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The global burden of heart failure attributable to interstitial lung diseases: insights from the global burden of disease study 2021

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Abstract

Background The burden of interstitial lung disease (ILD)-associated heart failure (HF) poses a significant challenge to the prognosis of ILD patients. This study aimed to characterize the disease burden and analyse future trends of ILD-associated HF, offering valuable insights to inform targeted prevention and control strategies.

Methods Data on the prevalence and years lived with disability (YLDs) of ILD-associated HF were retrieved from the Global Burden of Disease (GBD) database for the period 1990–2021. Trends in ILD-associated HF were evaluated using average annual percentage change (AAPC) and percentage change analyses. Future prevalence data were projected up to 2050 using predictive modelling.

Results Globally, the number of patients with ILD-associated HF increased from 20,229 in 1990 to 104,059 in 2021, with the prevalence rising from 0.53 to 1.41 per 100,000 population. Prevalence rates were disproportionately higher in older populations, with individuals over 95 years experiencing a 17.78-fold increase over the study period. Additionally, a positive correlation was observed between higher socioeconomic development index (SDI) levels and ILD-associated HF prevalence. Among 204 countries, 71.1% exhibited an increasing trend in prevalence. However, Bayesian age-period-cohort (BAPC) modelling predicts a declining trend over the next 28 years.

Conclusion Over the past three decades, the global burden of ILD-associated HF has escalated, particularly among individuals aged over 65 and in regions with high SDI levels. These findings underscore the need for region-specific, personalized intervention strategies to mitigate disease progression and enhance the quality of life for ILD patients.

Keywords Interstitial lung diseases, Heart failure, Global burden of disease, Prevalence, Prediction

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Introduction

Interstitial lung diseases (ILD) encompass over 200 confirmed types, ranging from extremely rare to relatively common conditions [1]. ILD is commonly classified into idiopathic interstitial pneumonias (IIPs), autoimmune ILDs, hypersensitivity pneumonitis, sarcoidosis, and other ILDs [2]. Among these, IIP represents the predominant category, with idiopathic pulmonary fibrosis (IPF) being the most frequently observed subtype. These diseases are characterized by inflammation and/or fibrosis within the interstitial spaces of the lung, primarily resulting in impaired gas exchange [1]. Systemic diseases, environmental exposures, and genetic predispositions contribute to the aetiology of ILD, further complicating its clinical management [3]. The heterogeneous and multifaceted nature of ILD poses significant challenges in its treatment [4].

Pulmonary hypertension (PH) is a frequent comorbidity among patients with ILD, particularly in those with IPF, connective tissue disease (CTD)-associated ILD, and sarcoidosis [5–8]. In a large trial involving patients with advanced IPF, 46% exhibited PAH [5, 9]. The prevalence of PH among IPF patients awaiting lung transplantation has been reported to range from 39.7–84% [10], underscoring the high disease burden. ILD-associated PH is linked to increased oxygen requirements, diminished quality of life, and elevated early mortality rates [5]. A key pathological consequence of PH is its deleterious impact on right ventricular function [5]. Initial compensatory right ventricular hypertrophy in response to pressure overload progresses to right ventricular dilation and failure as the ventricle becomes unable to sustain increasing afterload [9]. Additionally, studies in CTD-ILD have highlighted a significantly elevated cardiovascular risk, with an overall cardiovascular disease risk 1.65 times higher than in CTD patients without ILD [11].

A more comprehensive understanding of the burden of heart failure (HF) associated with ILD could inform public health strategies aimed at improving early diagnosis and targeted prevention efforts. Globally, disparities in healthcare resource distribution contribute to delayed diagnosis and suboptimal management of ILD and its associated complications, including HF.

The Global Burden of Disease (GBD) database provides impairment data derived from disease registries, medical records, and population health surveys across diverse countries and regions. These data are evaluated using clinical assessment tools and advanced statistical methods such as Bayesian meta-regression to estimate the incidence and severity of various dysfunctions [12], including anaemia, epilepsy, hearing loss, HF, intellectual disability, infertility, vision loss, Guillain-Barré syndrome, and pelvic inflammatory disease [12].

