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Global disease burden of interstitial lung disease and pulmonary sarcoidosis, 1990-2021, and forecast analysis over the next decade

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Abstract. *Background and aim:* Interstitial lung disease is a major class of disease that affect lung health, however, there is a lack of epidemiological studies related to the global burden of this disease. Data from the Global Burden of Disease Study 2021 (GBD 2021) were utilized to evaluate the global burden of interstitial lung disease and pulmonary sarcoidosis comprehensively in 21 global regions, 204 countries and territories from 1990 to 2021, examining their association with the sociodemographic index, and forecasting trends for the forthcoming decade. *Methods:* Using GBD 2021 data, we analyzed interstitial lung disease and pulmonary sarcoidosis prevalence, incidence, mortality, and disability-adjusted life years. We calculated age-standardized rate trends (1990–2021) through generalized linear models and assessed disease burden inequalities using the sociodemographic index, slope index, and concentration index. Global maps and regional comparisons visualized burden distribution. Decomposition analysis quantified impacts of population growth, aging, and epidemiological changes. Future burden trends (next decade) were projected using Bayesian Age-Period-Cohort modeling. *Results:* From 1990 to 2021, the global burden of interstitial lung disease and pulmonary sarcoidosis has been on the rise. Generally, Higher age-standardized rates of interstitial lung disease and pulmonary sarcoidosis were observed in higher age groups and areas with a high socio-demographic index. Moreover, population growth and ageing are the main causes of the increased burden of disease. Projections indicate that by 2034, the number of cases, illnesses, deaths, and disability-adjusted life years associated with interstitial lung disease and pulmonary sarcoidosis will continue to rise, while age-standardized rates are expected to plateau. *Conclusions:* The global disease burden of interstitial lung disease and pulmonary sarcoidosis remains significant and deserves our attention. People aged 70-84 and high sociodemographic index group should be the focus of attention.

Key words: interstitial lung disease, pulmonary sarcoidosis, prevalence, incidence, mortality, disability-adjusted life years, global burden of disease

Introduction

Interstitial lung diseases (ILD)s are characterized by various degrees of inflammation, injury, and fibrosis of the lung parenchyma, and encompasses over 200 heterogeneous pulmonary diseases. The most common form of ILD is idiopathic pulmonary fibrosis (1), which can lead to respiratory failure and significantly impair the quality life of ILD patients (2). In recent years, there has been an increasing number of studies related to ILDs. The pathogenesis, diagnosis, and treatment progress of idiopathic pulmonary fibrosis, connective tissue disease-associated interstitial lung disease, pulmonary sarcoidosis, and progressive pulmonary fibrosis are still the focus topics of ILDs for experts at home and abroad in 2023 (3). The international

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guidelines divide ILDs into four groups: 1) ILD of known causes; 2) idiopathic interstitial pneumonias; 3) sarcoidosis and granulomatous diseases; 4) miscellaneous. Pulmonary sarcoidosis (PS) is classified within the ILD category of granulomatous lung diseases (4). Although PS is categorized as an ILD, the Global Burden of Disease (GBD) database ranks PS alongside ILD, while pneumoconiosis, also an interstitial lung disease, is classified separately and is not included within the scope of this study. Numerous medical studies have indicated that the pathogenesis of ILD may be associated with genetic factors (5, 6), environmental factors (7, 8), and immune factors (9, 10) and so on. Genetic and geographic influence on phenotypic variation in European sarcoidosis patients (11). The different classifications of ILD are essential to provide treatment decisions. Till now, immunosuppression is still the primary treatment for ILD, except for idiopathic pulmonary fibrosis, including corticosteroids (12), mycophenolate (13, 14), azathioprine (15), methotrexate (15), cyclophosphamide (14, 16), and rituximab (17, 18). The limited treatment options, adverse drug-related side effects, and inadequate diagnosis and prognosis have resulted in a significant disease burden for both patients and society (1, 19). Between 1990 and 2019, the Age-standardized incidence rate (ASIR) and the age-standardized prevalence rate (ASPR) of interstitial lung disease and pulmonary sarcoidosis (ILD&PS) increased worldwide (20). Given its substantial population base, the disease burden of ILD&PS in Asia warrants significant attention. Nevertheless, systematic investigations into the disease burden of ILD&PS remain relatively scarce at this time. This article presents a systematic and comprehensive updated analysis of the disease burden associated with ILD&PS, utilizing the recently released GBD 2021 dataset. The objective of this study is to examine the prevalence, incidence, mortality, and disability-adjusted life years (DALY) of ILD&PS on a global scale, as well as across various countries, regions, age groups, and genders. The insights derived from our findings may assist national health authorities in gaining a comprehensive understanding of the global burden of ILD&PS, formulating reasonable prevention and control policies, allocating health resources, and the enhancement of prognostic outcomes for patients with ILD&PS.

Study Design and Methods

Data acquisition and sources

The data for this study were obtained from the GBD 2021 dataset, which provides comprehensive information on the global and regional burden of 369 diseases, injuries, and 88 risk factors across 204 countries and territories from 1990 to 2021 (21, 22). Specifically, data on ILD&PS were extracted, including prevalence, incidence, mortality, DALY, and their corresponding age-standardized rates (ASRs). The data were accessed and downloaded via the Global Health Data Exchange platform (http://ghdx.healthdata.org/gbd-results-tool). Sociodemographic Index data were also obtained to assess the impact of socioeconomic factors on disease burden.

Global and regional burden analysis

To analyze the global distribution and regional differences in the burden of ILD&PS disease, we generated global maps and regional comparative analyses. The data were aggregated by geographical regions as defined by the GBD study, and maps were created using R (version 4.3.3) (https://www.r-project.org/) with the 'ggplot2' and 'sf' packages (https://cran.r-project.org/) to visualize the distribution of disease burden.

Population analysis

Population-level analyses were conducted to explore the distribution of ILD&PS disease across different demographic groups, including age, sex, and specific subpopulations. The data were stratified by twenty age groups (e.g., 65-69 years, 70-74 years.). Statistical analyses were performed using R, and results were visualized using the 'ggplot2' package.

Sociodemographic index analysis

The relationship between sociodemographic index (SDI) and the burden of ILD&PS disease was examined by calculating SDI-specific disease rates. SDI types (low, low-middle, middle, high-middle, and high) were used to compare the disease burden across different levels of socioeconomic development. The 'dplyr' and 'ggplot2' packages (https://cran.r-project.org/) in R were employed for data manipulation and visualization.

The estimated annual percentage change

To further quantify trends in the burden of ILD&PS for global and subgroups over the period 1990-2021, the estimated annual percentage change (EAPC) was calculated, reflecting the annual change over a specific time period. The age normalization rate (ASR) exhibits an upward trend when both the EAPC value and the lower bound of the 95% confidence interval (CI) are larger than 0. On the other hand, a declining trend is indicated when the EAPC value and the 95% CI's lower bound are both less than zero. If not, ASR is regarded as steady.

Bayesian age-period-cohort model for forecasting

To predict the future burden of ILD&PS, we applied a Bayesian Age-Period-Cohort (BAPC) model. The BAPC model, implemented using the 'INLA' and 'BAPC' packages (https://cran.r-project.org/) in R, allowed us to forecast the DALY and mortality of the disease through next decade. This model considers the impacts of cohort, age, and period, providing a comprehensive approach to understanding future trends in disease burden.

Statistical analysis

All statistical analyses and data visualizations were performed using R (version 4. 3. 3). Descriptive statistics were generated for all key variables, and results were expressed as means with 95% uncertainty intervals (UIs). For trend analyses, p-values < 0.05 were considered statistically significant.

Function of the financial source

The study's design, data collection, analysis, interpretation, and report writing were all done without the funders' input. Complete access to the study data was granted to the authors, who also ultimately decided whether to submit the report for publication.

Results

Prevalence

The number of people with ILD&PS worldwide in 2021 is 4,306,628 (95% UI: 3802,951-489,8714), compared to 1,887,445 (95% UI: 160,9369-2206,969) in 1990, the number of cases of ILD&PS in 2021 is about 2.28 times that of 1990, and the ASPR for ILD&PS has increased from 45.99 per 100,000 population in 1990 (95% UI: 39.42-53.78) to 50.01 per 100,000 population by 2021 (95% UI: 44.24-56.77) (Table S1). Among 21 GBD regions, high-income Asia Pacific had the highest ASPR, with 134.65 per 100,000 people in 1990 (95% UI: 115.3-156.65) and 151.6 (95% UI: 134.19-172.06) per 100,000 people in 2021. The ASPR in Western Sub-Saharan Africa is lowest in 2021 (Table S1, Figure 1). From 1990 to 2021, the global prevalence and ASPR of ILD&PS increased (EAPC = 0.36 [0.29-0.44]) (Table S1, Figure 2). Among 5 SDI groups, high SDI group had the highest number of cases and ASPR in 2021, while low SDI group having the lowest (Table S1, Figure 3). While high SDI group had a larger illness burden, the other four SDI groups also showed substantial rises in ASPR (Figure 4). In 2021, the number of ILD&PS cases rose with age in various age categories, reaching a peak in the 70–74-year age group before subsequently falling (Figure 5). The prevalence of ILD&PS increases with age, with the highest prevalence in the 85–89 years age group, and the global increase is most pronounced in the 85–89 years age group from 1990 to 2021 (Figure 5, Figure 6). In addition, age-standardized prevalence, morbidity, and disability-adjusted life years of ILD&PS in 2021 are higher for men than for women (Figure S1).

Incidence

Globally, an estimated 390,267 (95% UI: 346393-433,403) people developed new ILD&PS in 2021, and the age-standardized rate of ILD&PS incidence data is 4.54 per 100,000 people (95% UI: 4.05-5.04). Andean Latin America had the highest ASIR with 20.47 per 100,000 (95% UI: 19.15-21.69), and Eastern Europe had the lowest ASIR with 1.04 per 100,000 (95% UI: 0.89-1.21) in 2021. Comparatively the global incidence of ILD&PS in 1990 was 157,441 (95% UI: 136,251-179,472), and the ASIR of ILD&PS was 3.77 per 100,000 people (95% UI: 3.27-4.28) (Table S2). The incidence of ILD&PS worldwide exhibited an increasing trend between 1990 and 2021 (EAPC = 0.72 [0.63-0.82]), with the largest increasing trend in Australasia (EAPC = 2.15 [1.94-2.36]). The downward trend is most obvious in Eastern Europe (EAPC = -2.56

