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Original article

Global, regional, and national burden of chronic respiratory diseases and the COVID-19 pandemic-driven estimates, 1990-2021: a Global Burden of Disease Study

Running title: Global burden of chronic respiratory diseases

GBD 2021 Chronic Respiratory Disease Collaborators

Abstract

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

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

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

INTRODUCTION

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

Sustainable Development Goal (SDG) target 3.4, adopted by the United Nations, advocates for a one-third reduction in premature mortality due to NCDs by 2030 compared to the rates observed in 2015.[5] It is imperative to reduce the prevalence and disability-adjusted life years (DALYs) of CRDs to achieve this goal by minimizing exposure to modifiable risk factors, such as smoking, air pollution, occupational dust, and chemicals.

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

This manuscript was produced as part of the GBD Collaborator Network following the GBD Protocol.[2,9]

METHODS

Overview

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

Case definition and input data

For CRDs, GBD 2021 produced estimates for four categories: COPD, asthma, pneumoconiosis, and ILD and pulmonary sarcoidosis.[2,9] COPD is defined in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.[11,12] Asthma is a chronic respiratory condition induced by allergic reactions or hypersensitivity that results in bronchial spasms and breathing difficulties. Pneumoconiosis is a chronic lung disease that results from lung scarring and interstitial damage caused by prolonged exposure to dust and other contaminants; GBD 2021 estimated pneumoconiosis by incorporating diagnoses of specific conditions such as silicosis and asbestosis. ILD and pulmonary sarcoidosis encompass various chronic respiratory conditions that affect lung function and oxygen absorption owing to scarring and/or inflammation. The definition provided by the American Thoracic Society for ILD is the gold standard. In addition to the CRD discussed earlier, there are other CRDs and their associated complications. Further details, including International Classification of Diseases (ICD) codes for each disease, are provided in the **Supplementary Methods**.[4]

Prevalence estimates

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

Mortality estimates

The modeling framework for mortality estimation is described briefly below with further detail provided in the summary cause of death publication for GBD 2021.[12] The cause-of-death ensemble model (CODEm) was used to simulate the majority of cause-of-death estimates for illnesses and injuries. CODEm tests covariate combinations based on the out-of-sample predictive validity using an ensemble of statistical models. The results were then combined to estimate deaths by cause, location, age, sex, and year.[14] CODEm was run separately for each sex and region with and without comprehensive vital registration data to reduce the potential increase in uncertainty due to heterogeneous data.[13] The estimation of mortality due to CRDs relied on various sources, including vital registration and verbal autopsy, with outlier data points excluded based on criteria such as implausible values, inconsistent age or time trends, and significant discrepancies with other sources.[12] Models with the smallest mean squared error were weighted more heavily to create the final ensemble model. The GBD 2021 methodology adheres to ICD-9 and 10, attributing each death to the underlying cause and initiating the chain of events leading to death.[2,9] CRD mortality estimates were scaled using a procedure known as CoDCorrect to ensure consistency between the sum of cause-specific mortality and the total envelope of all-cause mortality.[12]

DALY estimates

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

Risk factor analysis

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

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

The selection of risk-outcome pairs was established based on the presence of strong or probable evidence, evaluated according to the methods and criteria set by the World Cancer Research Fund[16], availability of exposure data, feasibility of behavioral changes, and public health relevance.

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

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

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

As a secondary analysis, we used GBD estimates to assess the expected number of deaths from CRDs for 2020—2021, based on estimates from 2015 to 2019 and a quasi-Poisson regression model.[8,18] Although the Poisson distribution is appropriate for modeling the number of events occurring within a specified time frame or geographic area, the inherent variability in event frequency observed in real-world data can result in overdispersion.[17] Accordingly, a quasi-Poisson regression model was selected to address this overdispersion and to accurately model the variability in count data.[8] Through this analysis, we compared the predicted mortality numbers with the observed figures for CRDs by age group and calculated the differences and ratios between the observed and expected deaths.[8]

SDI

SDI is a composite measure that includes a country's lag-distributed income per capita, average years of educational attainments, and the total fertility rate in females <25 years, and it varies from 0.0 to 1.0.[19] Further details can be found in **Supplementary Methods**.

Data presentation

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

Role of funding source

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

RESULTS

Overview

In 2021, there were 468.3 million (95% UI, 428.9 to 513.1) individuals with CRD worldwide, representing an age-standardized rate of 5,785.4 per 100,000 (**Figure S1**). The global age-standardized prevalence rate decreased by 27.2% from 7,936.4 in 1990, and 20 of the 21 GBD regions showed significant declines. The most significant reduction in the age-standardized prevalence rate was observed in the high-income Asia Pacific (−50.3% [−46.9 to −53.3]), followed by Eastern Europe (−38.4% [−35.0 to −41.4]; **Table S1**). However, high-income North America revealed a stable trend (2.8% [−1.4 to 7.4]; **Figure 1A**) and had the highest age-standardized prevalence rate (14,879.6 [13.883.8 to 16054.1]). At the national level, the age-standardized prevalence rate ranged from 3,207.8 in Cabo Verde to 13,316.0 in the United States in 2021.