Using updated GBD 2021 data, this study examines the prevalence and years lived with disability (YLDs) attributable to ILD-associated HF from 1990 to 2021 at global, regional, and national levels. It further explores the distribution and temporal trends in the burden of HF across different age groups, offering valuable insights for future healthcare interventions.

Methods

Data source

The GBD database serves as the core data platform for global disease burden research, systematically quantifying the health impacts of diseases, injuries, and risk factors worldwide. Maintained and led by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington, this database integrates comprehensive data from countries and regions globally, supporting evidence-based public health decision-making and policy formulation. The GBD 2021 study provides comprehensive epidemiological data on 371 diseases and injuries across 21 global regions and 204 countries from 1990 to 2021. Data for the present analysis were obtained from the Global Health Data Exchange (GHDx) platform (http://ghdx.healthdata.org/gbd-2021/sources) [12].

Definition

The GBD database defines ILD as including interstitial pulmonary disease (ICD-10 code J84.9), pulmonary sarcoidosis (ICD-10 code D86.2), and sarcoidosis unspecified in site (ICD-10 code D86.9) [13]. The dataset al.so integrates HF attributable to ILD as a key contributor to disease burden.

Years lived with disability were calculated using estimated prevalence data for non-fatal disease sequelae, adjusted for age, sex, location, and year. These estimates were combined with disability weights specific to each sequela [12]. The resulting rates were standardized per 100,000 individuals. Prevalence and YLDs associated with ILD-related HF were quantified using age-standardized rates (ASRs), with 95% uncertainty intervals (UIs) [12].

Socio-demographic index and decomposition methodology

The socio-demographic index (SDI) is a composite metric reflecting a country's or region's developmental status, based on the total fertility rate, mean years of education, and per capita income [12]. SDI scores range from 0 (indicative of low income, limited education, and high fertility) to 100 (indicative of high income, extensive education, and low fertility). The 204 included countries and territories were stratified into five SDI categories: low, low-middle, middle, high-middle, and high [12].

A decomposition methodology was employed to analyse the contributions of population growth, age structure, and epidemiological changes to variations in the prevalence and YLDs of ILD-associated HF [14].

Projection analysis

The Bayesian age-period-cohort (BAPC) model was utilized to project the future disease burden of ILD-associated HF from 2022 to 2050. This log-linear Poisson model assumes that age, period, and cohort exert multiplicative effects on the disease burden, with outcomes modelled using a Poisson distribution and a designated link function [14, 15].

Statistical analysis

Joinpoint regression analysis was conducted to evaluate prevalence trends over time. The analysis identified statistically significant shifts, termed "joinpoints," where changes in trend direction occurred [16, 17]. Annual percentage change (APC) values were calculated between joinpoints [18], while the average annual percentage change (AAPC) quantified overall temporal trends. Time-series data, including prevalence rates, were log-transformed, with time treated as the independent variable to derive regression coefficients (β1) [19]. The following formula was applied to calculate AAPC [19]:

$$\mathrm{AAPC} = (e^{\beta 1} - 1) \times 100\%$$

Additionally, the association between SDI and the burden of ILD-associated HF was analysed across geographical locations.

Joinpoint analyses were conducted using Joinpoint Regression 5.1 software, while additional statistical analyses were performed using R 4.3.3, incorporating the R packages BAPC (version 0.0.36), INLA (version 23.06.29), and ggplot2 (version 3.4.2). Statistical significance was defined as $p < 0.05$.

Results

Global burden of ILD-associated HF from 1990 to 2021 and projections to 2035

Globally, the burden of ILD-associated HF has demonstrated a marked upward trend from 1990 to 2021, as reflected in both prevalence and YLD metrics (Figure S1). The prevalence of ILD-associated HF increased from 20,229 cases in 1990 to 104,059 in 2021, representing a 4.14-fold rise. Concurrently, the age-standardized prevalence rate (ASPR) rose by 1.41 times over the same period (Table 1). Similarly, YLD cases increased from 1,873.77 in 1990 to 9,519.61 in 2021, a 4.08-fold rise, accompanied by a 1.38-fold increase in the YLD rate (Table S1). Annually, while the absolute number of cases and YLDs were consistently higher among women, the prevalence rate and YLD rate were notably higher in men (Figure S1).