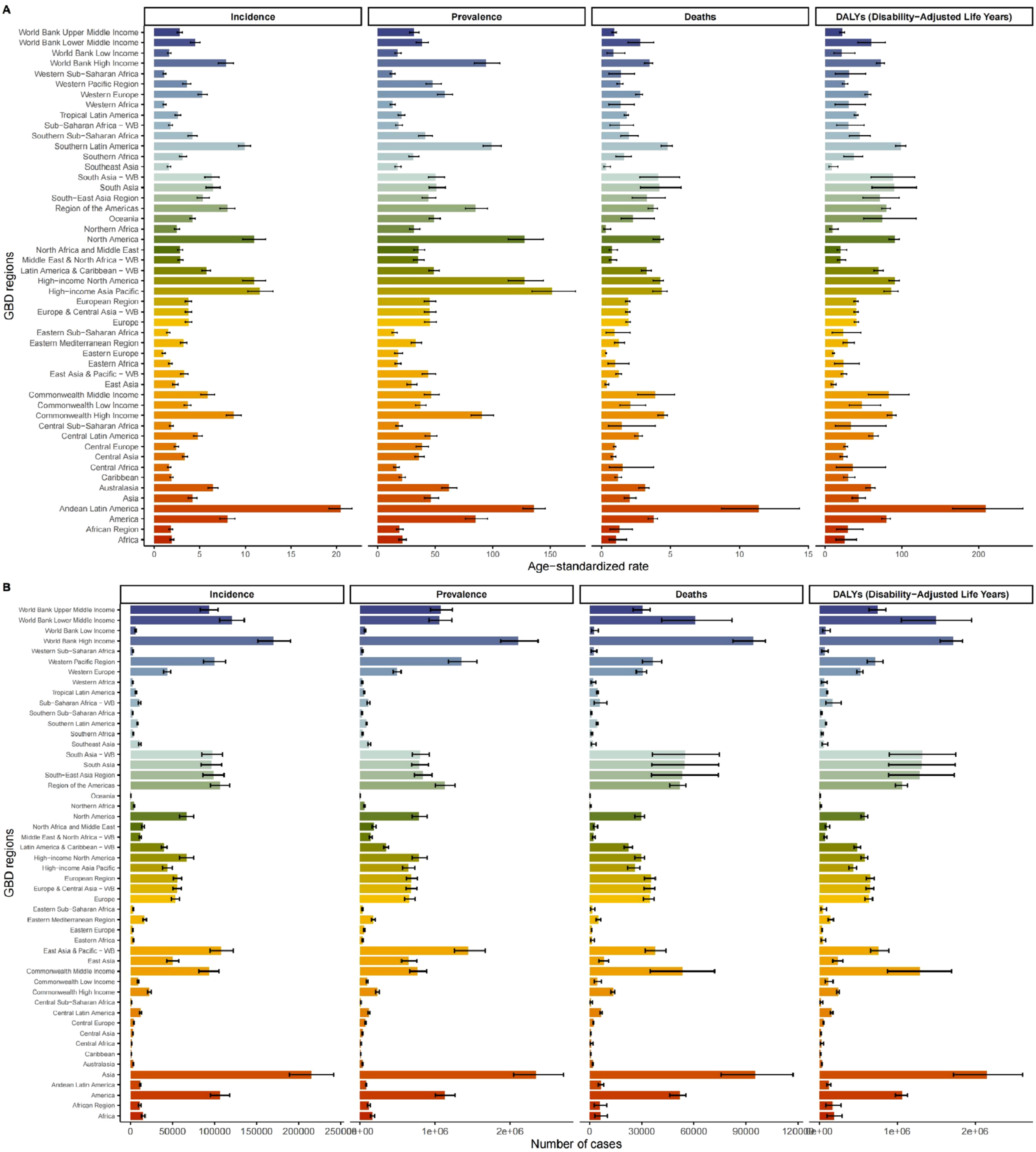

Figure 1. The disease burden of interstitial lung disease and pulmonary sarcoidosis in global regions in 2021. Their number of the Incidence, prevalence, death and disability-adjusted life years (B), and their age-standardized rates (A).

[-2.68--2.45]) (Table S2, Figure 2). The ASIR in all five SDI groups showed a growing tendency, with the high SDI group (EAPC = 0.92 [0.8-1.04]) exhibiting the most pronounced increase, followed by the intermediate SDI group (EAPC = 0.91 (0.81-1.02) (Table S2, Figure 4). In 2021, the relationship between the number of cases and incidence in the five SDI groups is as figures (Figure 3). The incidents and ASIR of ILD&PS rose with age in 2021 throughout a range of age groups (Figure 5). And the incidence

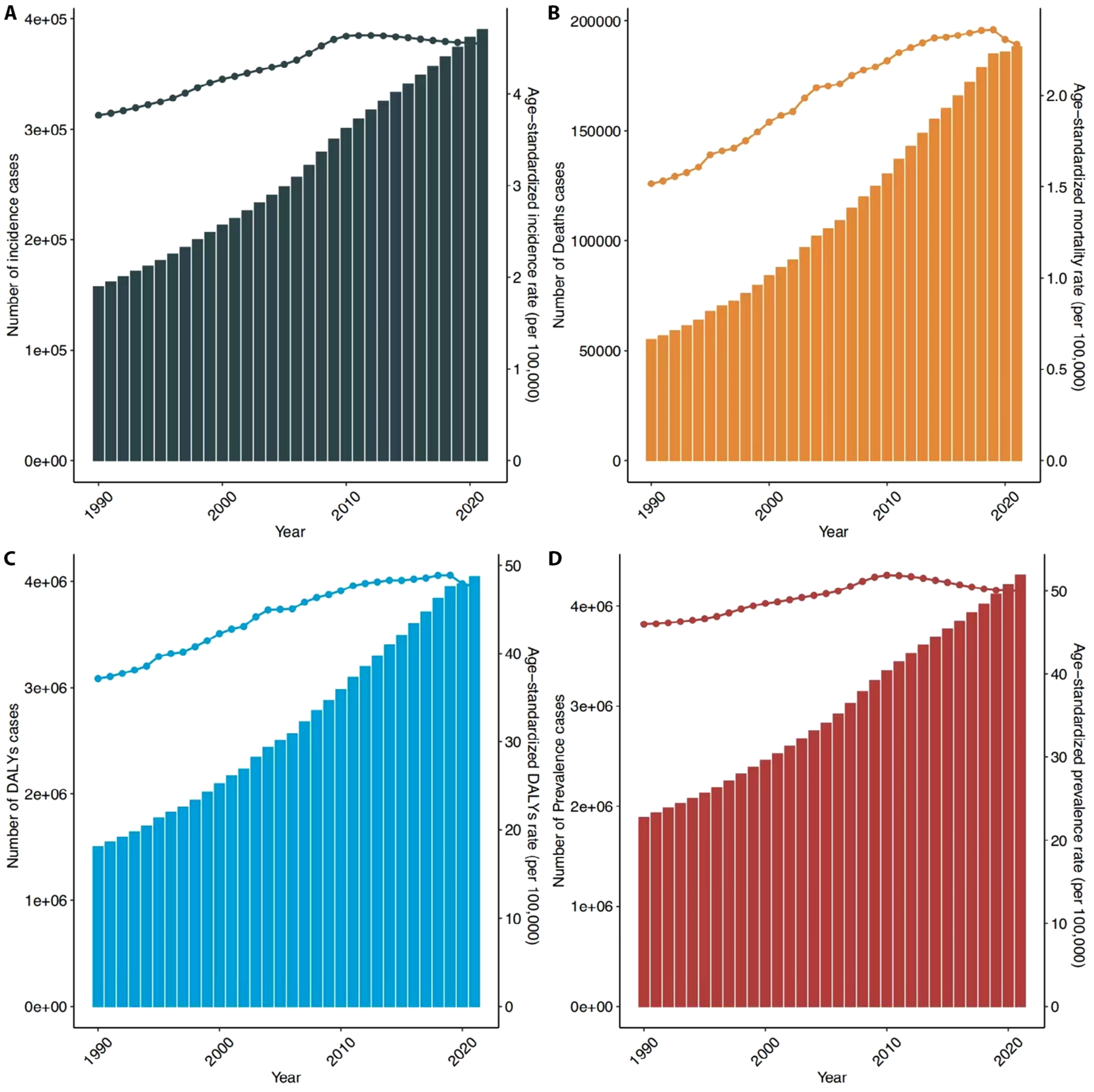

Figure 2. Global prevalent cases, age-standardized incidence rate (A), age-standardized mortality rate (B), age-standardized DALYs rate (C), age-standardized prevalence rate (D) of interstitial lung disease and pulmonary sarcoidosis from 1990 to 2021. Bar charts are stand for cases and line charts are stand for corresponding age-standardized rates.

of ILD&PS in the 60+ age group exhibited a significant upward trend from 1990 to 2021 (Figure 6).

Disability-adjusted life years

In 2021, ILD&PS were responsible for 4042150 (95% UI: 3489775-4516883) DALYs, up from 1501028 in 1990 (95% UI: 1221197-1850557), with an increase of about 169.3%. From 1990 to 2021, the global trend in age standardized DALYs rate (ASDR) for ILD&PS is increasing (EAPC = 0.95 (0.86-1.05)). The trend of ASDR increased the most in Australasia (EAPC = 3.1 (2.56-3.64), followed by Western Europe (EAPC = 3 (2.66-3.33)). The downward trend was most significant in Eastern Europe (EAPC = -4.56 (-5.23 -- 3.87) (Table S3).

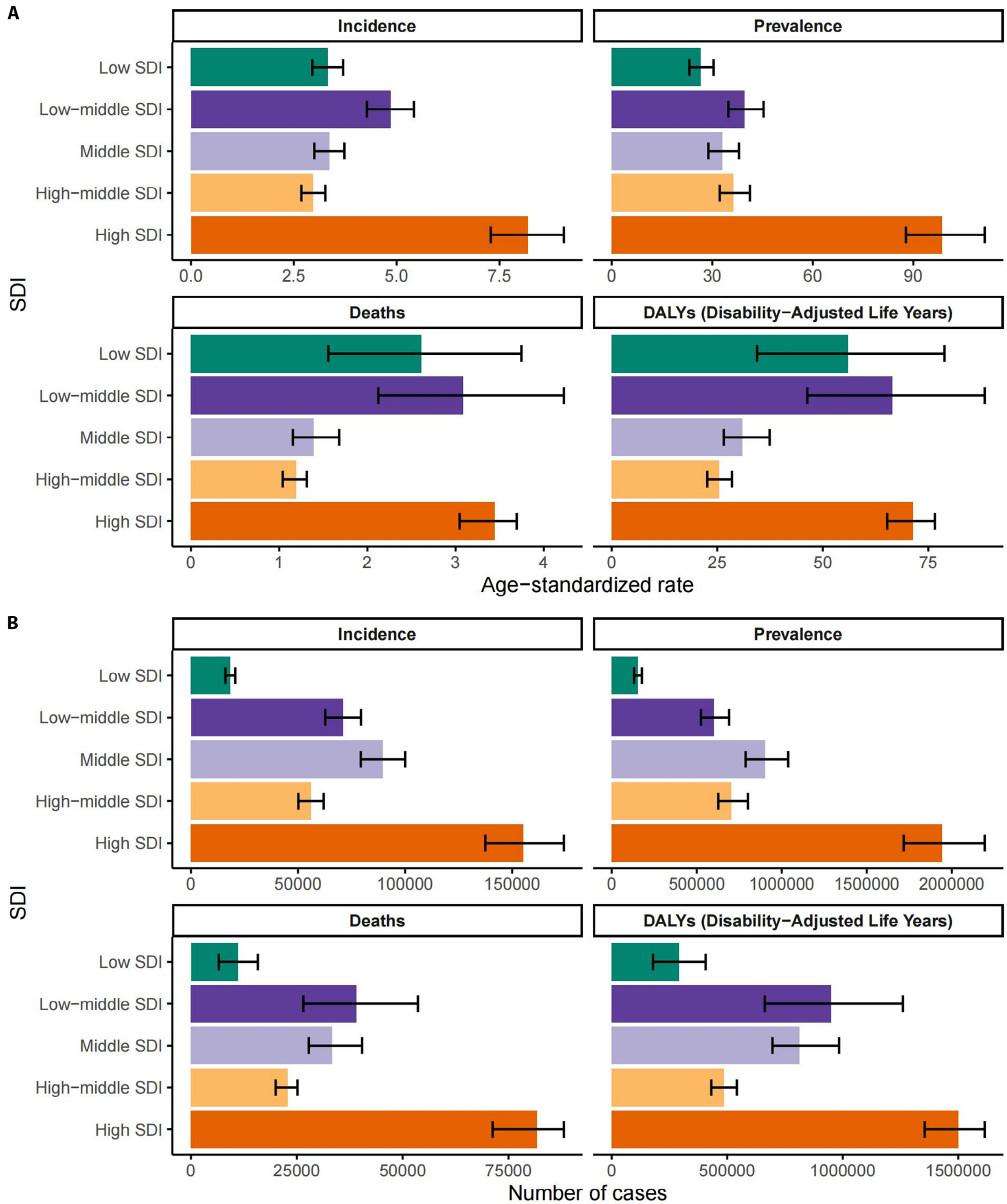

Figure 3. The disease burden of interstitial lung disease and pulmonary sarcoidosis in five sociodemographic index groups in 2021.