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

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

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

Trends in age-sex-specific CRD burden

Figure 4 presents the trends in age-sex-specific death rates for four CRDs from 1990 to 2021. For COPD, age-specific death rates were higher in males across all age groups and showed substantial declines across all age-sex groups from 1990 to 2021. Females aged 15-44 years had the greatest reduction of 55.2%, from 1.8 per 100,000 in 1990 to 0.8 per 100,000 in 2021, among all age-sex groups. For asthma, we observed a significant reduction in the age-sex-specific death rates across all groups, most pronounced in males aged <15 years (1.5 per 100,000 population in 1990; 0.4 per 100,000 population in 2021; -73.3% percentage change). As a result, in 2021, death rates were higher among females in most age groups, with rates increasing progressively with advanced age. Pneumoconiosis also showed a declining trend in all age-sex groups, and males had a greater mortality burden of pneumoconiosis than females of all ages. Last, age-sex-specific death rates for ILD and pulmonary sarcoidosis increased in most groups, most pronounced in those aged ≥ 75 years, with an increase of 105.9% in females and 84.1% in males from 1990 to 2021. Conversely, individuals aged <15 years had a marked reduction in death rates (-45.9% in females; -48.3% in males). More details on the global age and sex distributions of COPD, asthma, pneumoconiosis, and ILD and pulmonary sarcoidosis prevalence and death are shown in **Figures S6-S8**.

Risk factors attributable to COPD, asthma, and pneumoconiosis

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

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

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

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

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

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

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

DISCUSSION

Key findings of this study

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

Plausible mechanisms

Globally, substantial progress has been made in reducing the burden of asthma, COPD, and pneumoconiosis. This achievement is partly attributed to various efforts to improve prevention and therapeutics through targeted strategies and actions.[20] For instance, adopting the World Health Organization Framework Convention on Tobacco Control in 2005, which includes raising taxes on tobacco and enforcing a ban on advertising, marking a significant turning point for enhancing global tobacco control efforts and preventing CRDs.[21] Considering that some resource-limited countries have shown slow implementation of policies[21], there is potential for further reduction in the disease burden, with overall advances in healthcare access and patient education. In recent decades, innovations in targeted therapies have contributed to a better prognosis for patients with chronic respiratory conditions. Novel targeted treatments, such as anti-IgE or anti-IL-5 monoclonal antibodies, represent a substantial advancement for patients with asthma refractory to conventional treatments, which could further contribute to a reduction in premature deaths.[22] For severe COPD, triple therapy, a combination of a long-acting muscarinic antagonist, a long-acting beta-agonist, and an inhaled corticosteroid in a single inhaler, has shown improved outcomes.[23]

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

Notably, high-income North America had the highest age-standardized prevalence rate of CRDs. This is primarily due to asthma, which accounts for more than half of CRD cases, driving the overall trend of the prevalence rate (**Figure 2**). Asthma has been historically more common in Western countries due to a complex interplay of genetic and environmental factors.[27] In addition, high-income North America exhibited an increase in age-standardized mortality rates for CRD from 1990 to 2021. Specifically, the age-standardized mortality rates for ILD and pulmonary sarcoidosis showed a marked rise, while those for asthma and 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 inflammation[29], 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 factors[31] may have prompted more frequent hospital visits, along with the increased number of CT scans performed[32], during the pandemic and led to incidental diagnoses of underlying conditions, such as asthma or COPD.[33] This increased healthcare engagement and heightened awareness and monitoring of pulmonary health during the pandemic might have contributed to better detection of previously undiagnosed cases.

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

Overall, the impact of the COVID-19 pandemic on CRDs is less pronounced than in tuberculosis and non-COVID-19 lower respiratory infections.[7,8] Unlike these acute conditions, the nature of chronic diseases may have made them less immediately affected by the pandemic. In addition, the interactions between COVID-19 and CRDs are complex and bidirectional. Individuals with a history of COVID-19 are more likely to develop a range of pulmonary sequelae[38,39], while those with pre-existing chronic respiratory conditions are more susceptible to severe COVID-19 outcomes when infected.[40,41] These factors may lead to an underestimation of the true extent of excess mortality related to CRDs, as some of these cases may be recorded as COVID-19-related fatalities.[42] Therefore, further studies are needed to better understand the full impact of the COVID-19 pandemic on CRDs and to clarify the factors contributing to variations in disease outcomes across different CRDs.

Policy and clinical implications

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

For instance, we noted that household air pollution from solid fuels, rather than smoking, primarily contributed to the COPD burden among females in low SDI settings. Therefore, using cleaner fuel or technology for domestic work is required to reduce solid fuel exposure in these countries[45], which aligns with the Clean Cooking Alliance, a leading global initiative to make clean cooking more accessible.[46] Enhancing access to modern energy for cooking is crucial to meet the UN's SDG by 2030, and this shift can reduce the disease burden, contribute to climate change mitigation, and protect terrestrial ecosystems. High DALY rates for asthma, COPD, and pneumoconiosis in low-SDI regions, despite lower prevalence, suggest that poor healthcare access, suboptimal treatment, and unhealthy environments amplify the burden.[47] Therefore, prevention, diagnostic, and therapeutic approaches in limited-source settings should be addressed at a global level.