Joinpoint regression analysis revealed varying degrees of increase in ASPR between 1990 and 2018, with the most significant growth occurring from 1995 to 2004, representing a 4.86-fold increase ($P < 0.001$). However, from 2018 to 2021, the ASPR exhibited a slight, non-significant decline ($P = 0.154$) (Figure S2, Table S2).

Subgroup analyses by age revealed no documented cases of ILD-associated HF in individuals aged 0–15 years (Table S3). In populations aged 15 years and older, the prevalence of ILD-associated HF displayed a consistent upward trajectory across the 32 years from 1990 to 2021, with increasing age amplifying this trend. Notably, individuals aged 95 years and older experienced a 17.78-fold rise in prevalence during this period (Fig. 1A–D, Table S3). Across HF subtypes, trends remained relatively consistent, with severe HF representing the largest proportion of cases (Fig. 1A–D, Table S3). Additionally, the proportion of ILD-associated HF cases in individuals aged 65 years and older increased significantly by 2021 compared with 1990 (Fig. 1E).

Globally, in the population aged 15 years and older, the AAPC in prevalence rates and YLDs rates exhibited a sustained upward trend, with the increase being more pronounced among older populations. For individuals aged 60 years and older, the AAPC escalated with advancing age (Fig. 2).

Future trends, modelled using a BAPC framework, suggest a declining trajectory in the ASPR of ILD-associated HF from 2021 to 2050. By 2050, the estimated prevalence is projected to decline to 1.27×10^{-5} per 100,000 men and 8.47×10^{-6} per 1,000,000 women (Figure S3).

Global burden of ILD-associated HF stratified by SDI and GBD region

The global burden of ILD-associated HF varies significantly across five SDI regions. In 2021, the High SDI region exhibited the greatest number of prevalent cases and YLDs, as well as the highest prevalence and YLDs rates compared to other regions. Specifically, the High SDI region recorded 55,838 prevalent cases, corresponding to a prevalence rate of 2.54 per 100,000 individuals (Table 1, Table S1). The High-middle SDI region demonstrated the highest relative increases in prevalence and YLDs over the study period, with prevalent cases rising 5.43-fold and YLDs increasing 5.35-fold from 1990 to 2021 (Table 1, Table S1). Across all SDI regions, the majority of prevalent cases were observed among individuals aged 65–84 years. Over the 32-year period, the proportion of cases among those aged 65 and older increased across all regions, with the most notable rise occurring in the High SDI region (Fig. 1). The AAPC in prevalence and YLDs increased across all age groups