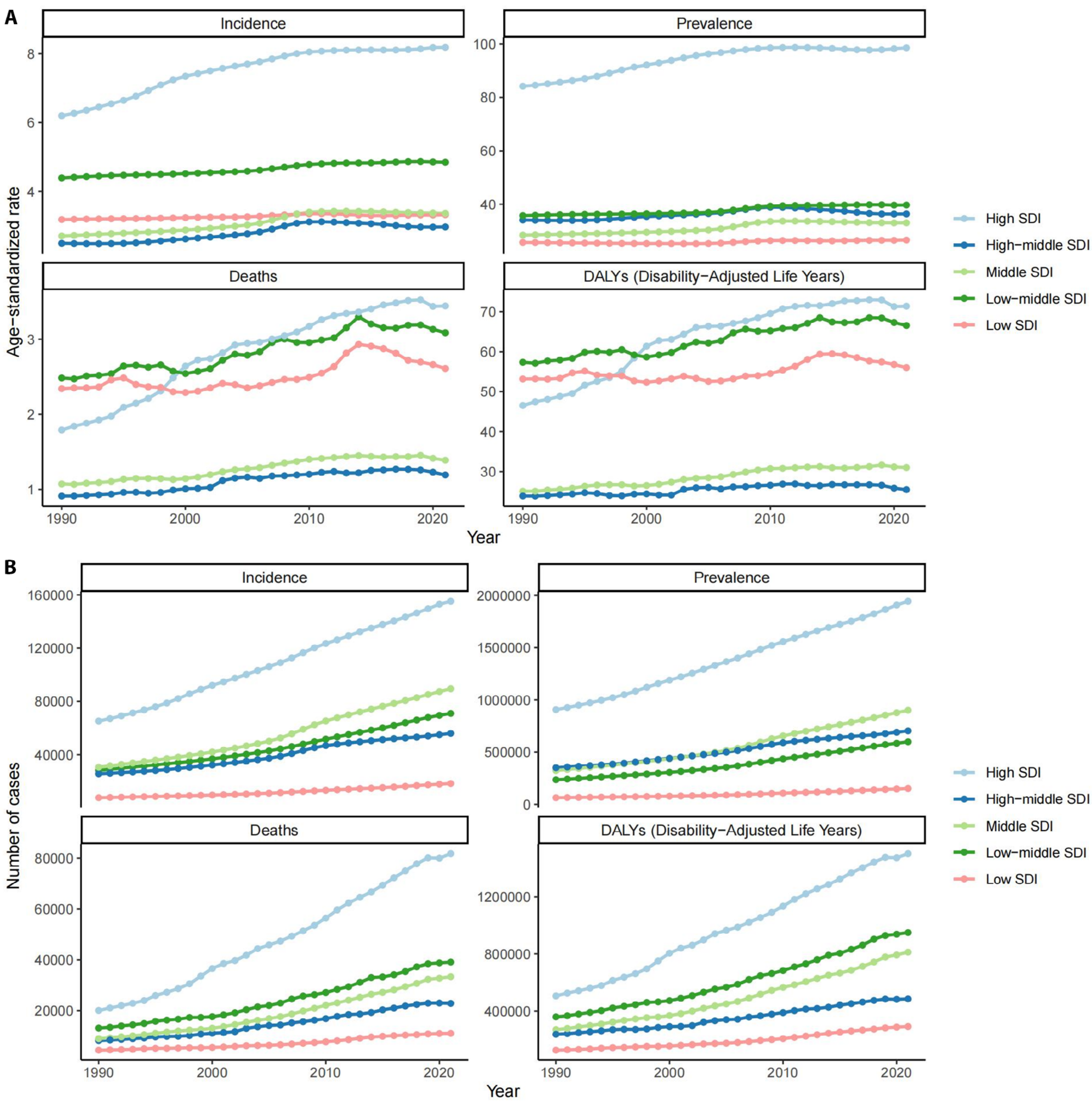

Figure 4. From 1990 to 2021, the variation tendency of disease burden of interstitial lung disease and pulmonary sarcoidosis in five socio-demographic index (SDI) groups.

In 2021, South Asia, followed by high-income North America, had the highest number of DALYs, while the Caribbean having the lowest number of DALYs. The ASDR among the five SDI groups increased between 1990 and 2021, with high SDI group (EAPC = 1.54 (1.34-1.74) and middle SDI group (EAPC = 0.83 (0.76-0.91)) having the largest increase (Table S3, Figure 4). In 2021, the 70-74 year age group had the highest DALYs. And the ASDR of ILD&PS also increased with age groups, peaking the highest in the 90-94 years age group (Figure 5).

Mortality

The number of ILD&PS deaths in 2021 is 188,222 (95% UI: 161,406-212,252), and the

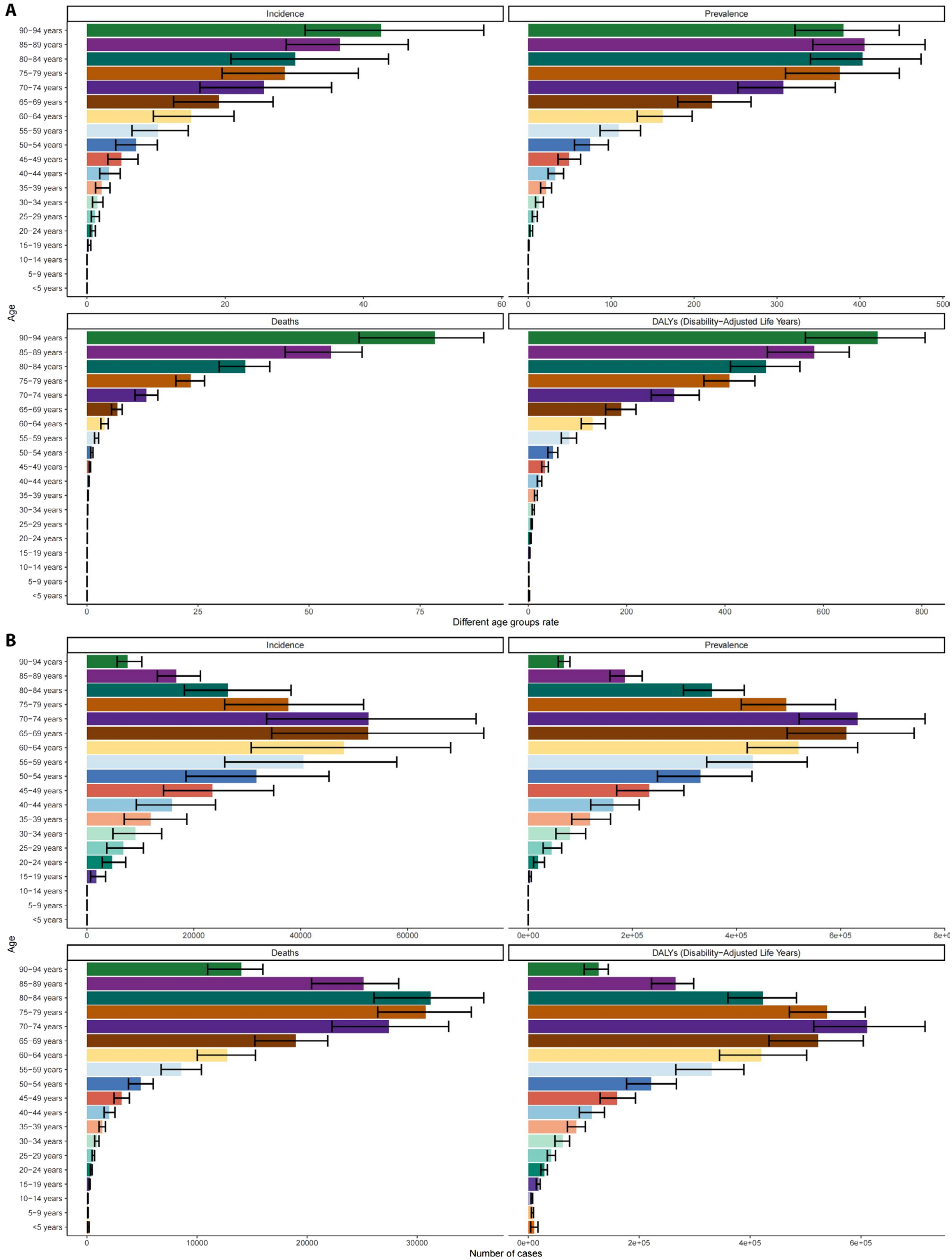

Figure 5. The disease burden of interstitial lung disease and pulmonary sarcoidosis in different age groups in 2021.

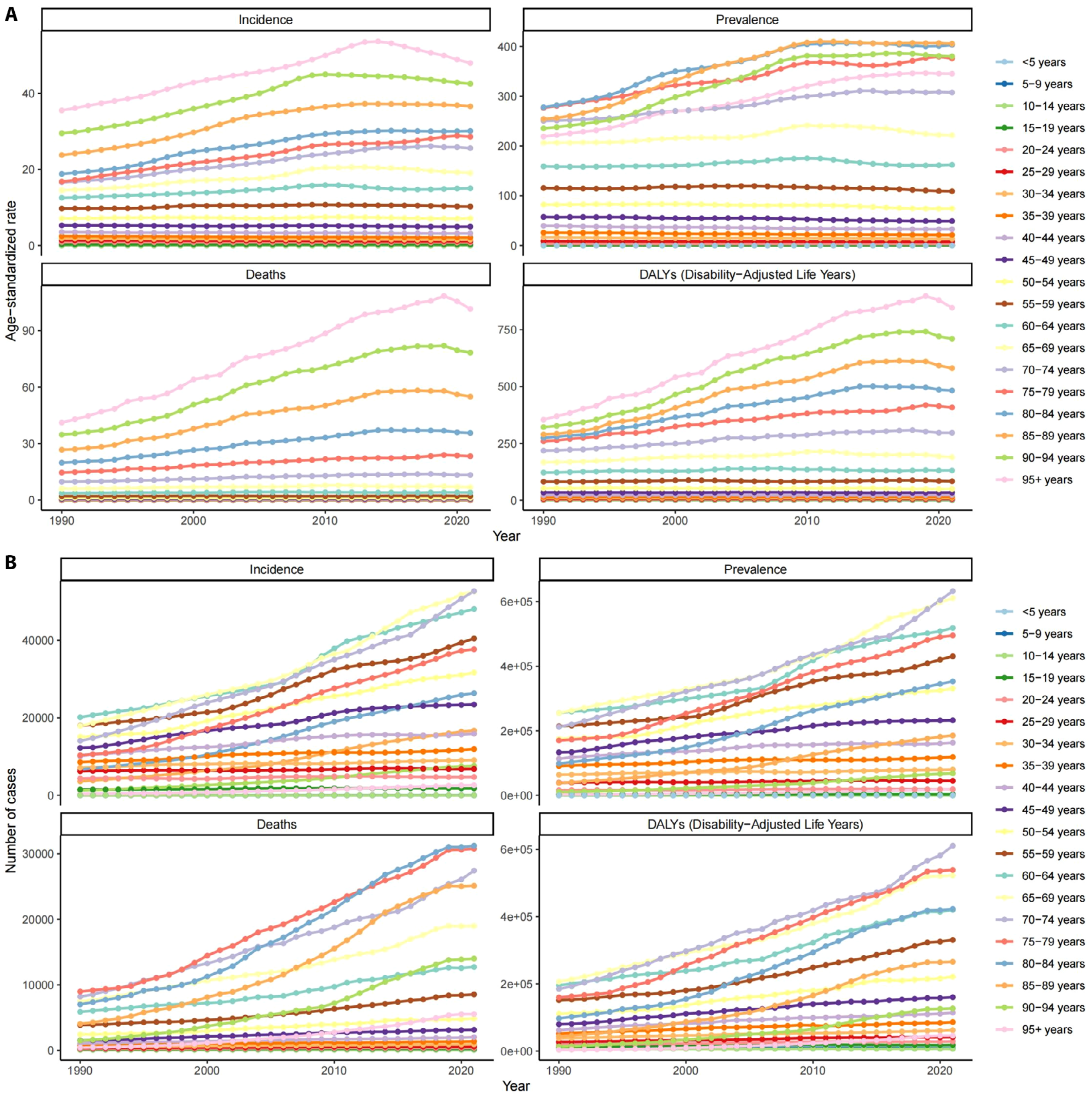

Figure 6. From 1990 to 2021, the variation tendency of disease burden of interstitial lung disease and pulmonary sarcoidosis in different age groups.

