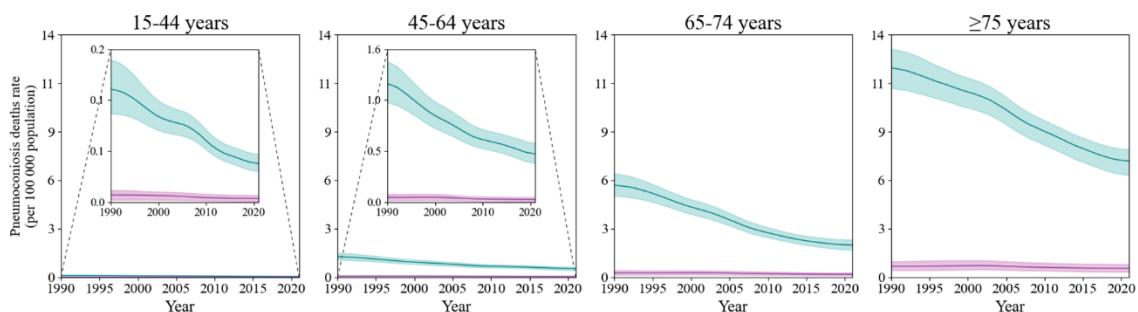
(A) COPD death rates



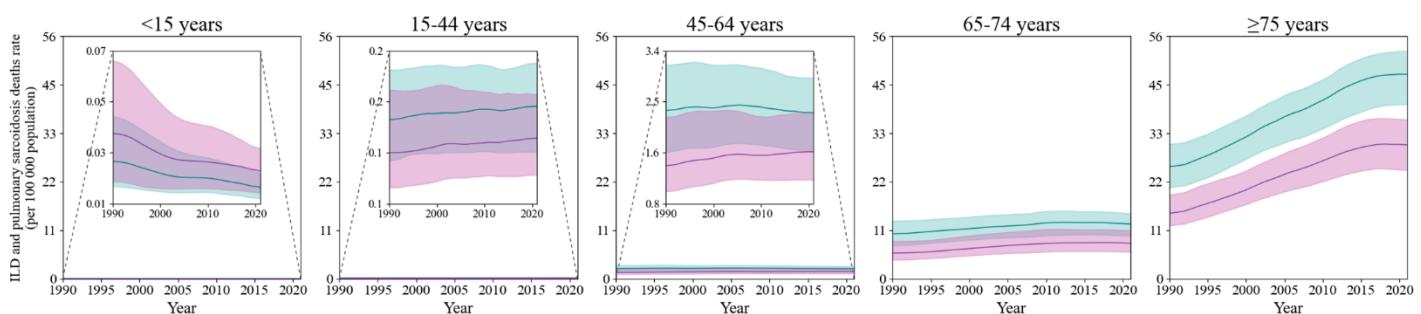
(B) Asthma death rates



(C) Pneumoconiosis death rates



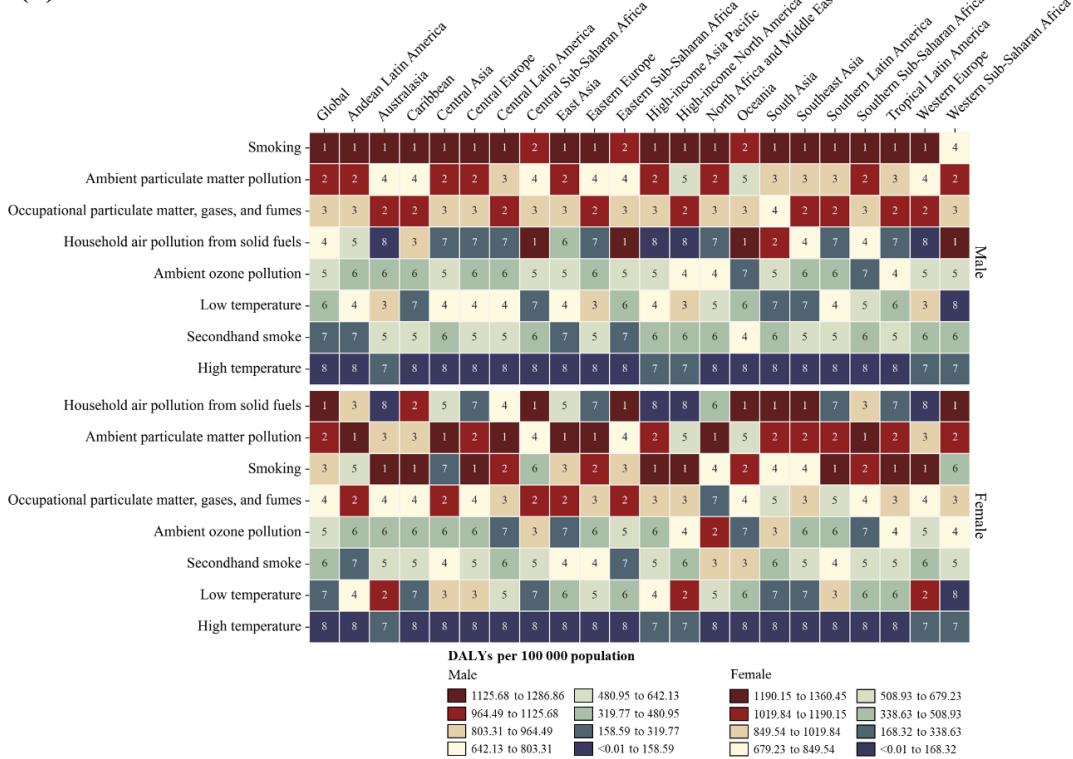
(D) ILD and pulmonary sarcoidosis death rates



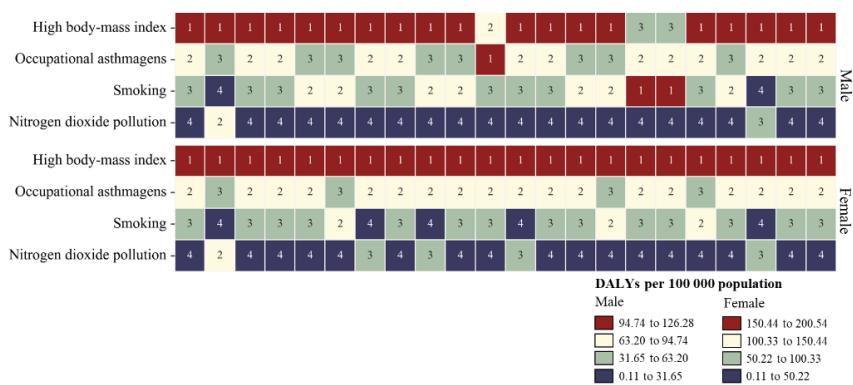
623 **Figure 5. Global and regional distribution of age-standardized DALY rates for COPD (A),**
 624 **asthma (B), and pneumoconiosis (C) by risk factor in males and females, 2021.**
 625 Abbreviations: COPD, chronic obstructive pulmonary disease; DALYs, disability-adjusted
 626 life-years; GBD, Global Burden of Disease.