Table 1 The prevalence of ILD-associated HF cases and rates in 1990 and 2021

Location	Prevalent cases			Age-standardized prevalent rates			AAPC
	1990 (95% UI)	2021 (95% UI)	Percentage change	1990_per 100 000(95% UI)	2021_per 100 000(95% UI)	Percentage change	
Global	20228.72 (16194.39,25346.46)	104058.82 (80411.77,130772.42)	4.14 (3.61,4.71)	0.52 (0.42,0.66)	1.26 (0.97,1.58)	1.41 (1.21,1.63)	2.88
Low SDI	1853.77 (1381.18,2422.55)	4903.54 (3660.37,6485.74)	1.65 (1.53,1.77)	0.79 (0.61,1.02)	0.9 (0.68,1.17)	0.13 (0.08,0.19)	0.40
Low-middle SDI	3609.72 (2896.61,4475.44)	11859.98 (9314.92,15124.53)	2.29 (2.08,2.51)	0.65 (0.52,0.82)	0.89 (0.69,1.15)	0.36 (0.28,0.45)	1.00
Middle SDI	3484.16 (2848.99,4270.74)	17827.54 (14037.4,22740.13)	4.12 (3.67,4.56)	0.37 (0.3,0.45)	0.73 (0.58,0.93)	1 (0.89,1.12)	2.26
High-middle SDI	2112.5 (1679.6,2651.85)	13579.61 (10820.32,16844.78)	5.43 (4.85,6.11)	0.22 (0.18,0.28)	0.72 (0.58,0.89)	2.22 (1.96,2.53)	3.85
High SDI	9156.48 (6990.32,11763.84)	55837.58 (41898.75,72455.41)	5.1 (4.27,6.05)	0.85 (0.66,1.08)	2.54 (1.94,3.23)	1.99 (1.63,2.37)	3.60
High-income Asia Pacific	1888.08 (1320.74,2584.61)	16914.83 (11662.83,23517.43)	7.96 (6.19,10.5)	0.98 (0.69,1.32)	3.19 (2.27,4.3)	2.26 (1.8,2.84)	3.88
High-income North America	4540.58 (3500.37,5793.35)	19284.58 (14541.8,25646.63)	3.25 (2.54,4.04)	1.31 (1.02,1.65)	2.92 (2.23,3.81)	1.23 (0.9,1.63)	2.63
Western Europe	2721.45 (2062.36,3547.15)	21739.73 (17267.01,27489.82)	6.99 (6.06,7.92)	0.48 (0.38,0.61)	2.25 (1.82,2.82)	3.72 (3.21,4.19)	5.13
Australasia	129.25 (99.06,167.99)	2121.8 (1689.49,2653.22)	15.42 (13.03,18.23)	0.55 (0.42,0.71)	3.7 (2.98,4.59)	5.76 (4.74,6.91)	6.36
Andean Latin America	724.23 (599.74,882.97)	4930.38 (3967.53,6132.09)	5.81 (5.07,6.54)	3.68 (2.99,4.5)	8.63 (6.92,10.8)	1.35 (1.09,1.59)	2.79
Tropical Latin America	349.28 (273.06,435.32)	2437.01 (1827.56,3275.6)	5.98 (4.66,7.4)	0.34 (0.27,0.42)	0.99 (0.74,1.32)	1.92 (1.49,2.32)	3.52
Central Latin America	634.97 (522.37,766.39)	4004.67 (3149.54,5082.06)	5.31 (4.58,6.07)	0.68 (0.55,0.83)	1.63 (1.28,2.06)	1.41 (1.22,1.61)	2.88
Southern Latin America	311.86 (245.57,394.68)	1892.88 (1428.02,2469.41)	5.07 (4.28,5.84)	0.69 (0.54,0.87)	2.15 (1.63,2.77)	2.1 (1.73,2.46)	3.72
Caribbean	67.21 (55.51,83.33)	306.81 (242.53,386.93)	3.56 (3.02,4.19)	0.25 (0.2,0.31)	0.58 (0.46,0.73)	1.33 (1.07,1.64)	2.76
Central Europe	342.61 (270.94,431.91)	1011.57 (789.93,1311.14)	1.95 (1.63,2.31)	0.25 (0.2,0.31)	0.54 (0.43,0.66)	1.14 (0.95,1.35)	2.49
Eastern Europe	476.78 (363.47,622.6)	334.52 (232.04,482.2)	-0.3 (-0.4,-0.15)	0.19 (0.15,0.24)	0.1 (0.07,0.14)	-0.46 (-0.53,-0.37)	-1.94
Central Asia	160.87 (128.8,201.69)	156.52 (126.16,193.8)	-0.03 (-0.11,0.06)	0.32 (0.25,0.41)	0.2 (0.16,0.25)	-0.38 (-0.44,-0.32)	-1.54
North Africa and Middle East	281.81 (236.79,333.07)	1539.22 (1276.08,1828.21)	4.46 (4.05,4.91)	0.15 (0.13,0.18)	0.31 (0.26,0.37)	1.03 (0.89,1.2)	2.32
South Asia	3945.8 (3134.16,4926.97)	14717.46 (11230.07,19564.4)	2.73 (2.41,3.09)	0.83 (0.66,1.05)	1.11 (0.84,1.47)	0.33 (0.22,0.44)	0.93
Southeast Asia	193.09 (161.91,232.41)	768.49 (633.06,960.01)	2.98 (2.69,3.26)	0.08 (0.06,0.1)	0.13 (0.11,0.17)	0.7 (0.6,0.81)	1.72
East Asia	854.36 (665.43,1092.66)	6126.02 (4444.67,8592.44)	6.17 (5.36,7.14)	0.1 (0.08,0.13)	0.3 (0.22,0.41)	1.83 (1.55,2.17)	3.42
Oceania	16.37 (13.28,19.55)	44.95 (36.72,53.78)	1.75 (1.54,1.98)	0.44 (0.36,0.54)	0.53 (0.44,0.65)	0.2 (0.11,0.31)	0.60
Western Sub-Saharan Africa	1139.3 (790.99,1504.77)	2468.34 (1727.81,3312.91)	1.17 (1.04,1.3)	1.08 (0.76,1.46)	0.96 (0.68,1.31)	-0.12 (-0.15,-0.08)	-0.40
Eastern Sub-Saharan Africa	630.47 (446.02,873.62)	1566.82 (1106.56,2166.2)	1.49 (1.37,1.62)	0.69 (0.49,0.94)	0.7 (0.5,0.97)	0.02 (-0.03,0.06)	0.06
Central Sub-Saharan Africa	175.14 (120.51,252.69)	448.79 (303.04,642.63)	1.56 (1.34,1.83)	0.67 (0.47,0.94)	0.67 (0.47,0.94)	0 (-0.08,0.1)	0.00
Southern Sub-Saharan Africa	645.2 (473.93,843.7)	1243.43 (893.76,1655.12)	0.93 (0.83,1.04)	2.2 (1.62,2.89)	2.04 (1.48,2.71)	-0.07 (-0.11,-0.02)	-0.23