Limitations and strengths

This is the first study to examine the global, regional, and national burden of CRDs during the COVID-19 pandemic across 204 countries and territories. In addition to providing updated comprehensive estimates of the disease, we analyzed the potential impact of the pandemic on the mortality of CRD. However, this study has several limitations, primarily due to the limited amount and high input data variability. First, despite the massive use of international vital registration and insurance claims data to construct the GBD model, numerous locations and years lack primary data, particularly in low- and middle-income countries (LMICs). This led to lower certainty and generalizability of our findings, highlighting the importance of improved data collection in LMICs to ensure that the estimates from the modeling process are grounded in more primary data. Second, while there is evidence suggesting an association between air pollution and ILD and between occupational risk and pneumoconiosis, the GBD model has not yet incorporated these risk-outcome pairs.[12,48] This gap limits our understanding of how environmental factors contribute to these diseases.[49] Meanwhile, this lag in risk factor integration may reflect the rigorous selection criteria of the GBD framework[10], which requires sufficient evidence of causation for each risk-outcome pair, as determined by the Bradford Hill criteria. These criteria also mandate the availability of risk exposure data and ensure the relevance of the risk for modification and policy implementation.[50] As such, emerging exposures, such as vaping and cannabis use, remain yet excluded due to the lack of standardized global data or insufficient evidence to satisfy these criteria.[51] Expanding the list of risk factors is strong motivation of GBD, and more risk factors are expected to be included in future GBD iterations.[10] Third, the diagnostic criteria for CRDs and interpretation of spirometry results were heterogeneous across input data sources and regions, which may influence the reliability of the estimates, although GBD 2021 adjusted for input data that did not use the reference definition.

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

CONCLUSION

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

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

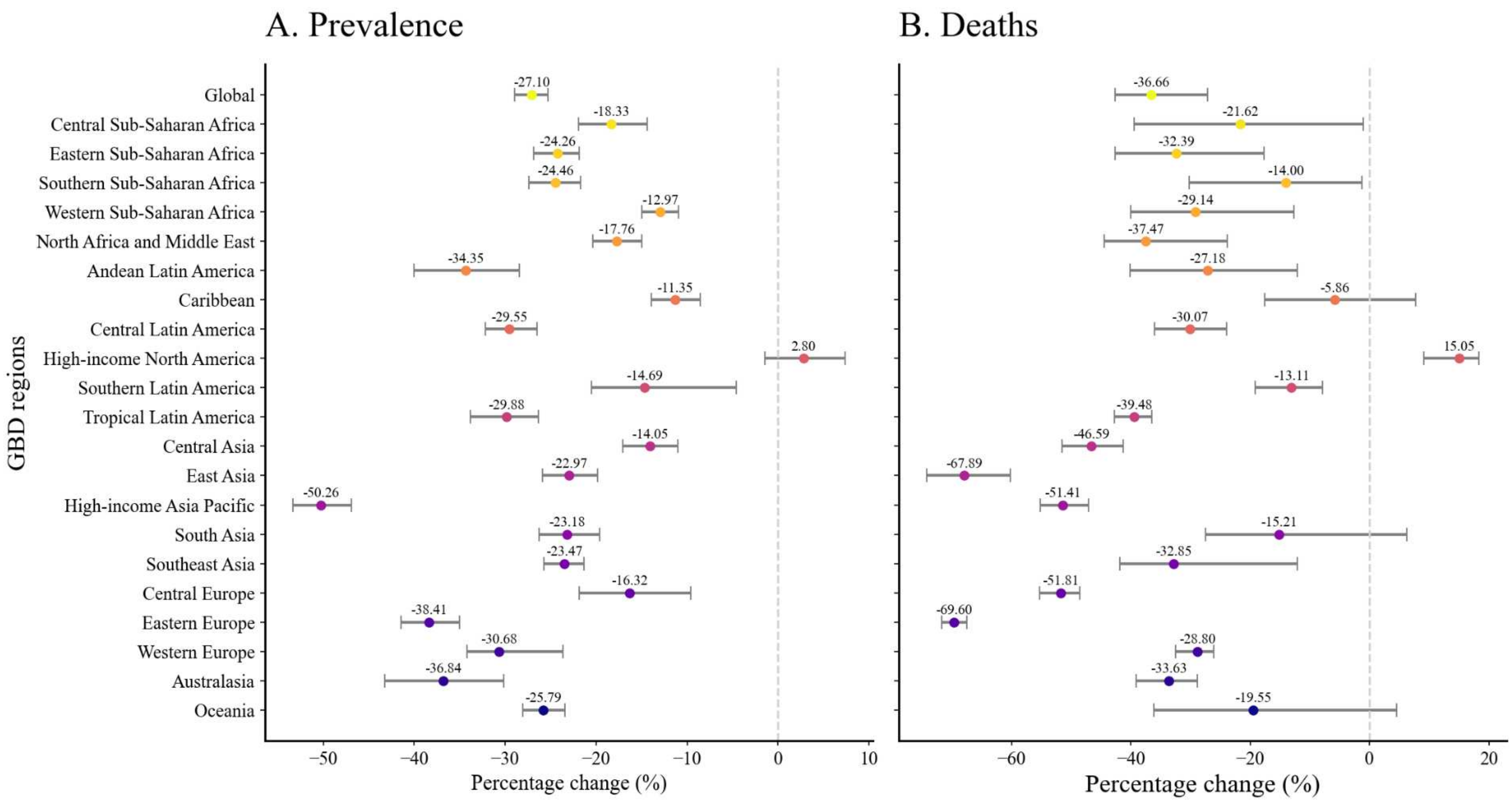


Figure 2. World map of age-standardized prevalence rates for COPD (A), asthma (B), pneumoconiosis (C), and ILD and pulmonary sarcoidosis (D) in 2021. Abbreviation: COPD, Chronic obstructive pulmonary disease; ILD, interstitial lung disease.