age-standardized mortality rate (ASMR) is 2.28 (95% UI: 1.96-2.56). Among them, Andean Latin America had the highest mortality rate in ILD&PS, and Asia had the highest number of deaths (Table S4, Figure 1). Compared to the 1990 ILD&PS death toll of 54,967 (95% UI: 447,61-68,391) and ASMR 1.52 (95% UI: 1.25-1.87), the global trend of ILD&PS mortality from 1990 to 2021 shows an upward trend (EAPC = 1.55 [1.42-1.69]). In addition, the number of deaths and ASMR in the five SDI groups showed an increasing trend from 1990 to 2021, with the most significant increasing trend in High SDI group (EAPC = 1.24 (1.09-1.39)). In 1990, the highest mortality rates were found in low-middle SDI group, and by 2021, the highest mortality rates were found in high SDI group (Figure 4). In the age group analysis, it was found that the number of deaths in the age group over 50 years of age increased from 1990

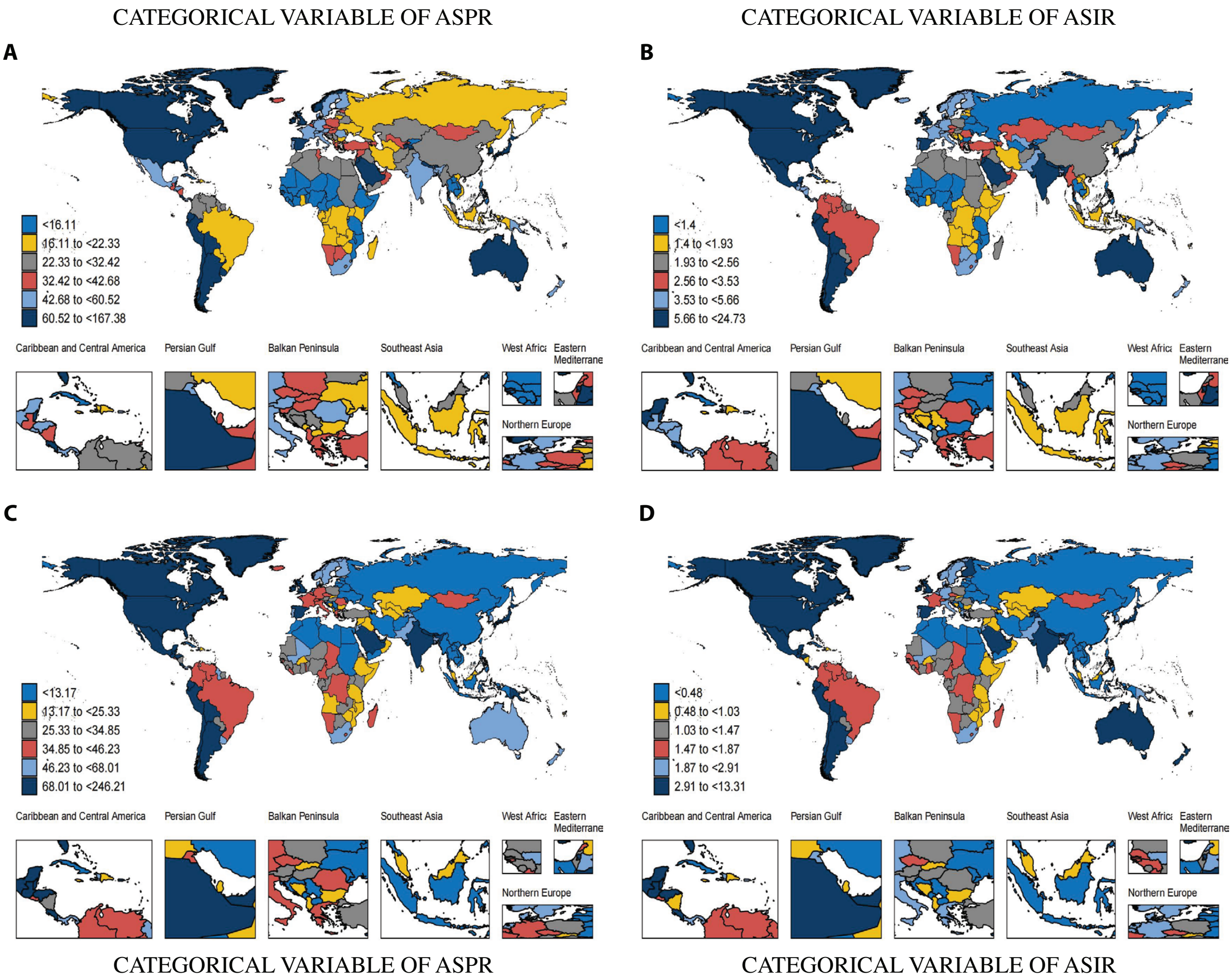

Figure 7. Categorical variable of age-standardized rates for prevalence (A), incidence (B), disability-adjusted life years (C), mortality (D) in 204 countries and territories in 2021.

to 2021 (Figure 6). The number of ILD&PS deaths in 2021 was the highest in the 80–84-year age group and then declined, and the ASMR of ILD&PS increased with increasing age, reaching the highest in the 90–94-year age group (Figure 5).

Global distribution of ILD&PS disease burden by region and country, 2021

The world map illustrates that the disease burden of ILD&PS in 2021 varies significantly between countries (Figure 7).

Relationship between EAPC and ASRs/HDI

As shown in the figure (Figure 8). Our study found a significant positive association between the EAPC of ILD&PS disease burden and the 2021 age-standardized prevalence rate (ASPR 2021) and the 2021 Human Development Index (HDI 2021). The ILD&PS' age-standardized rates (ASRs) reflect the disease pool, while the HDI can serve as a proxy for the level and accessibility of healthcare in each country. The higher the HDI, the higher the ASRs of ILD&PS, and the greater the EAPC. The circles represent the countries for which HDI data are available, and the size of the circles is proportional to the number of ILD&PS cases.

SDI and ILD&PS ASRs trends by region or country from 1990 to 2021.

From 1990 to 2021, the global ASRs are on the rise with the increase of SDI. In the 21 regions with

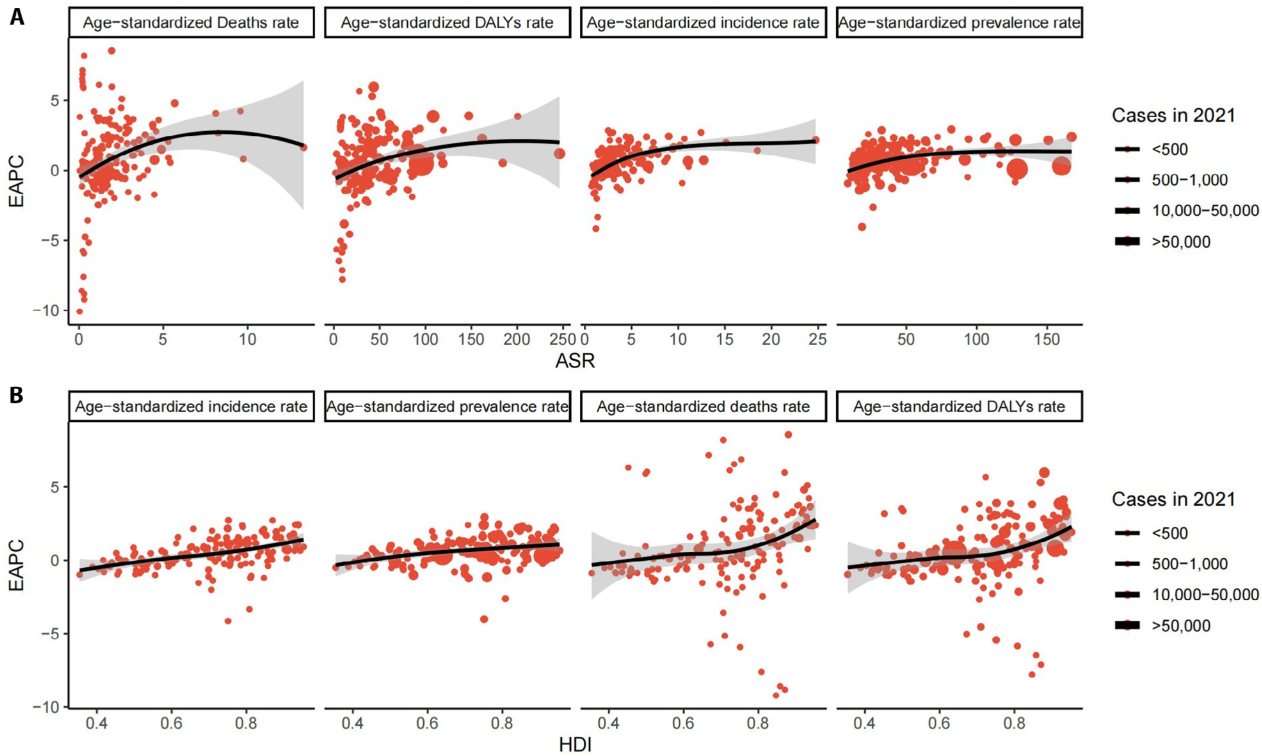

Figure 8. Correlation between estimated annual percentage change (EAPC) and age-standardized rates (ASRs) (A) human development index (HDI) (B) of interstitial lung disease and pulmonary sarcoidosis in 2021. The size of the circle is proportional to the number of interstitial lung disease and pulmonary sarcoidosis cases.

different SDI, the ASRs in most regions increased with the increase in SDI between 1990 and 2021 (Figure 9). In this context, Andean Latin America, South Asia, and Southern Latin America exceeded expectations in all years. Figure 9 illustrates the link between ASRs and SDI for different countries and regions in 2021. At the national level, ASRs also indicated a general rising tendency with the increase of SDI, which is similar to the regional pattern. After the SDI exceeds 0.75, this upward trend suddenly becomes more pronounced.

Health inequalities

The SDI was combined with the inequality slope index and the concentration index to perform a health inequality analysis to assess differences in disease burden in ILD&PS. As shown in the figure, the burden of disease is higher in areas with a high relative ranking of SDI. The inequality slope index shows a larger gap in disease burden between the highest and lowest SDI countries in 2021 compared to 1990. Incidence concentration index from 0.27(95% CI 0.21-0.34) in 1990 to 0.32(95% CI 0.25-0.39) in 2021; prevalence concentration index from 0.39(95% CI 0.32-0.46) in 1990 to 0.41(95% CI 0.33-0.48) in 2021; mortality concentration index from 0.17(95% CI 0.1-0.25) in 1990 to 0.32(95% CI 0.22-0.42) in 2021. The concentration index of DALYs ranges from 0.15(95% CI 0.08-0.21) in 1990 to 0.24(95% CI 0.15-0.32) in 2021, all of which indicate that inequality persists and increases (Figure 10).

Decomposition analysis

Disaggregated analysis was used to determine the impact of population growth, aging, and epidemiological changes on the burden of disease. The findings show that global population growth and aging contribute the most to the increase in ILD&PS disease burden through 2021, followed by epidemiological changes. However, the most important factors leading to the increase of mortality and DALY burden in high SDI group are aging and epidemiological change, followed by population growth.

The contribution of population growth to the burden of disease is highest in South Asia. In addition, among the five SDI groups, the contribution of aging to the prevalence burden is most obvious in high SDI group, followed by middle SDI group, and the increase in prevalence burden in low SDI group is mainly due to population growth (Figure 11).

ILD&PS global burden of disease projections

Based on comprehensive GBD data from 1990 to 2021, we use the BAPC model to estimate that the number of deaths and DALYs of ILD&PS in both men and women globally will continue to increase over the next decade, while ASDR will plateau (Figure 12).