Abbreviations: AAPC, average annual percentage change; ILD, interstitial lung disease; SDI, Socio-demographic Index; UI, uncertainty interval

within the five SDI regions. The High SDI region experienced the most significant growth in individuals aged 65 and older, whereas the High-middle SDI region exhibited the largest increase among individuals under 65 years (Fig. 2). Decomposition analysis revealed that both population growth and epidemiological shifts substantially contributed to the increasing burden of ILD-associated HF across all SDI regions. In the High and High-middle SDI regions, population ageing emerged as an additional critical driver of this trend (Fig. 3).

Analysis of the 21 GBD regions revealed a widespread increase in the proportion of individuals aged 65 and older among the ILD-associated HF population. By 2021, Australasia recorded the highest proportion of cases within this demographic (Fig. 1). Australasia also exhibited significantly higher AAPC values for prevalence and YLDs across most age groups compared with other regions, with the AAPC reaching 7.11 for the 80–84 age group. In contrast, Central Asia and Eastern Europe experienced declining AAPC values for both prevalence and YLDs across all age groups (Fig. 2). Decomposition analysis indicated that, while population growth and epidemiologic changes contributed to the burden in most regions, the declining demographic-adjusted epidemiological changes in Central Asia and Eastern Europe led to reductions in the prevalence and YLDs of ILD-associated HF (Fig. 3).

The SDI serves as a comprehensive measure of regional development and is closely related to population health outcomes. A significant positive correlation was identified between ASPR and SDI ($R = 0.2311$, $P < 0.001$), suggesting that higher SDI levels are associated with increased prevalence of ILD-associated HF. This trend was most pronounced in High SDI regions. Notable intraregional disparities in ASPR were also observed, particularly within Andean Latin America (Fig. 4A).

Global burden of ILD-associated HF across countries

At the national level, the ASPR of ILD-associated HF exhibits a positive correlation with the SDI ($R = 0.2263$, $P < 0.001$), with a pronounced increase observed when the SDI surpasses 0.7. Among all countries, Peru demonstrated the highest ASPR in 2021, reaching 11.97 per 100,000 population, substantially exceeding the rates observed in other nations (Fig. 4B). Canada ranked second, with an ASPR of 5.62 per 100,000 population, while Moldova reported the lowest ASPR, at 0.009 per 100,000 population (Fig. 5A, Table S4). Between 1990 and 2021, 71.1% of countries exhibited an increasing trend in the ASPR of ILD-associated HF. Italy recorded the most pronounced rise, with a total percentage change of 14.89 and an AAPC of 9.33. The Kingdom of the Netherlands followed, with a total percentage change of 8.97 and an AAPC of 7.70. Conversely, Moldova displayed the most substantial decline, characterized by a total percentage change of -0.91 and an AAPC of -7.31 (Fig. 5B, Table S4).