627 The number in each cell represents the rank of risk factors associated with the disease.

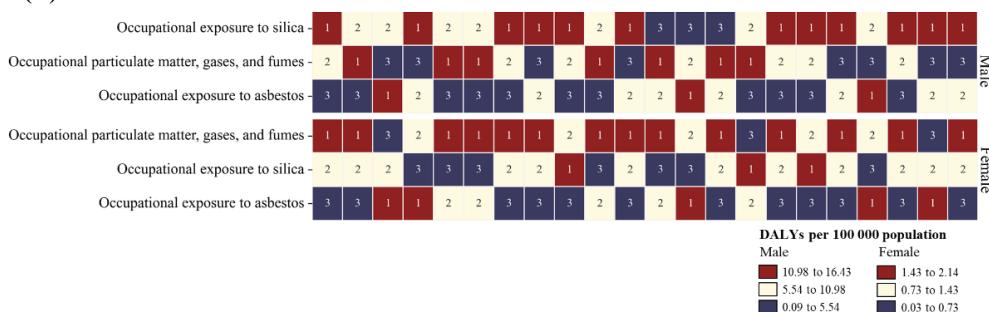
(A) COPD



(B) Asthma

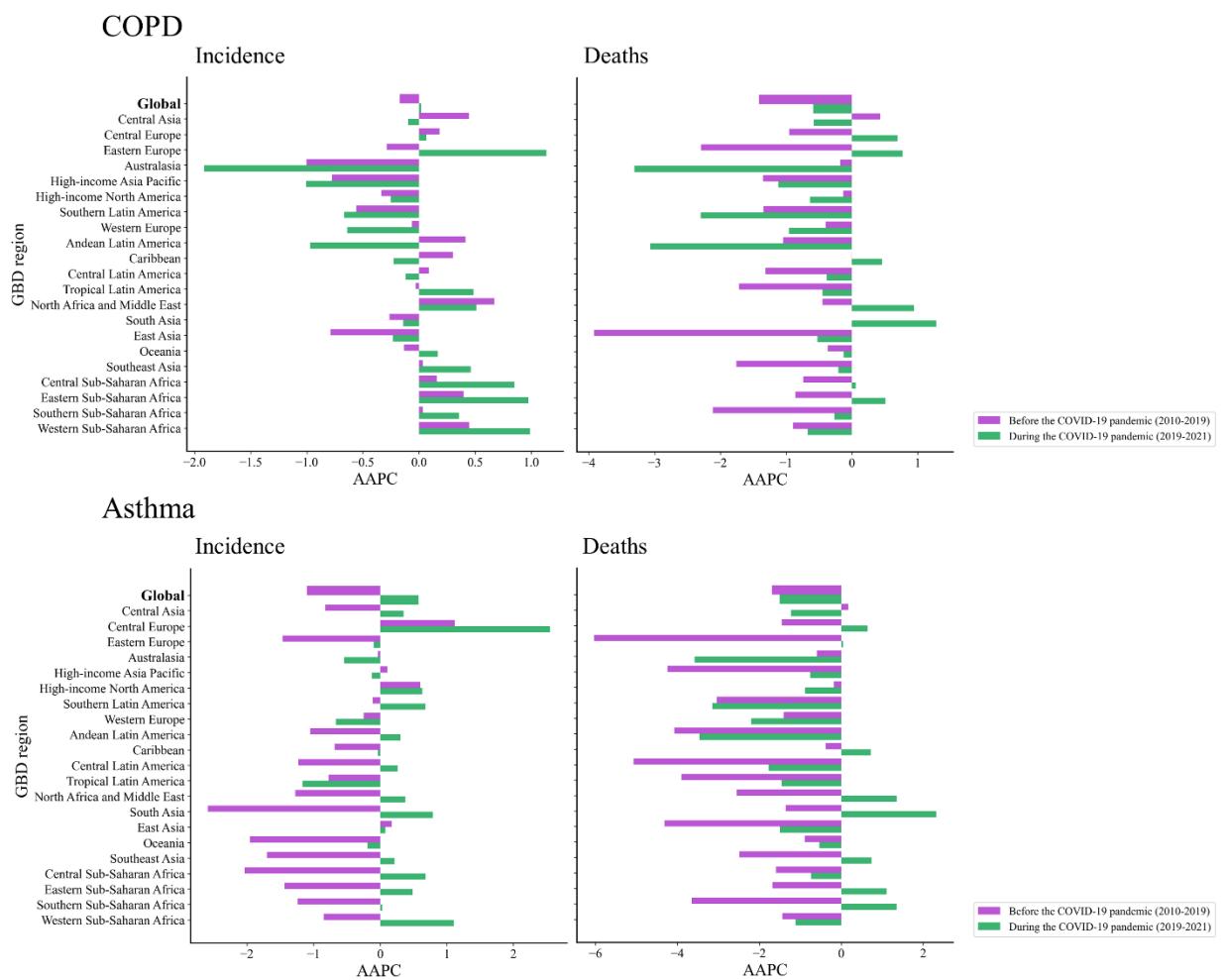


(C) Pneumoconiosis

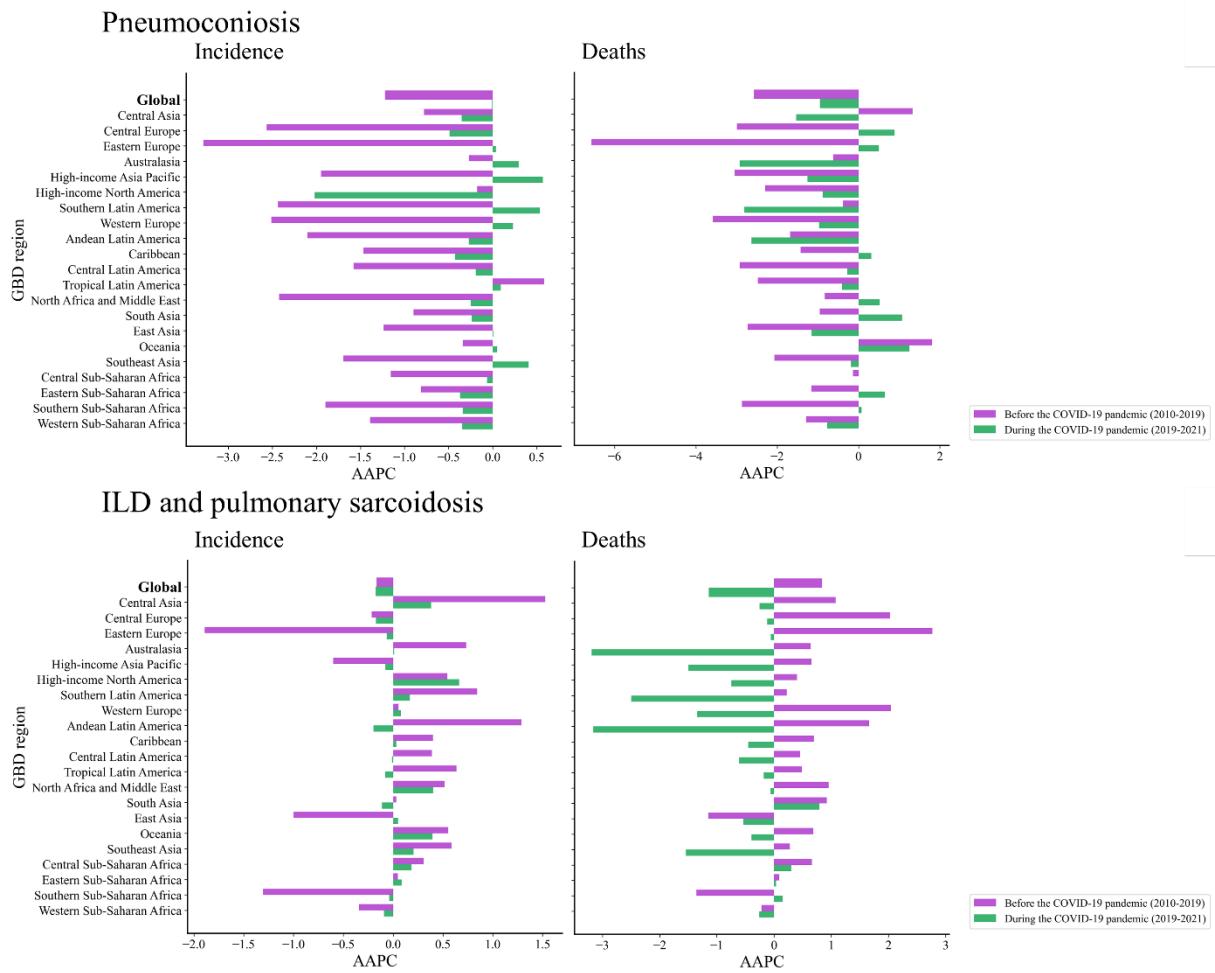


628 **Figure 6. Average annual percentage change of age-standardized incidence and death**
 629 **rates for COPD, asthma, pneumoconiosis, and ILD and pulmonary sarcoidosis by GBD**
 630 **region during the pre-COVID-19 (2010–2019) and pandemic period (2019–2021).**

631 Abbreviation: COPD, chronic obstructive pulmonary disease; GBD, Global Burden of Disease,
 632 Injuries, and Risk Factors Study; ILD, Interstitial lung disease.