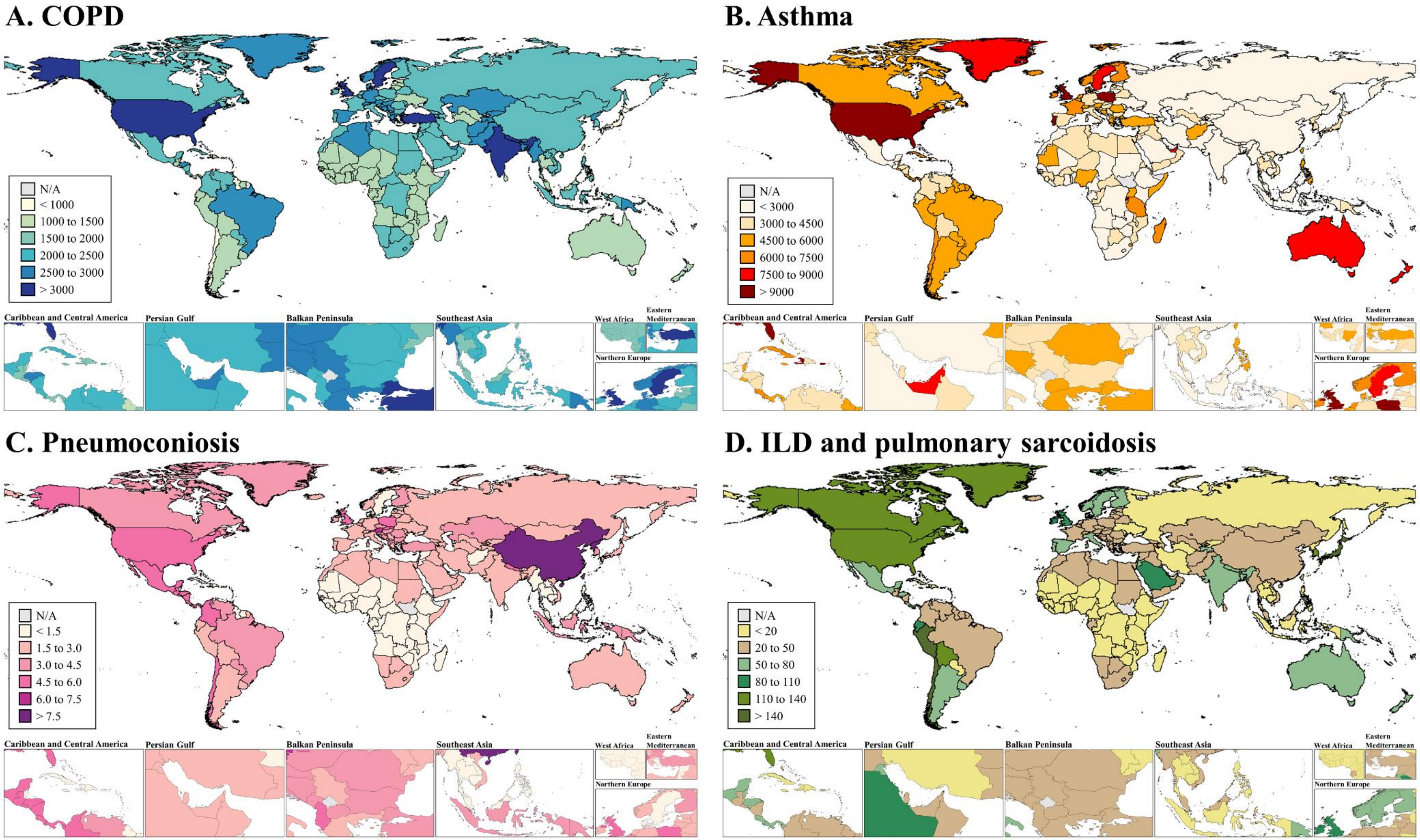


Figure 3. World map of age-standardized death rates for COPD (A), asthma (B), pneumoconiosis (C), and ILD and pulmonary sarcoidosis (D) in 2021. Abbreviation: COPD, Chronic obstructive pulmonary disease; ILD, interstitial lung disease.