Discussion

Interstitial lung disease is a heterogeneous and complex group of inflammatory and fibrotic conditions primarily affecting the lung interstitium [1]. The co-occurrence of HF in patients with ILD significantly worsens prognosis and is associated with increased mortality risk [20]. Notably, ILDs such as IPF and CTD-ILD are frequently complicated by PH [21]. A critical cardiovascular manifestation in ILD is the heightened vascular resistance within the precapillary pulmonary circulation, leading to elevated pulmonary arterial pressure (PAP) and the development of pulmonary hypertension [22]. The retrograde transmission of elevated PAP increases intraluminal pressure, exerting additional stress on the walls of the right ventricle [22]. Over time, the right ventricle, being structurally ill-equipped to withstand sustained pressure overload, experiences a progressive decline in myocardial contractility and subsequent dilation. This triggers a deleterious cycle characterized by increased right ventricular wall tension, heightened oxygen demand, and compromised myocardial perfusion, ultimately culminating in right ventricular failure [22, 23]. These pathophysiological processes significantly contribute to elevated mortality rates [22, 24, 25]. In cases of pulmonary hypertension, the incidence and severity of biventricular dysfunction are notably exacerbated [22]. This study is the first to evaluate the disease burden and temporal trends associated with HF in the context of ILD.

Our findings indicate that in 2021, more than 100,000 patients with ILD developed HF, representing a fivefold increase compared with 1990, with an AAPC of 2.88. Furthermore, a marked rise in the prevalence of ILD-associated HF has been observed across most countries and regions globally. This upward trend may be attributable to demographic expansion and shifts in epidemiologic patterns. With the increasingly widespread use of chest computed tomography (CT) since the 1990s, different subtypes of interstitial lung disease (ILD) have been further refined [26]. The diagnostic paradigm for interstitial lung disease (ILD) has progressively shifted toward multidisciplinary evaluation over recent decades [26]. Initial guidance from the 2002 American Thoracic Society/European Respiratory Society (ATS/ERS) consensus advocated integrated clinical, imaging, and pathological case reviews for indeterminate ILD classifications [27]. Subsequent refinements in the 2013 update formally recommended multidisciplinary team (MDT) consensus as the gold standard for ILD diagnosis [28]. Multidisciplinary team (MDT) discussions have become the reference standard for diagnosis, which has significantly improved the diagnostic accuracy of ILD [26, 28]. In the