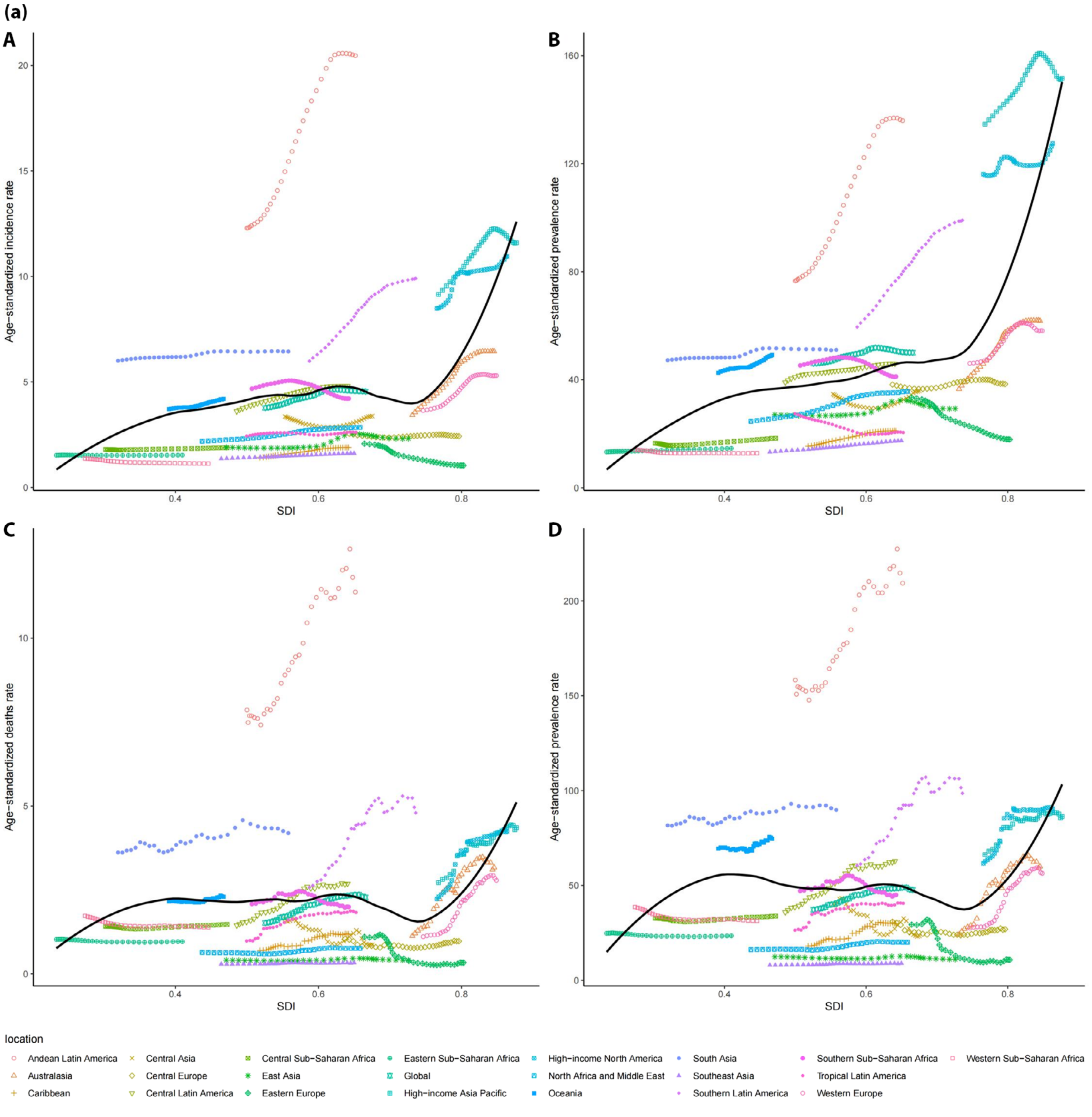

Figure 9. (a) Trend in age-standardized rates of interstitial lung disease and pulmonary sarcoidosis among/across 21 regions based on sociodemographic index (SDI) in 2021. For each region, points from left to right depict estimates from each year from 1990 to 2021, with expected values shown as the black line. (b) Age-standardized rates of interstitial lung disease and pulmonary sarcoidosis across 204 countries and territories by SDI in both sexes, 2021. Expected values are shown as the black line. Each point shows observed age-standardized rates for a certain country in 2021.

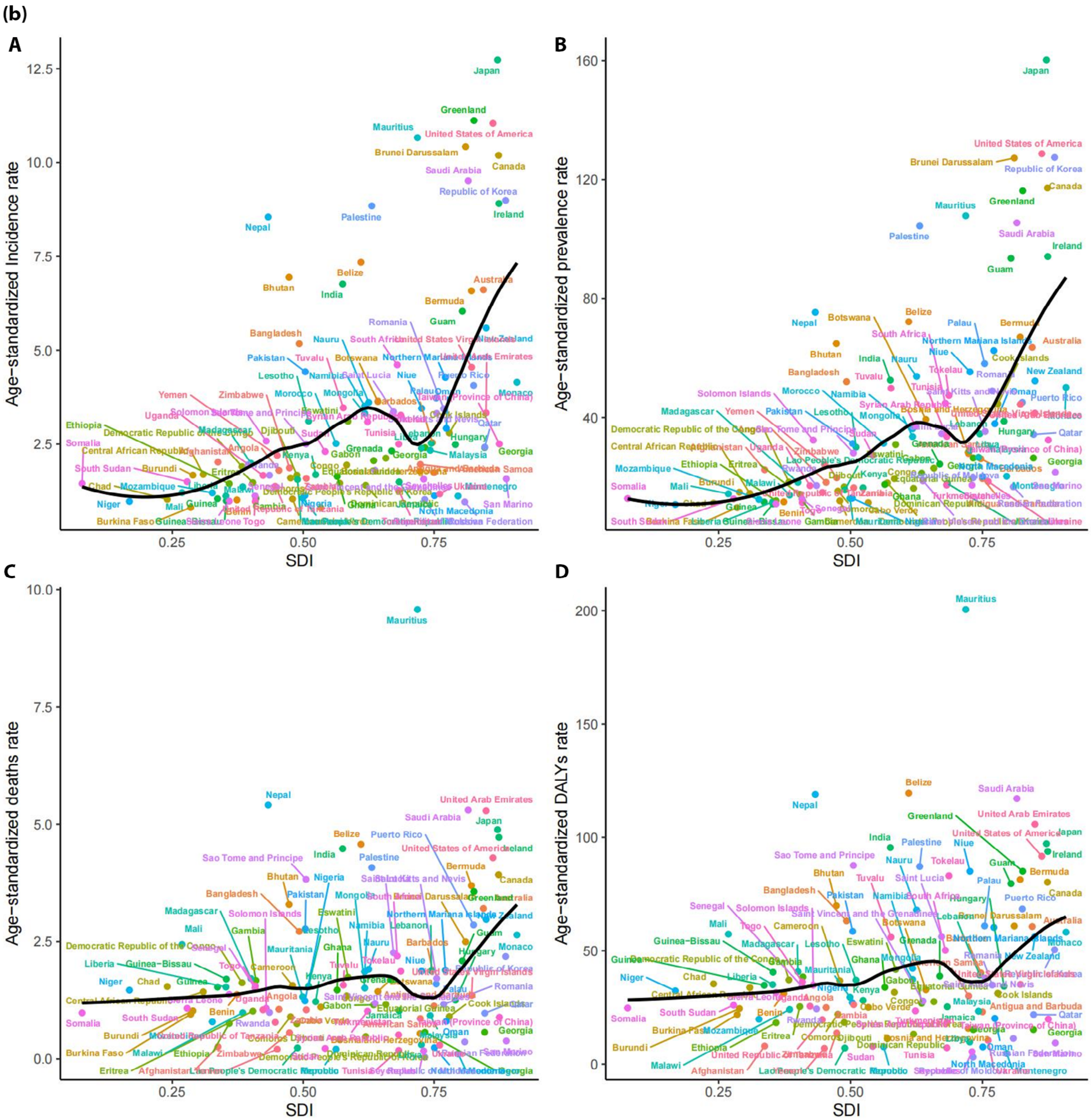

Figure 9. (*Continued*)

Discussion

Despite global initiatives aimed at alleviating the burden of chronic respiratory diseases, the burden associated with ILD&PS remains significantly high and warrants attention (23). This study systematically reviews the global disease burden of ILD&PS from 1990 to 2021, examining temporal trends, regional and demographic distribution characteristics, as well as projections extending to 2034. Our findings indicate that, consistent with the work of Zeng, Qi (24) et al., the global prevalence of cases,

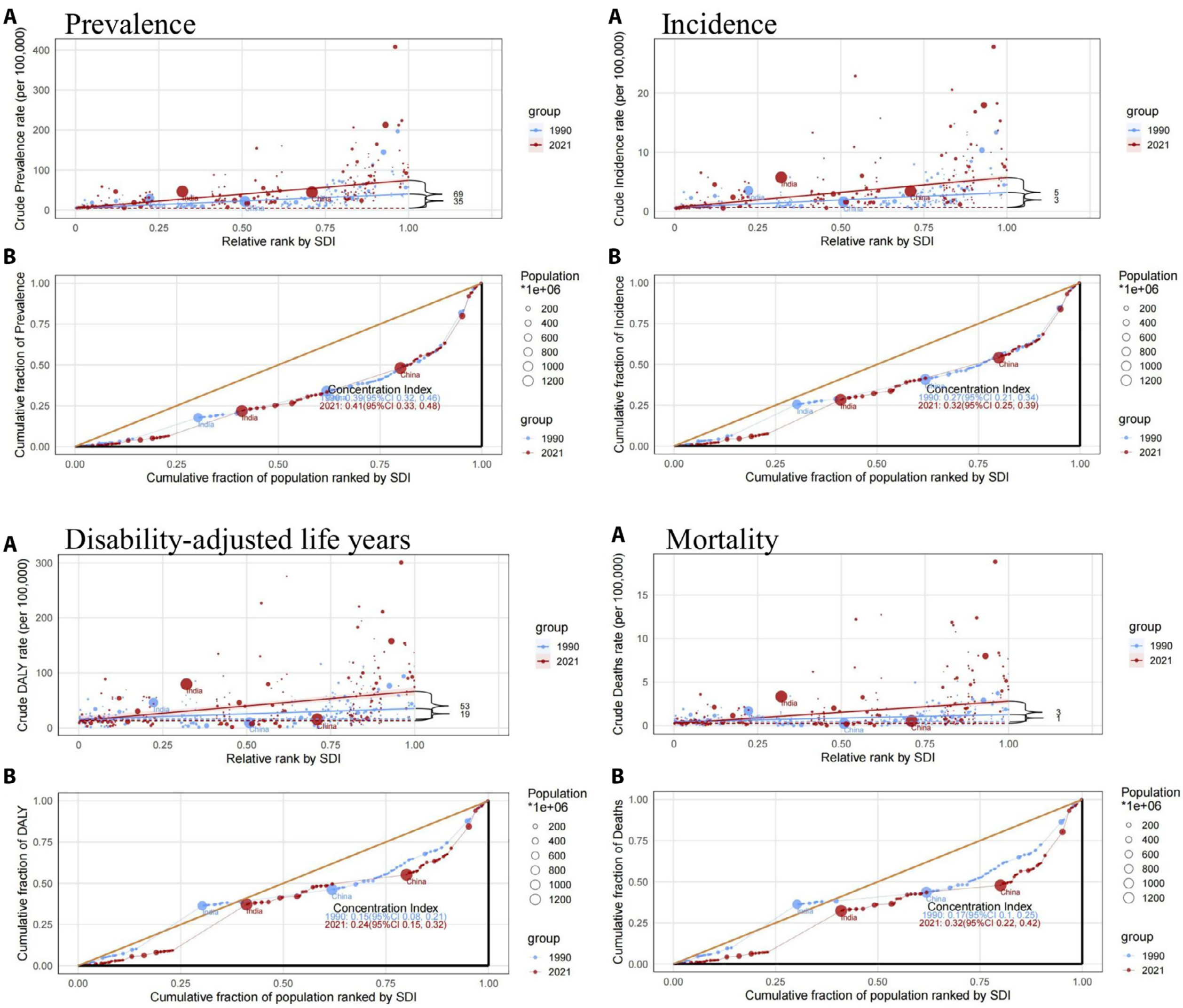

Figure 10. Panels A illustrate the inequality slope index, depicting the relationship between sociodemographic index (SDI) and age-standardized rates for each condition, with points representing individual countries sized by population. Panels B present the concentration index, which quantifies relative inequalities by integrating the area under the Lorenz curve, aligning age-standardized rates distribution with population distribution by SDI. Blue represents data from 1990, and red represents data from 2021.