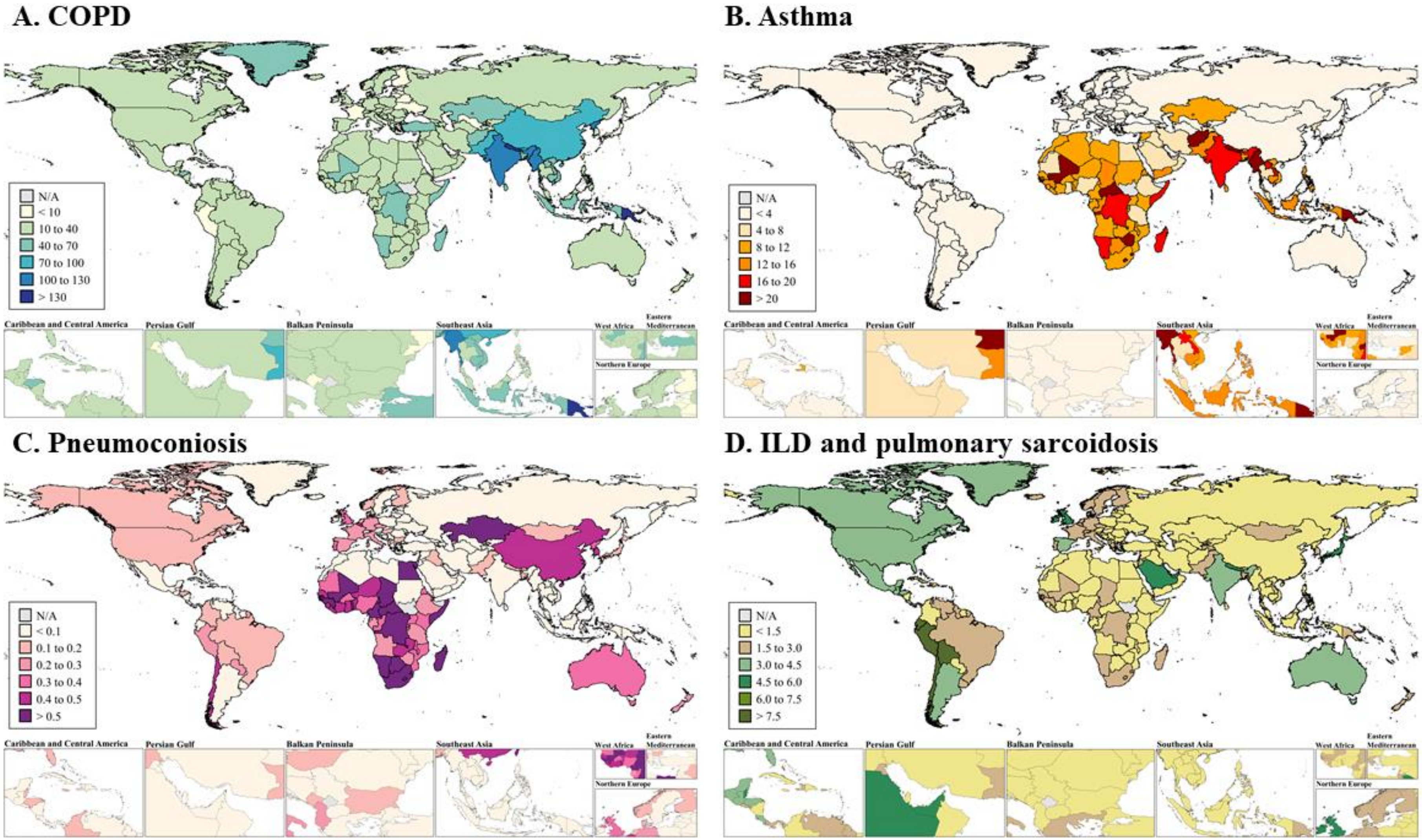


Figure 4. Global age-sex-specific COPD (A), asthma (B), pneumoconiosis (C), ILD and pulmonary sarcoidosis (D) death rates, 1990–2021. Abbreviation: COPD, Chronic obstructive pulmonary disease; ILD, interstitial lung disease.