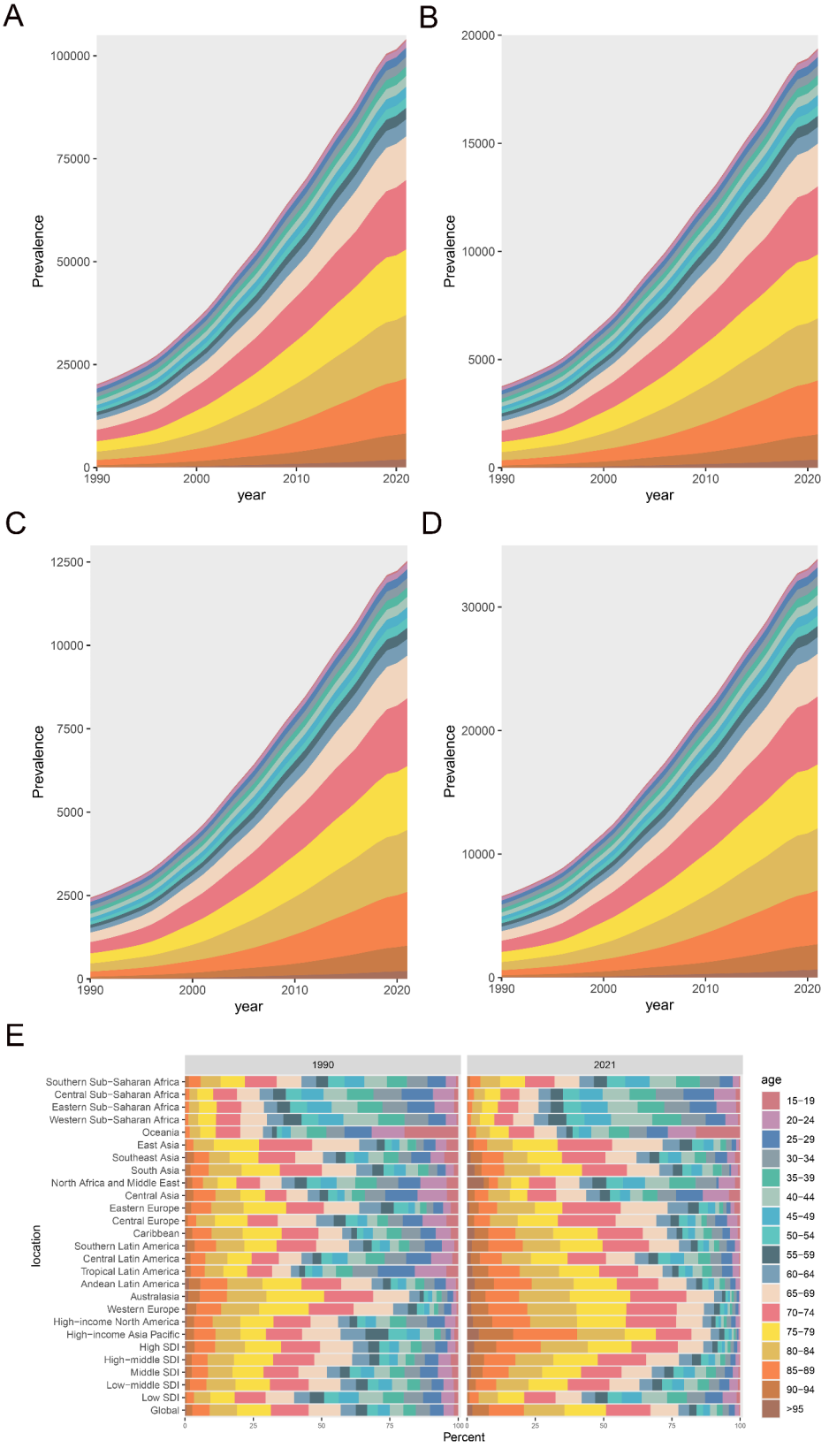

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Fig. 1 Time trend of the burden of ILD-associated HF by age group. (**A**) Prevalent cases of ILD-associated HF by age group globally from 1990 to 2021; (**B**) Prevalent cases of ILD-associated mild HF by age group globally from 1990 to 2021; (**C**) Prevalent cases of ILD-associated moderate HF by age group globally from 1990 to 2021; (**D**) Prevalent cases of ILD-associated severe HF by age group globally from 1990 to 2021; (**E**) The distribution of prevalent cases as percentages across different age groups globally, in five territories, and across 21 GBD regions in 1990 and 2021. Abbreviations: GBD, Global Burden of Disease; HF, heart failure; ILD, interstitial lung disease

context of global ageing, the ageing population in most regions adversely influences the prevalence of ILD-associated HF, partially accounting for the projected decline in ILD-associated HF over the next 28 years.

Our analysis also reveals that the prevalence rate and YLD rate of ILD-associated HF are higher in men compared with women. Prior studies have identified advanced age, smoking history, male sex, gastro-oesophageal reflux disease, and reduced baseline pulmonary function as significant risk factors associated with increased incidence, disease progression, and reduced survival in IPF [29, 30]. These disparities may be attributed to the higher proportion of men engaged in industrial and labour-intensive occupations, which involve greater exposure to occupational hazards such as silica, asbestos, and hard metals, increasing their susceptibility to related ILDs [31, 32]. Additionally, research on occupational lung diseases has predominantly focused on male populations, potentially introducing challenges and biases in assessing the risks encountered by women in specific occupational settings, thereby contributing to delayed diagnoses [31, 33].