morbidity, deaths, and DALYs, along with ASPR, ASIR, ASMR and ASDR, increased from 1990 to 2021. There is an urgent necessitating in many countries for appropriate and effective management of ILD&PS. In 2021, Andean Latin America exhibited the highest ASIR, ASMR, and ASDR for ILD&PS, and the highest ASPR was observed in the high-income Asia Pacific region. The incidence of these diseases was lowest in Eastern Europe. In terms of prevalence, Western Sub-Saharan Africa reported the lowest figures, while Southeast Asia recorded the lowest mortality and DALYs. The disparities in disease burden across different regions may be closely associated with factors such as the classification of ILD&PS, genetic predisposition, environmental influences, lifestyle choices, and the development level of the regions. Given the diverse nature of ILD&PS, which often present diagnostic challenges, various types necessitate distinct treatment approaches, leading to markedly different prognoses (1). Further research is essential to establish a comprehensive and uniform method for the therapy of individuals with various forms of interstitial lung disease (ILD), including those categorized as non-classifiable (25). Sandra et al., (26) identified a significant association between polymorphisms in the tumor necrosis

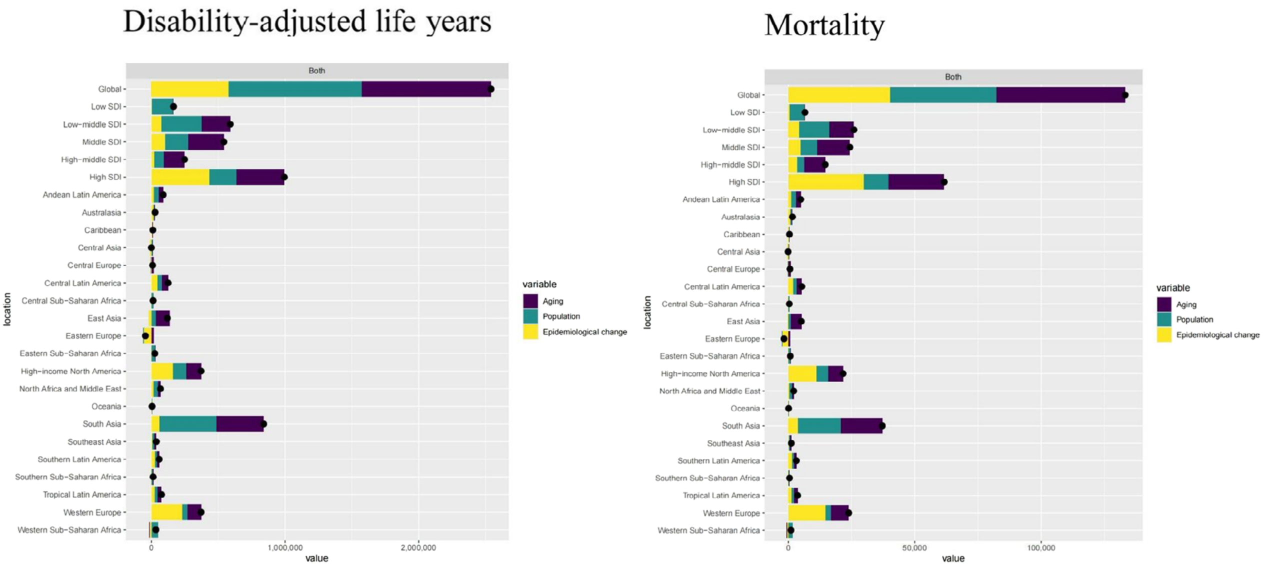

Figure 11. Changes in disability-adjusted life years and mortality (both male and female) of interstitial lung disease and pulmonary sarcoidosis, according to population-level determinants of aging, population growth, and epidemiological change, from 1990 to 2021 at the global level, SDI quintile and the regions.

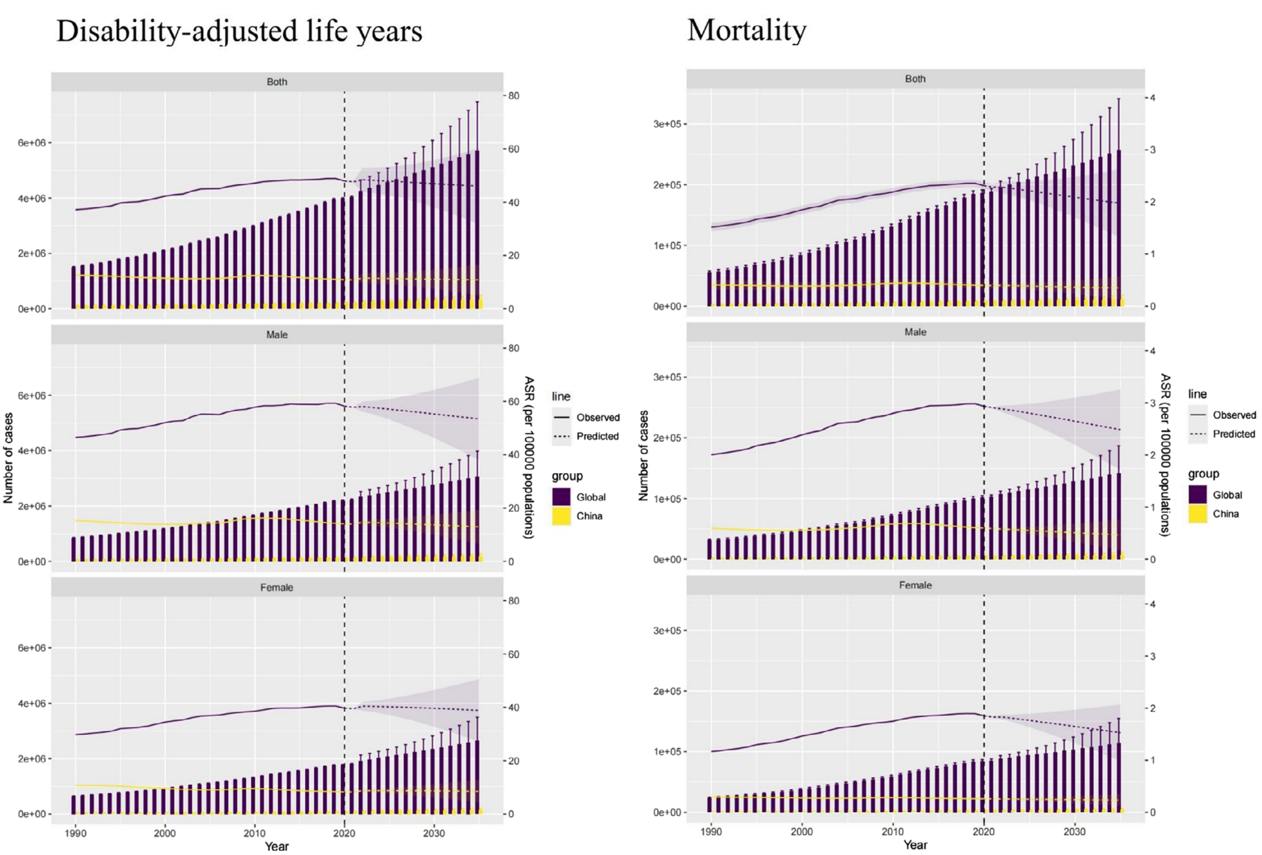

Figure 12. Observed and predicted trends of cases and age-standardized rates of interstitial lung disease and pulmonary sarcoidosis by sex globally from 1990 to 2034 using the BAPC model. The shadow in the figure represents uncertainty intervals, suggesting that mortality could fluctuate dramatically as the corresponding rates rise or fall by 1% per year, with each shade corresponding to a change of 1%. Bar charts are stand for cases and line charts are stand for corresponding age-standardized rates.

factor promoter region and the onset of PS, which was correlated with a favorable prognosis. Furthermore, significant markers were identified across various regions, with notable differences in clinical manifestations (i.e., phenotypes) observed among these regions. This finding suggests a relationship between genetic factors specific to certain areas and the diverse traits associated with the disease. The HLA-associated phenotype, gene associations, familial aggregation and racial prevalence support the concept of genetic susceptibility to ILD&PS, which is further influenced by environmental factors. Environmental factors have been identified in more than one third of ILD patients, notably air pollution (27). Numerous studies have demonstrated that ILD may be exacerbated by air pollution, including that caused by transportation, construction materials, and agriculture (28, 29). High SDI group (30) is characterized by the accessibility and availability of abundant medical resources. This environment enhances the capacity for diagnosing ILD&PS, potentially contributing to a higher prevalence of these conditions. From the viewpoint of global social evolution, economic development has facilitated advancements in medical technology, particularly in imaging and functional testing, which have contributed to more accurate and widespread diagnoses of ILD&PS. Consequently, this has resulted in an observed increase in the prevalence of ILD&PS. Notably, in 2021, regions with high SDI scores exhibited the highest mortality rates, a finding that contradicts the availability of adequate medical resources and healthcare systems. This discrepancy reflects poor prognoses, limited treatment options, and inadequate management strategies for ILD&PS. The significant variations in disease burden across different countries and regions, as well as the trends in disease burden from 1990 to 2021, can be attributed to differing local health policies and the impact of changes in these policies (31). In the analysis of gender subgroups, it was noted that the global prevalence, morbidity, mortality, and disability-adjusted life years associated with ILD&PS are significantly higher in males than in females. This disparity may be attributed to the effects of sex hormones (32, 33). The epidemiological relationship between sex differences and the disease burden of ILD&PS has stimulated research into the influence of sex and sex hormones on the pathogenesis and treatment of pulmonary fibrosis. The regulation of sex hormones is critical in modulating pro-inflammatory and pro-fibrotic factors; specifically, estrogen is known to exacerbate inflammation and tissue remodeling, while androgens may exert an opposing effect (34). In addition, relevant studies have found that smoking is a major risk factor for chronic respiratory disease-related disability in men in all regions (23) and an established risk factor for interstitial lung disease (35), so smoking may make an important contribution to the disease burden of interstitial lung disease in men. This study found that the prevalence, incidence, mortality, and DALYs of ILD&PS increased progressively with age, especially in people over 70 years old. The association between age and ILD&PS disease burden may be related to the accumulation of senescent cells, DNA mutations, protein aggregates, and lipid metabolic waste (lipofuscin) with age (36). In addition, global demographic changes have also led to an increase in the burden of age-related ILD&PC diseases, and by the beginning of the 20th century, the population growth rate had shifted from linear to exponential, with the elderly population growing faster than the younger population (37). In addition, related studies have shown that comorbidities such as cardiovascular diseases and depression can affect the disease burden of IPF (38, 39). However, the elderly are often accompanied by more chronic non-communicable diseases, such as cardiovascular and cerebrovascular diseases, chronic obstructive pulmonary disease, diabetes, cancer, and depression. Other chronic diseases are common in the elderly group, and chronic respiratory diseases are most associated with aging (40, 41). In addition, relatively poor medical compliance in the elderly may also affect the prognosis of ILD (42). Therefore, for countries facing an aging population, the social burden of chronic diseases such as ILD&PS should be seriously considered.

There are some limitations to this study. The data of this study comes from GBD 2021, the inclusion of original data may be biased, and the data information of some countries is incomplete, and the quality is relatively low. The GBD database was established in 1990, and its data sources mainly include international organizations and institutions, national health departments, academic research, medical institutions, and other survey data. However, from 1990 to the present, the nomenclature of ILD has undergone multiple updates (43), which may result heterogeneity in the data investigated and registered by the above-mentioned organizations and institutions. Nevertheless, such heterogeneity is inevitable in studies using the GBD database, which is also an important limitation of this study. Because of the nature of the database, our study could not distinguish specific types of ILD as it does not provide detailed information on the types of ILD beyond broader categories. There are disparities in the definitions and diagnostic criteria for ILD&PS worldwide, and the economic development of various countries or regions is uneven. In low-income countries, especially in areas where modern imaging technologies are not widely available, the actual disease burden of ILD&PS may be severely underestimated due to the lack of diagnostic tools and complete disease registries. The database still lacks information on risk factors for ILD&PS. ILD&PS remains an international health challenge, and further research on this disease requires more comprehensive data (Table S5).

Conclusions

Our research indicates that over the past 30 years, the global disease burden of interstitial lung disease and pulmonary sarcoidosis has increased, with a particularly notable upward trend in the high sociodemographic index group. The disease burden is more severe in the 70-84 age group and in the high sociodemographic index group. Current preventive and treatment measures need to be further improved, and corresponding interventions should be carried out in areas and populations with high disease burdens to reduce the burden of interstitial lung disease and pulmonary sarcoidosis and improve patient outcomes.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Authors' Contributions: Xinlian Li conceived and designed the study, collected the data and performed the preliminary analysis. Both Xinlian Li and Zhihong Zhang were involved in drafting and critical revision of the manuscript. All authors accepted the final version and are responsible for the integrity of the entire work.