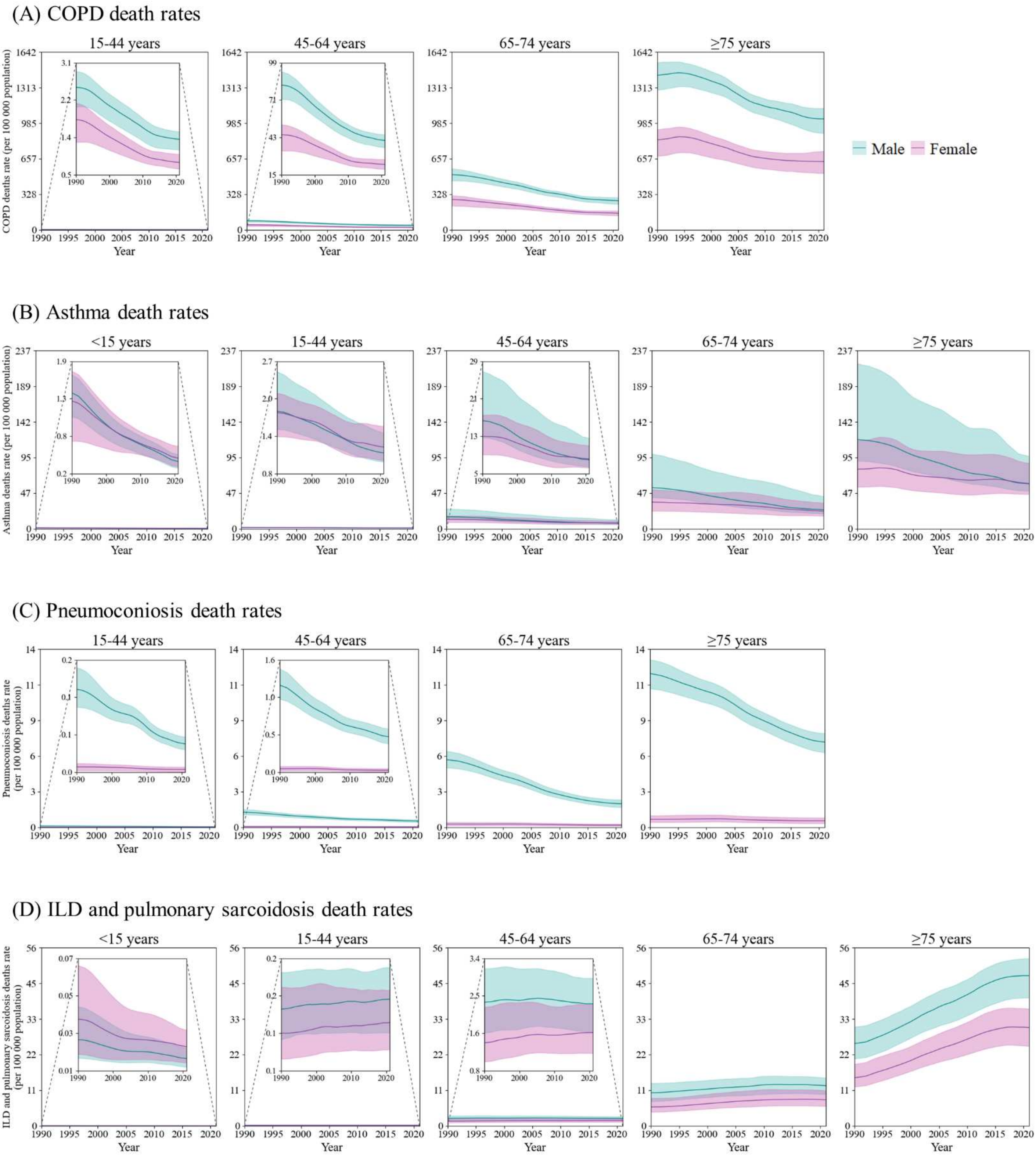


Figure 5. Global and regional distribution of age-standardized DALY rates for COPD (A), asthma (B), and pneumoconiosis (C) by risk factor in males and females, 2021. Abbreviations: COPD, chronic obstructive pulmonary disease; DALYs, disability-adjusted life-years; GBD, Global Burden of Disease.