633



634

635

636 **Table 1.** Global and regional age-standardized mortality rates from chronic respiratory disease
 637 in 2021 and percentage change from 1990 in both sexes combined.

Location	Year	CRDs	Cause-specific				
			COPD	Asthma	Pneumoconiosis	ILD and pulmonary sarcoidosis	Other CRDs
Global	2021	53.56 (48.46 to 59.09)	45.22 (40.61 to 49.70)	5.20 (4.27 to 6.59)	0.22 (0.19 to 0.25)	2.28 (1.96 to 2.56)	0.65 (0.51 to 0.80)
	% change	-36.66 (- 42.64 to - 27.11)	-37.12 (- 43.37 to - 27.68)	-46.08 (- 53.01 to - 35.29)	-52.82 (-59.92 to -44.43)	50.31 (31.72 to 74.28)	-0.37 (-0.46 to -0.19)
Central Europe, Eastern Europe, and Central Asia	2021	16.19 (15.21 to 17.05)	14.24 (13.36 to 15.00)	1.03 (0.94 to 1.13)	0.07 (0.07 to 0.08)	0.62 (0.57 to 0.67)	0.22 (0.20 to 0.26)
	% change	-60.88 (- 62.71 to - 58.99)	-58.43 (- 60.38 to - 56.39)	-79.49 (- 81.30 to - 77.55)	-70.56 (-74.18 to -65.82)	-45.80 (-49.51 to -41.77)	-0.68 (-0.73 to -0.63)
Central Asia	2021	27.33 (24.63 to 30.27)	21.27 (19.12 to 23.46)	4.34 (3.78 to 5.09)	0.13 (0.09 to 0.17)	0.87 (0.71 to 1.06)	0.72 (0.58 to 0.89)
	% change	-46.59 (- 51.49 to - 41.22)	-41.44 (- 46.91 to - 35.23)	-62.15 (- 68.56 to - 54.67)	-36.08 (-59.93 to -0.42)	-47.17 (-58.99 to -31.50)	-0.53 (-0.65 to -0.39)
Central Europe	2021	18.00 (16.51 to 19.36)	16.03 (14.70 to 17.22)	0.79 (0.72 to 0.86)	0.09 (0.08 to 0.10)	0.97 (0.88 to 1.06)	0.12 (0.10 to 0.14)
	% change	-51.81 (- 55.35 to - 48.61)	-47.71 (- 51.51 to - 44.20)	-83.49 (- 85.29 to - 81.98)	-78.43 (-81.76 to -74.79)	-6.65 (-15.94 to 3.84)	-0.75 (-0.78 to -0.70)
Eastern Europe	2021	12.69 (11.69 to 13.65)	11.72 (10.79 to 12.62)	0.46 (0.43 to 0.50)	0.05 (0.04 to 0.06)	0.34 (0.31 to 0.37)	0.12 (0.11 to 0.13)
	% change	-69.60 (- 71.75 to - 67.46)	-67.23 (- 69.62 to - 64.92)	-88.66 (- 89.48 to - 87.76)	-69.86 (-75.07 to -61.68)	-69.55 (-72.21 to -66.80)	-0.81 (-0.83 to -0.78)
High-income	2021	24.02 (21.24 to 25.39)	19.11 (16.86 to 20.21)	0.75 (0.67 to 0.80)	0.18 (0.16 to 0.19)	3.65 (3.23 to 3.89)	0.33 (0.30 to 0.34)
	% change	-19.33 (- 23.20 to - 17.08)	-18.88 (- 22.73 to - 16.58)	-77.00 (- 78.82 to - 75.08)	-65.22 (-67.71 to -62.91)	109.34 (96.67 to 119.57)	-0.53 (-0.55 to -0.51)
Australasia	2021	23.87 (21.07 to 25.64)	18.89 (16.66 to 20.42)	1.14 (1.02 to 1.24)	0.31 (0.27 to 0.36)	3.17 (2.69 to 3.46)	0.36 (0.30 to 0.42)
	% change	-33.63 (- 39.16 to - 28.85)	-35.78 (- 41.33 to - 30.94)	-72.19 (- 74.85 to - 69.30)	67.83 (41.23 to 105.28)	180.27 (151.69 to 209.00)	-0.68 (-0.73 to -0.63)
High-income Asia Pacific	2021	12.15 (10.31 to 13.31)	6.68 (5.70 to 7.37)	0.66 (0.53 to 0.84)	0.22 (0.19 to 0.25)	4.36 (3.73 to 4.76)	0.23 (0.21 to 0.25)