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Annex

Table S1. Prevalence

location_name	Num_1990	ASR_1990	Num_2021	ASR_2021	EAPC_CI
Andean Latin America	15935 (14531-17510)	76.6 (69.74-84.04)	79687 (73988-85343)	135.98 (126.12-145.58)	2.37 (2.21-2.52)
Australasia	8622 (7526-9870)	36.58 (31.86-42.01)	32955 (29675-36525)	61.8 (55.39-68.95)	1.77 (1.58-1.95)
Caribbean	4238 (3555-4977)	15.36 (13-18.01)	11198 (9897-12639)	21.09 (18.65-23.82)	1.16 (1.07-1.26)
Central Asia	17284 (15188-19815)	34.69 (30.71-39.36)	31350 (27948-35422)	35.86 (32.32-40.28)	0.14 (-0.1-0.38)
Central Europe	56134 (48055-65349)	38.21 (32.69-44.77)	70262 (62022-79643)	38.39 (33.44-44.05)	0.24 (0.15-0.32)
Central Latin America	35146 (29813-40967)	39.05 (33.59-45.27)	116101 (103369-130258)	45.91 (41.07-51.56)	0.45 (0.41-0.49)
Central Sub-Saharan Africa	4362 (3559-5232)	16.45 (13.78-19.46)	12478 (10451-14822)	18.3 (15.77-21.18)	0.42 (0.29-0.54)
East Asia	260268 (213539-316112)	27.06 (22.44-32.71)	647955 (552500-759163)	29.3 (25.22-34.2)	0.58 (0.4-0.75)
Eastern Europe	90879 (75717-107683)	33.43 (27.72-39.85)	52794 (43745-62989)	17.88 (14.66-21.42)	-2.28 (-2.36--2.21)
Eastern Sub-Saharan Africa	11901 (9600-14376)	13.24 (10.93-15.74)	30904 (25480-36978)	14.57 (12.34-17.07)	0.31 (0.29-0.33)
Global	1887445 (1609369-2206969)	45.99 (39.42-53.78)	4306628 (3802951-4898714)	50.01 (44.24-56.77)	0.36 (0.29-0.44)
High-income Asia Pacific	274572 (234702-319642)	134.65 (115.3-156.65)	642118 (564110-731622)	151.6 (134.19-172.06)	0.43 (0.3-0.56)
High-income North America	393391 (338218-460044)	116.11 (100.03-135.71)	787779 (695020-893374)	127.5 (113.42-143.85)	0.19 (0.13-0.26)
High-middle SDI	351806 (300238-413792)	34.1 (29.26-39.96)	704696 (626654-800963)	36.39 (32.23-41.24)	0.38 (0.27-0.49)
High SDI	907884 (783539-1058221)	84.18 (72.93-97.79)	1944286 (1717676-2193797)	98.58 (87.8-111.3)	0.55 (0.46-0.63)
Low-middle SDI	236665 (198227-278344)	35.77 (30.26-41.93)	600253 (524700-690438)	39.7 (34.81-45.31)	0.43 (0.38-0.47)
Low SDI	64790 (54155-76331)	25.68 (21.67-30.09)	152796 (131759-177190)	26.57 (23.17-30.4)	0.16 (0.12-0.21)
Middle SDI	324844 (271303-385905)	28.48 (24.08-33.82)	902158 (787326-1037655)	33.03 (28.83-37.97)	0.64 (0.56-0.73)
North Africa and Middle East	48261 (40001-57470)	24.62 (20.9-28.99)	185663 (160883-214498)	35.72 (31.4-40.69)	1.38 (1.29-1.47)
Oceania	1718 (1501-1963)	42.55 (37.75-48.11)	4880 (4391-5411)	49.16 (44.66-54.3)	0.39 (0.34-0.44)
South Asia	293638 (246481-345906)	47.25 (39.91-55.76)	791408 (688352-911272)	51.07 (44.55-58.79)	0.32 (0.27-0.38)
Southeast Asia	37166 (30050-45335)	13.22 (10.95-15.79)	120933 (103687-141729)	17.4 (15.03-20.22)	0.9 (0.88-0.91)
Southern Latin America	27842 (25031-30972)	59.53 (53.6-66.25)	85609 (78825-92601)	99.07 (91.46-107.24)	1.67 (1.57-1.78)
Southern Sub-Saharan Africa	13392 (11191-15782)	45.27 (38.3-53.16)	25863 (22187-30077)	41.18 (35.6-47.56)	-0.42 (-0.57--0.28)
Tropical Latin America	28813 (23850-34562)	27.45 (22.97-32.54)	52675 (45618-60595)	20.45 (17.76-23.47)	-1.12 (-1.28--0.96)
Western Europe	249467 (219645-284531)	46.08 (40.1-53.29)	491893 (441707-547311)	58.14 (52-65.11)	0.98 (0.79-1.16)
Western Sub-Saharan Africa	14419 (11654-17390)	14.07 (11.53-16.78)	32122 (26136-38830)	12.79 (10.7-15.15)	-0.29 (-0.35--0.23)

Table S2. Incidence

location_name	Num_1990	ASR_1990	Num_2021	ASR_2021	EAPC_CI
Andean Latin America	2440 (2228-2662)	12.29 (11.13-13.46)	11838 (11094-12531)	20.47 (19.15-21.69)	2.13 (1.98-2.28)
Australasia	798 (717-885)	3.43 (3.08-3.8)	3392 (3070-3718)	6.45 (5.88-7.02)	2.15 (1.94-2.36)
Caribbean	394 (344-448)	1.42 (1.25-1.6)	1003 (917-1094)	1.89 (1.73-2.07)	1.06 (0.98-1.14)
Central Asia	1672 (1504-1851)	3.36 (3.05-3.7)	2849 (2622-3094)	3.38 (3.12-3.65)	0.02 (-0.2-0.24)
Central Europe	3650 (3251-4100)	2.59 (2.3-2.9)	4034 (3661-4443)	2.42 (2.2-2.69)	0.02 (-0.07-0.1)
Central Latin America	3384 (2932-3876)	3.61 (3.14-4.1)	12172 (10943-13423)	4.81 (4.33-5.29)	0.95 (0.86-1.03)
Central Sub-Saharan Africa	456 (385-531)	1.8 (1.55-2.05)	1272 (1103-1455)	1.88 (1.66-2.1)	0.17 (0.13-0.2)
East Asia	19463 (16281-23141)	1.9 (1.6-2.23)	50031 (42927-57600)	2.31 (2.02-2.64)	1.12 (0.87-1.38)
Eastern Europe	5322 (4510-6209)	2.07 (1.78-2.4)	2682 (2299-3096)	1.04 (0.89-1.21)	-2.56 (-2.68--2.45)
Eastern Sub-Saharan Africa	1328 (1107-1559)	1.52 (1.31-1.74)	3244 (2780-3753)	1.53 (1.34-1.72)	-0.02 (-0.03--0.01)
Global	157441 (136251-179472)	3.77 (3.27-4.28)	390267 (346393-433403)	4.54 (4.05-5.04)	0.72 (0.63-0.82)
High-income Asia Pacific	18818 (16024-22064)	9.15 (7.82-10.66)	43787 (38399-49650)	11.59 (10.25-13.02)	0.79 (0.6-0.97)
High-income North America	28333 (24530-32456)	8.48 (7.37-9.71)	66609 (58423-75153)	10.95 (9.73-12.2)	0.75 (0.62-0.88)
High-middle SDI	25616 (22401-29235)	2.49 (2.2-2.83)	56001 (50155-61921)	2.97 (2.68-3.27)	0.85 (0.71-0.99)
High SDI	65229 (56925-73998)	6.2 (5.42-7.03)	155238 (137458-174122)	8.19 (7.29-9.07)	0.92 (0.8-1.04)
Low-middle SDI	28179 (23956-32565)	4.39 (3.76-5)	70990 (62702-79388)	4.85 (4.28-5.42)	0.38 (0.35-0.41)
Low SDI	7696 (6516-8958)	3.19 (2.74-3.64)	18292 (16089-20678)	3.33 (2.95-3.7)	0.16 (0.13-0.18)
Middle SDI	30615 (26132-35606)	2.71 (2.35-3.1)	89561 (79276-100011)	3.37 (3-3.73)	0.91 (0.81-1.02)
North Africa and Middle East	4326 (3720-5016)	2.19 (1.91-2.49)	15113 (13574-16831)	2.85 (2.58-3.15)	0.98 (0.93-1.03)
Oceania	155 (139-174)	3.72 (3.37-4.09)	419 (385-456)	4.2 (3.91-4.51)	0.39 (0.36-0.41)
South Asia	35968 (30515-41709)	6.01 (5.11-6.88)	96281 (84137-108635)	6.44 (5.65-7.26)	0.25 (0.22-0.28)
Southeast Asia	3839 (3218-4512)	1.36 (1.16-1.56)	11245 (9857-12738)	1.62 (1.42-1.81)	0.54 (0.53-0.56)
Southern Latin America	2750 (2529-2975)	5.99 (5.51-6.47)	8477 (7913-9062)	9.9 (9.26-10.57)	1.68 (1.53-1.82)
Southern Sub-Saharan Africa	1381 (1182-1597)	4.68 (4-5.36)	2577 (2241-2928)	4.21 (3.69-4.73)	-0.52 (-0.68--0.36)
Tropical Latin America	2580 (2184-3040)	2.44 (2.08-2.82)	6640 (5821-7441)	2.62 (2.29-2.94)	0.09 (0.02-0.16)
Western Europe	18948 (17007-20974)	3.64 (3.26-4.05)	43620 (39614-47749)	5.3 (4.82-5.81)	1.46 (1.29-1.62)
Western Sub-Saharan Africa	1436 (1204-1682)	1.37 (1.17-1.58)	2981 (2544-3486)	1.13 (0.99-1.28)	-0.65 (-0.71--0.58)