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

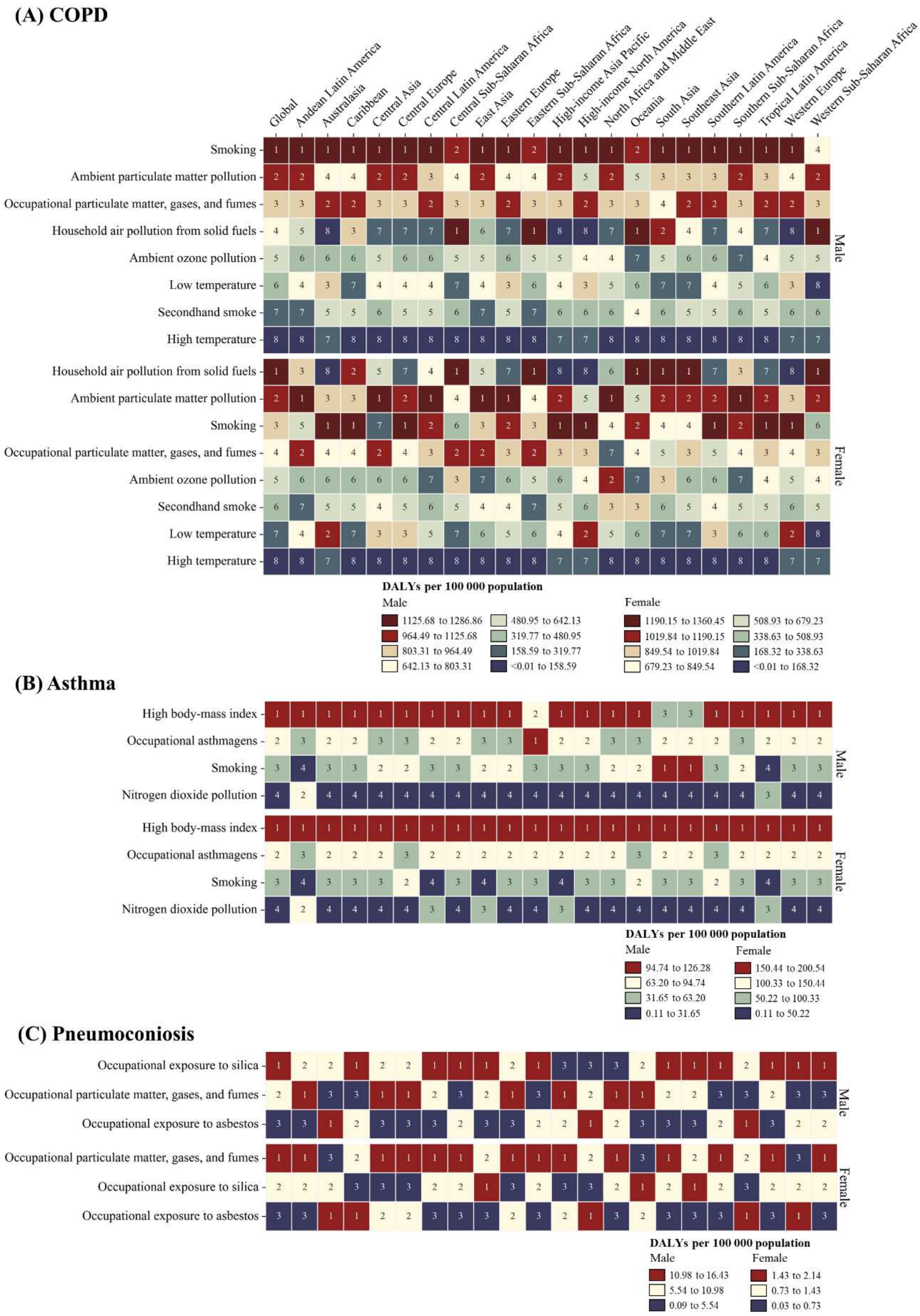
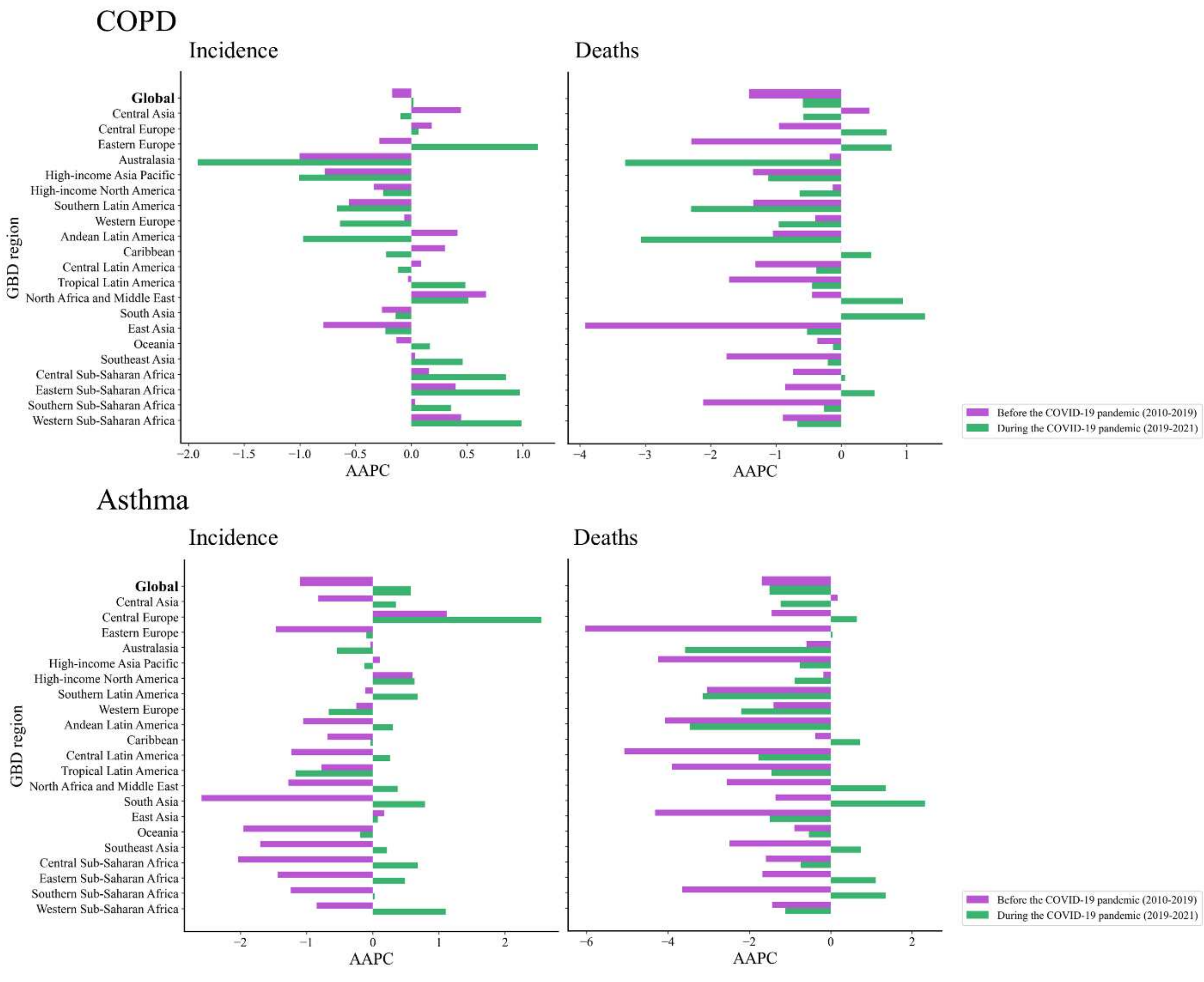


Figure 6. Average annual percentage change of age-standardized incidence and death rates for COPD, asthma, pneumoconiosis, and ILD and pulmonary sarcoidosis by GBD region during the pre-COVID-19 (2010–2019) and pandemic period (2019–2021). Abbreviation: COPD, chronic obstructive pulmonary disease; GBD, Global Burden of Disease, Injuries, and Risk Factors Study; ILD, Interstitial lung disease.