	% change	-51.41 (-55.14 to -47.14)	-52.84 (-56.34 to -48.45)	-90.90 (-92.60 to -87.56)	-59.22 (-64.14 to -53.91)	60.29 (43.91 to 74.79)	-0.30 (-0.38 to -0.22)
High-income North America	2021	35.50 (31.22 to 37.53)	29.89 (26.20 to 31.63)	0.78 (0.74 to 0.81)	0.12 (0.10 to 0.13)	4.25 (3.75 to 4.49)	0.46 (0.42 to 0.49)
	% change	15.05 (9.08 to 18.37)	13.73 (7.70 to 17.06)	-52.13 (-53.65 to -50.69)	-66.22 (-69.02 to -63.35)	90.18 (79.86 to 97.29)	0.28 (0.19 to 0.38)
Southern Latin America	2021	28.93 (26.31 to 30.87)	22.53 (20.53 to 24.07)	0.87 (0.79 to 0.92)	0.16 (0.14 to 0.18)	4.80 (4.31 to 5.15)	0.58 (0.51 to 0.64)
	% change	-13.11 (-19.13 to -7.86)	-16.33 (-22.08 to -10.66)	-64.39 (-67.92 to -60.65)	-43.70 (-53.49 to -32.41)	85.98 (68.66 to 103.98)	-0.46 (-0.55 to -0.37)
Western Europe	2021	21.68 (19.17 to 23.01)	17.82 (15.74 to 18.92)	0.67 (0.59 to 0.71)	0.19 (0.17 to 0.20)	2.79 (2.49 to 2.97)	0.22 (0.20 to 0.23)
	% change	-28.80 (-32.54 to -26.18)	-27.73 (-31.63 to -25.02)	-78.91 (-80.68 to -77.47)	-69.70 (-72.47 to -66.80)	151.38 (133.19 to 166.72)	-0.76 (-0.77 to -0.74)
Latin America and Caribbean	2021	29.88 (26.82 to 32.10)	24.68 (22.18 to 26.40)	1.30 (1.17 to 1.45)	0.13 (0.11 to 0.14)	3.02 (2.64 to 3.40)	0.75 (0.65 to 0.88)
	% change	-31.79 (-35.84 to -27.58)	-30.32 (-34.13 to -26.24)	-72.60 (-74.75 to -70.12)	-40.93 (-45.91 to -35.27)	66.19 (34.78 to 104.25)	-0.53 (-0.60 to -0.46)
Andean Latin America	2021	26.57 (21.66 to 31.66)	13.40 (10.93 to 16.29)	0.78 (0.59 to 0.99)	0.20 (0.15 to 0.28)	11.37 (8.69 to 14.33)	0.80 (0.62 to 1.03)
	% change	-27.18 (-40.17 to -12.10)	-31.06 (-44.04 to -13.59)	-80.89 (-86.57 to -74.81)	-22.35 (-49.19 to 10.64)	44.74 (-4.61 to 122.00)	-0.83 (-0.88 to -0.77)
Caribbean	2021	26.67 (23.11 to 31.05)	19.85 (17.47 to 22.49)	4.02 (3.09 to 5.63)	0.02 (0.02 to 0.02)	1.19 (0.99 to 1.45)	1.59 (1.01 to 2.35)
	% change	-5.86 (-17.52 to 7.73)	7.41 (-5.20 to 21.66)	-42.98 (-53.24 to -31.52)	-58.19 (-66.63 to -48.84)	70.29 (34.51 to 112.93)	-0.22 (-0.44 to 0.08)
Central Latin America	2021	31.57 (27.97 to 34.72)	26.92 (23.70 to 29.64)	1.08 (0.96 to 1.21)	0.09 (0.08 to 0.10)	2.69 (2.42 to 2.96)	0.79 (0.67 to 0.95)
	% change	-30.07 (-36.01 to -23.91)	-24.67 (-31.07 to -18.26)	-82.73 (-84.65 to -80.67)	-69.75 (-73.27 to -66.21)	86.03 (67.86 to 106.22)	-0.44 (-0.53 to -0.34)
Tropical Latin America	2021	29.91 (26.71 to 31.76)	26.32 (23.44 to 27.99)	1.09 (0.99 to 1.16)	0.16 (0.15 to 0.18)	1.83 (1.64 to 1.96)	0.50 (0.46 to 0.54)
	% change	-39.48 (-42.81 to -36.54)	-41.04 (-44.14 to -38.38)	-62.30 (-65.15 to -59.13)	-1.78 (-11.69 to 9.88)	86.70 (71.69 to 102.04)	-0.32 (-0.39 to -0.24)