Table S3. DALYs

location_name	Num_1990	ASR_1990	Num_2021	ASR_2021	EAPC_CI
Andean Latin America	33945 (24798-48280)	158.26 (116.08-221.6)	121673 (96602-150014)	209.34 (165.81-257.66)	1.47 (1.29-1.64)
Australasia	5708 (5219-6190)	24.12 (22.11-26.1)	33036 (28956-35886)	59.97 (53.13-64.9)	3.1 (2.56-3.64)
Caribbean	5040 (3866-6914)	18.07 (14.09-23.62)	15715 (12779-19981)	30 (24.15-38.6)	1.92 (1.74-2.11)
Central Asia	20131 (18089-22763)	40.3 (35.89-45.69)	19790 (16339-24518)	23.37 (19.37-28.78)	-1.98 (-2.38--1.59)
Central Europe	44912 (41926-48293)	30.89 (28.89-33.12)	53275 (48499-58218)	26.9 (24.41-29.45)	-0.13 (-0.37-0.12)
Central Latin America	33623 (31642-35884)	35.89 (33.81-38.25)	158077 (143505-173855)	62.84 (57.11-69.1)	1.92 (1.73-2.11)
Central Sub-Saharan Africa	8097 (2925-15524)	32.71 (12.32-68.73)	20545 (8467-44099)	33.84 (13.17-79.52)	0.09 (-0.01-0.19)
East Asia	115445 (86138-171274)	12.41 (9.41-18.31)	234266 (171305-301444)	11.01 (8.06-14.14)	-0.12 (-0.27-0.03)
Eastern Europe	79279 (72136-86326)	29.38 (26.78-31.98)	34252 (31151-37997)	10.78 (9.78-12)	-4.56 (-5.23--3.87)
Eastern Sub-Saharan Africa	22391 (7515-36232)	24.77 (9.3-43.15)	47826 (19642-93157)	23.45 (9.36-46.54)	-0.29 (-0.34--0.24)
Global	1501028 (1221197-1850557)	37.15 (30.62-45.37)	4042150 (3489795-4516883)	47.62 (41.26-53.16)	0.95 (0.86-1.05)
High-income Asia Pacific	132227 (120398-145561)	66.26 (60.19-72.9)	432703 (380225-475663)	86.32 (76.64-94.93)	0.71 (0.52-0.89)
High-income North America	210856 (195640-227583)	61.65 (57.12-66.57)	582575 (532853-621775)	90.44 (83.28-96.54)	1.28 (1-1.56)
High-middle SDI	237514 (213560-266885)	23.85 (21.53-26.81)	485512 (430896-541669)	25.48 (22.63-28.47)	0.41 (0.32-0.5)
High SDI	506205 (470841-546440)	46.54 (43.29-50.27)	1500930 (1354746-1614665)	71.4 (65.27-76.57)	1.54 (1.34-1.74)
Low-middle SDI	359489 (213852-552929)	57.35 (34.67-86.88)	949438 (662365-1260419)	66.55 (46.34-88.36)	0.64 (0.57-0.71)
Low SDI	126671 (60835-188619)	53.16 (27.07-75.28)	291855 (178640-406440)	56.02 (34.43-78.83)	0.31 (0.21-0.42)
Middle SDI	269856 (212977-366219)	25.08 (19.94-33.57)	812056 (695675-984262)	31 (26.55-37.41)	0.83 (0.76-0.91)
North Africa and Middle East	30115 (21398-44298)	16.19 (11.54-23.72)	97814 (75696-134363)	20.11 (15.54-28.24)	0.95 (0.81-1.09)
Oceania	3219 (2153-4773)	69.39 (47.61-104.63)	8024 (5581-12403)	74.63 (50.21-118.43)	0.25 (0.17-0.33)
South Asia	473028 (268377-740983)	81.68 (47.16-126.64)	1312644 (890806-1740639)	89.8 (61.01-118.92)	0.4 (0.33-0.47)
Southeast Asia	22495 (12087-47186)	8.01 (4.35-16.31)	59048 (34100-109402)	8.93 (5.18-16.51)	0.37 (0.32-0.42)
Southern Latin America	27989 (26106-29940)	60.45 (56.32-64.62)	86239 (79828-92166)	98.58 (91.54-105.26)	1.82 (1.53-2.12)
Southern Sub-Saharan Africa	13659 (8256-18871)	47.13 (27.18-67.43)	26228 (18455-34420)	45.01 (31.73-59.13)	-0.32 (-0.55--0.08)
Tropical Latin America	27651 (26178-29363)	26.41 (24.86-28.11)	102784 (95498-108206)	40.58 (37.64-42.74)	1.33 (1.06-1.6)
Western Europe	154697 (143923-165739)	27.51 (25.55-29.62)	526090 (478286-559276)	56.37 (51.97-59.88)	3 (2.66-3.33)
Western Sub-Saharan Africa	36522 (13623-55767)	38.64 (15.12-59.97)	69547 (29751-115085)	31.33 (13.04-52.94)	-0.61 (-0.73--0.5)

Table S4. Death

location_name	Num_1990	ASR_1990	Num_2021	ASR_2021	EAPC_CI
Andean Latin America	1444 (1045-2078)	7.86 (5.68-11.33)	6366 (4875-8022)	11.37 (8.69-14.33)	1.87 (1.69-2.05)
Australasia	263 (242-285)	1.13 (1.03-1.22)	1904 (1603-2088)	3.17 (2.69-3.46)	3.54 (3-4.09)
Caribbean	175 (141-219)	0.7 (0.57-0.86)	639 (534-773)	1.19 (0.99-1.45)	1.99 (1.78-2.2)
Central Asia	715 (616-821)	1.64 (1.38-1.91)	630 (515-779)	0.87 (0.71-1.06)	-2.05 (-2.49--1.62)
Central Europe	1513 (1420-1622)	1.04 (0.98-1.12)	2179 (1973-2369)	0.97 (0.88-1.06)	0.12 (-0.21-0.45)
Central Latin America	1120 (1064-1191)	1.44 (1.36-1.54)	6475 (5837-7126)	2.69 (2.42-2.96)	2.19 (1.97-2.41)
Central Sub-Saharan Africa	259 (88-549)	1.42 (0.49-3.37)	666 (242-1622)	1.47 (0.51-3.92)	0.09 (-0.01-0.19)
East Asia	3042 (2259-4831)	0.41 (0.31-0.66)	8190 (5177-10927)	0.41 (0.25-0.54)	0.38 (0.2-0.57)
Eastern Europe	2860 (2660-3060)	1.1 (1.02-1.18)	1154 (1054-1263)	0.34 (0.31-0.37)	-5.47 (-6.36--4.58)
Eastern Sub-Saharan Africa	687 (228-1206)	1.03 (0.35-1.93)	1484 (530-3098)	0.96 (0.33-2.08)	-0.32 (-0.37--0.26)
Global	54967 (44761-68391)	1.52 (1.25-1.87)	188222 (161406-212252)	2.28 (1.96-2.56)	1.55 (1.42-1.69)
High-income Asia Pacific	5196 (4709-5608)	2.72 (2.45-2.94)	26166 (21826-28826)	4.36 (3.73-4.76)	1.35 (1.12-1.58)
High-income North America	8066 (7442-8421)	2.23 (2.07-2.33)	29737 (26085-31529)	4.25 (3.75-4.49)	2.16 (1.81-2.52)
High-middle SDI	8238 (7611-9227)	0.91 (0.84-1.02)	22851 (20008-25163)	1.19 (1.04-1.31)	1.24 (1.09-1.39)
High SDI	20064 (18622-20871)	1.79 (1.66-1.86)	81732 (71244-88092)	3.44 (3.05-3.69)	2.3 (2.06-2.55)
Low-middle SDI	13153 (7523-20491)	2.48 (1.46-3.81)	39118 (26540-53612)	3.09 (2.12-4.23)	0.94 (0.83-1.06)
Low SDI	4478 (2158-6438)	2.34 (1.19-3.27)	11084 (6589-15794)	2.61 (1.56-3.75)	0.63 (0.45-0.81)
Middle SDI	8993 (7004-12322)	1.07 (0.85-1.45)	33342 (27822-40427)	1.39 (1.16-1.68)	1.15 (1.03-1.27)
North Africa and Middle East	919 (633-1433)	0.64 (0.44-1)	3051 (2249-4527)	0.76 (0.56-1.15)	0.87 (0.68-1.06)
Oceania	71 (48-110)	2.16 (1.45-3.46)	185 (119-304)	2.3 (1.42-3.85)	0.23 (0.17-0.3)
South Asia	17522 (9598-27913)	3.62 (2-5.65)	54724 (35863-74243)	4.19 (2.81-5.76)	0.67 (0.54-0.79)
Southeast Asia	659 (317-1480)	0.29 (0.14-0.66)	1877 (959-3772)	0.33 (0.17-0.66)	0.42 (0.34-0.5)
Southern Latin America	1140 (1066-1223)	2.58 (2.41-2.77)	4357 (3906-4681)	4.8 (4.31-5.15)	2.29 (1.92-2.67)
Southern Sub-Saharan Africa	493 (262-752)	2.08 (1.07-3.25)	986 (677-1309)	2 (1.39-2.65)	-0.34 (-0.58--0.1)
Tropical Latin America	847 (799-890)	0.98 (0.9-1.04)	4527 (4080-4836)	1.83 (1.64-1.96)	2.13 (1.8-2.46)
Western Europe	6645 (6204-6944)	1.11 (1.04-1.16)	30538 (26845-32788)	2.79 (2.49-2.97)	3.74 (3.39-4.09)
Western Sub-Saharan Africa	1332 (486-2109)	1.73 (0.66-2.77)	2386 (919-4115)	1.39 (0.54-2.41)	-0.64 (-0.75--0.52)

Table S5. The full name and explanations of abbreviations

Abbreviations	Full name	Explanations
ASDR	Age standardized DALYs rate	The DALY rate of ILD&PS in a specific time and region after age standardization
ASIR	Age standardized incidence rate	The incidence rate of ILD&PS in a specifictime and region after age standardization
ASMR	Age standardized mortality rate	The mortality rate of ILD&PS in a specifictime and region after age standardization
ASPR	Age standardized prevalence rate	The prevalence rate of ILD&PS in a specifictime and region after age standardization
DALY	Disability adjusted life year	The sum of the years of healthy life lost from the start of a disease to death due to ILD&PS
EAPC	Estimated annual percentage change	EAPC are calculated based on a linear regression mode of the age standardized rates and the calendar year to represent temporal trends
HDI	Human-development index	The social and economic development level of countries
SDI	Socio-demographic index	The sociodemographic development level of countries

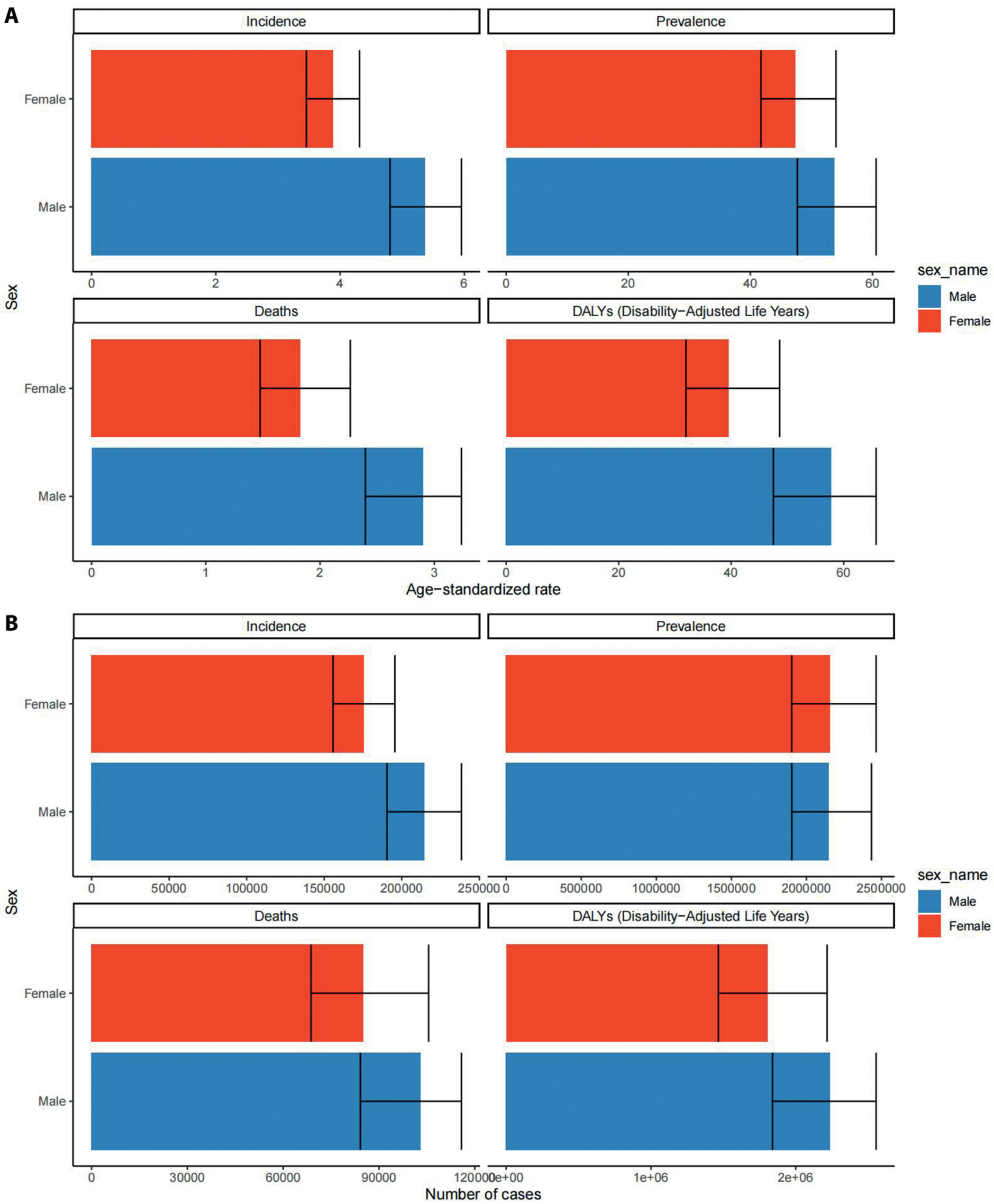

Figure S1. The disease burden of interstitial lung disease and pulmonary sarcoidosis between the two genders in 2021.