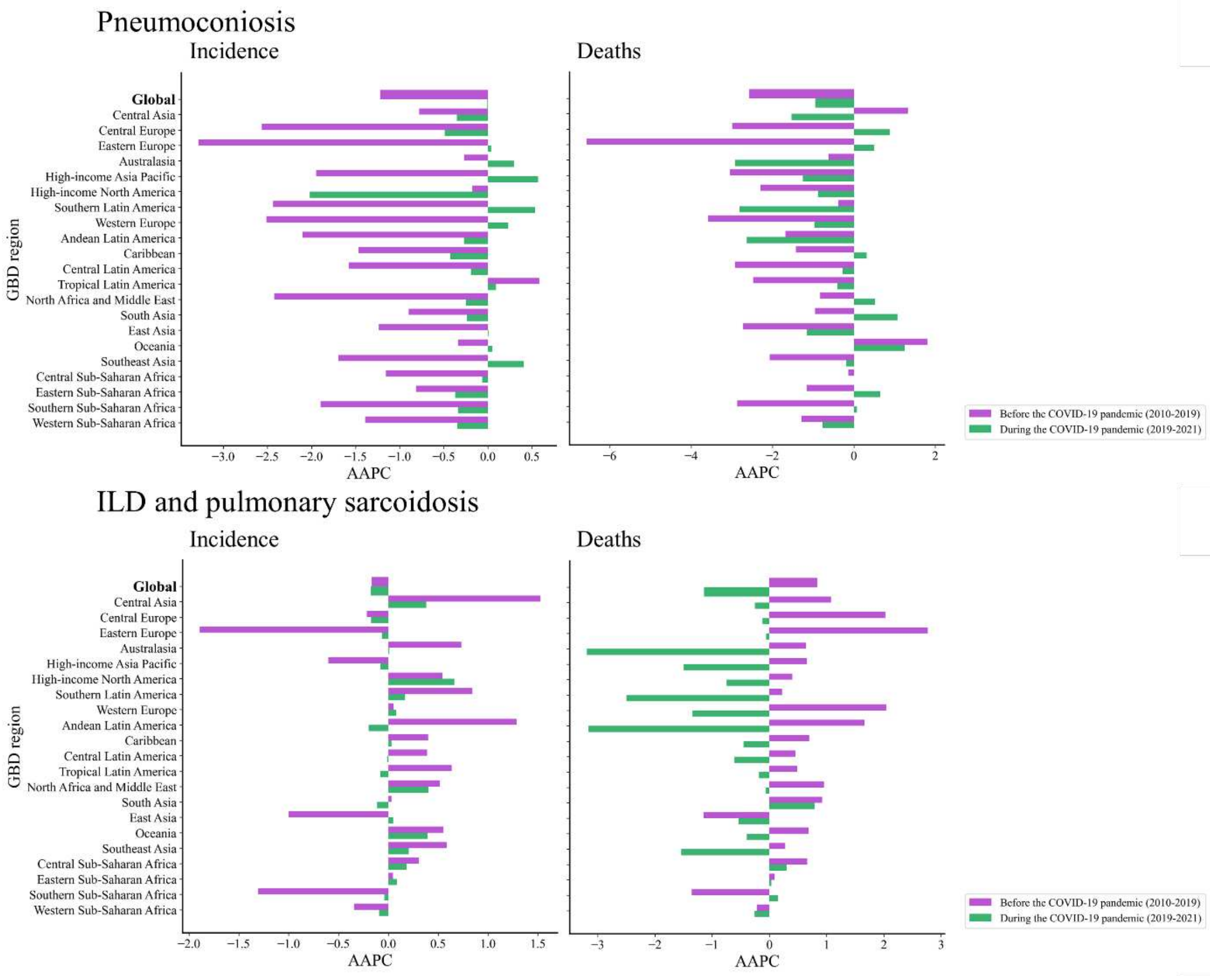

Pneumoconiosis
Incidence
Deaths
GBD region
Global
Central Asia
Central Europe
Eastern Europe
Australasia
High-income Asia Pacific
High-income North America
Southern Latin America
Western Europe
Andean Latin America
Caribbean
Central Latin America
Tropical Latin America
North Africa and Middle East
South Asia
East Asia
Oceania
Southeast Asia
Central Sub-Saharan Africa
Eastern Sub-Saharan Africa
Southern Sub-Saharan Africa
Western Sub-Saharan Africa
AAPC
Before the COVID-19 pandemic (2010-2019)
During the COVID-19 pandemic (2019-2021)
ILD and pulmonary sarcoidosis
Incidence
Deaths
AAPC

Table 1. Global and regional age-standardized mortality rates from chronic respiratory disease 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)

Uncertainty intervals represent 95% confidence intervals.

Abbreviation: COPD, chronic obstructive pulmonary disease; CRD, chronic respiratory disease; ILD, Interstitial lung disease.