North Africa and Middle East	2021	34.42 (30.59 to 38.34)	26.37 (23.19 to 29.31)	6.48 (5.65 to 7.36)	0.11 (0.08 to 0.14)	0.76 (0.56 to 1.15)	0.70 (0.51 to 0.84)
	% change	-37.47 (-44.46 to -23.82)	-27.11 (-36.93 to -5.37)	-60.84 (-69.96 to -51.30)	-39.06 (-53.50 to -18.00)	19.18 (-11.82 to 81.78)	-0.53 (-0.64 to -0.38)
South Asia	2021	124.97 (110.17 to 142.52)	101.63 (90.55 to 114.34)	17.68 (12.55 to 26.32)	0.15 (0.10 to 0.20)	4.19 (2.81 to 5.76)	1.32 (0.89 to 1.90)
	% change	-15.21 (-27.45 to 6.23)	-11.27 (-25.19 to 14.84)	-35.95 (-49.59 to -17.05)	-24.85 (-43.35 to 10.11)	15.95 (-8.96 to 73.64)	-0.08 (-0.26 to 0.28)
Southeast Asia, East Asia, and Oceania	2021	71.66 (60.43 to 82.88)	66.61 (55.77 to 77.41)	3.87 (3.42 to 4.36)	0.32 (0.25 to 0.41)	0.40 (0.29 to 0.56)	0.46 (0.38 to 0.54)
	% change	-62.30 (-68.67 to -53.73)	-62.69 (-69.14 to -54.04)	-60.71 (-69.71 to -50.94)	-52.39 (-66.31 to -34.62)	4.15 (-33.55 to 58.31)	-0.23 (-0.45 to 0.16)
East Asia	2021	74.84 (61.58 to 88.33)	72.20 (59.32 to 85.26)	1.52 (1.23 to 1.82)	0.41 (0.32 to 0.52)	0.41 (0.25 to 0.54)	0.31 (0.21 to 0.38)
	% change	-67.89 (-74.25 to -60.15)	-67.95 (-74.24 to -60.20)	-74.94 (-84.49 to -64.14)	-53.35 (-67.08 to -35.81)	-0.32 (-42.78 to 53.73)	-0.30 (-0.59 to 0.04)
Oceania	2021	157.62 (128.99 to 188.69)	118.21 (96.32 to 144.59)	33.98 (24.05 to 51.08)	0.05 (0.02 to 0.12)	2.30 (1.42 to 3.85)	3.07 (2.03 to 4.29)
	% change	-19.55 (-36.13 to 4.56)	-18.06 (-35.44 to 6.40)	-27.64 (-44.40 to -1.63)	86.08 (0.91 to 259.92)	6.41 (-32.27 to 54.46)	0.23 (-0.08 to 0.73)
Southeast Asia	2021	55.50 (49.46 to 62.20)	43.14 (38.24 to 48.54)	11.37 (10.01 to 12.98)	0.01 (0.01 to 0.02)	0.33 (0.17 to 0.66)	0.65 (0.51 to 0.91)
	% change	-32.85 (-41.80 to -12.08)	-28.31 (-39.04 to -2.65)	-46.36 (-56.78 to -31.54)	-34.34 (-53.90 to 1.38)	13.05 (-11.19 to 66.25)	-0.33 (-0.51 to 0.07)
Sub-Saharan Africa	2021	41.87 (36.39 to 51.25)	28.60 (24.91 to 33.18)	10.69 (8.49 to 15.65)	0.38 (0.23 to 0.60)	1.33 (0.59 to 2.39)	0.86 (0.43 to 1.44)
	% change	-27.15 (-35.83 to -15.92)	-21.98 (-30.97 to -8.89)	-39.01 (-48.09 to -26.66)	-31.66 (-42.78 to -15.69)	-13.38 (-34.64 to 12.46)	-0.27 (-0.47 to -0.01)
Central Sub-Saharan Africa	2021	61.45 (42.48 to 104.20)	42.82 (29.63 to 65.02)	15.79 (8.99 to 37.27)	0.45 (0.17 to 1.01)	1.47 (0.51 to 3.92)	0.92 (0.42 to 1.97)
	% change	-21.62 (-39.46 to -1.02)	-18.17 (-37.34 to 5.85)	-31.17 (-50.15 to -7.48)	-14.44 (-44.44 to 33.59)	3.88 (-31.28 to 49.80)	-0.23 (-0.48 to 0.16)
Eastern Sub-Saharan Africa	2021	41.53 (35.00 to 52.58)	29.91 (24.41 to 35.14)	9.42 (6.67 to 15.60)	0.31 (0.14 to 0.52)	0.96 (0.33 to 2.08)	0.94 (0.46 to 1.74)

	% change	-32.39 (-42.63 to -17.64)	-29.29 (-39.44 to -14.81)	-42.20 (-54.63 to -20.84)	-33.77 (-47.60 to -13.57)	-6.22 (-38.58 to 38.83)	-0.31 (-0.54 to 0.02)
Southern Sub-Saharan Africa	2021	51.81 (47.87 to 55.42)	34.78 (31.93 to 37.34)	13.89 (12.43 to 15.40)	0.48 (0.42 to 0.56)	2.00 (1.39 to 2.65)	0.66 (0.53 to 0.82)
	% change	-14.00 (-30.25 to -1.30)	-7.01 (-21.83 to 4.47)	-28.53 (-49.25 to -8.56)	-16.96 (-35.65 to 5.63)	-4.11 (-34.84 to 39.81)	-0.11 (-0.29 to 0.08)
Western Sub-Saharan Africa	2021	34.22 (29.56 to 39.19)	22.07 (19.45 to 25.05)	9.52 (7.82 to 11.70)	0.40 (0.23 to 0.62)	1.39 (0.54 to 2.41)	0.22 (0.20 to 0.23)
	% change	-29.14 (-40.07 to -12.67)	-22.63 (-34.47 to -2.48)	-41.63 (-51.11 to -27.18)	-36.41 (-49.30 to -19.80)	-19.61 (-41.48 to 10.19)	-0.24 (-0.42 to 0.01)

638 Uncertainty intervals represent 95% confidence intervals.

639 Abbreviation: COPD, chronic obstructive pulmonary disease; CRD, chronic respiratory

640 disease; ILD, Interstitial lung disease.