Across the five SDI regions, the highest prevalence and prevalence rates of ILD-associated HF are observed in the High SDI regions compared with other SDI regions. Among the 21 global geographical regions, Australasia demonstrates the most pronounced increase in ILD-associated HF prevalence, with a 15.42-fold growth over 32 years and an AAPC of 6.36. Further analysis of the correlation between SDI and prevalence highlights a positive association, suggesting that advancements in diagnostic technologies and increased awareness of follow-up care among ILD patients may underlie this trend [34, 35]. However, in low- and middle-income countries (LMICs), the diagnosis of chronic respiratory diseases (CRDs) remains hindered by limited access to diagnostic tools, such as spirometry and chest imaging, at the primary care level, as well as a shortage of trained healthcare professionals capable of performing and interpreting these tests [36]. Over the past 32 years, the prevalence of ILD-associated HF in Andean Latin America has exceeded that of other geographical regions, with Peru recording the highest prevalence among 204 countries. According to 2019 GBD data, Andean Latin America also exhibits the highest mortality rate associated with ILD-associated HF [36]. This may reflect inadequate diagnostic capabilities within the region, as many patients present to ILD referral centres at advanced disease stages [37, 38]. Pulmonary arterial hypertension, a frequent complication in the later stages of IPF, significantly impacts survival outcomes [24]. In LMICs, population ageing exhibits a negative correlation with the disease burden of ILD-associated HF, potentially reflecting the reduced life expectancy of patients with ILD-associated HF in these settings.

In terms of age-related patterns, the burden of ILD-associated HF exhibits a marked increase with advancing age. Globally, the prevalence of ILD-associated HF among individuals aged 95 years and older is estimated at 36.23 per 100,000, representing the demographic with the most rapid growth in case numbers. Over the past 32 years, the prevalence of ILD-associated HF in this age group has increased 17.78-fold. Evidence indicates that advancing age is strongly correlated with a heightened susceptibility to ILD, particularly IPF [39]. This

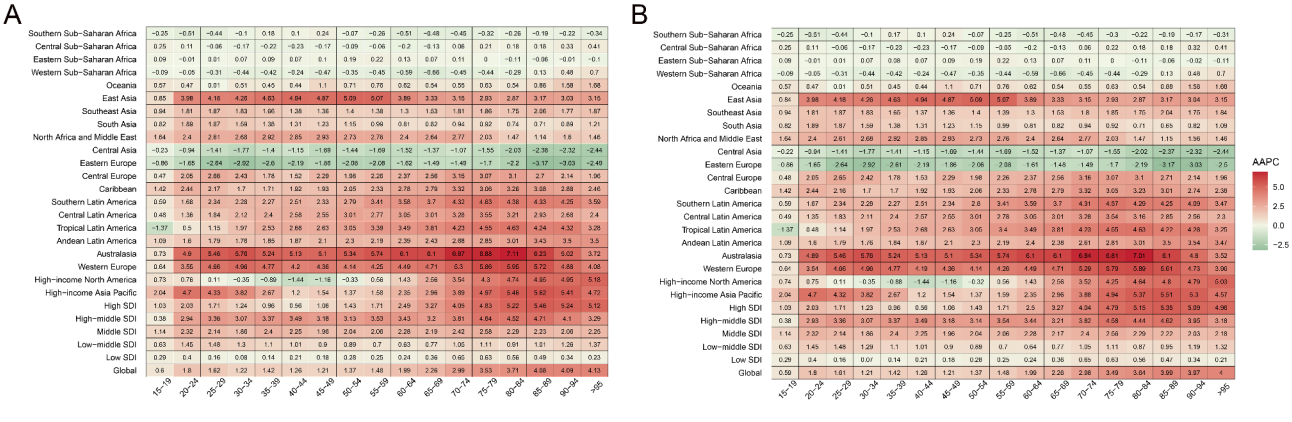

Fig. 2 AAPC in age-specific prevalence rates and YLDs for ILD-associated HF by age groups and regions from 1990 to 2021. (**A**) AAPC of prevalence; (**B**) AAPC of YLDs. Abbreviations: AAPC, average annual percent change; HF, heart failure; ILD, interstitial lung disease; YLDs, years lived with disability

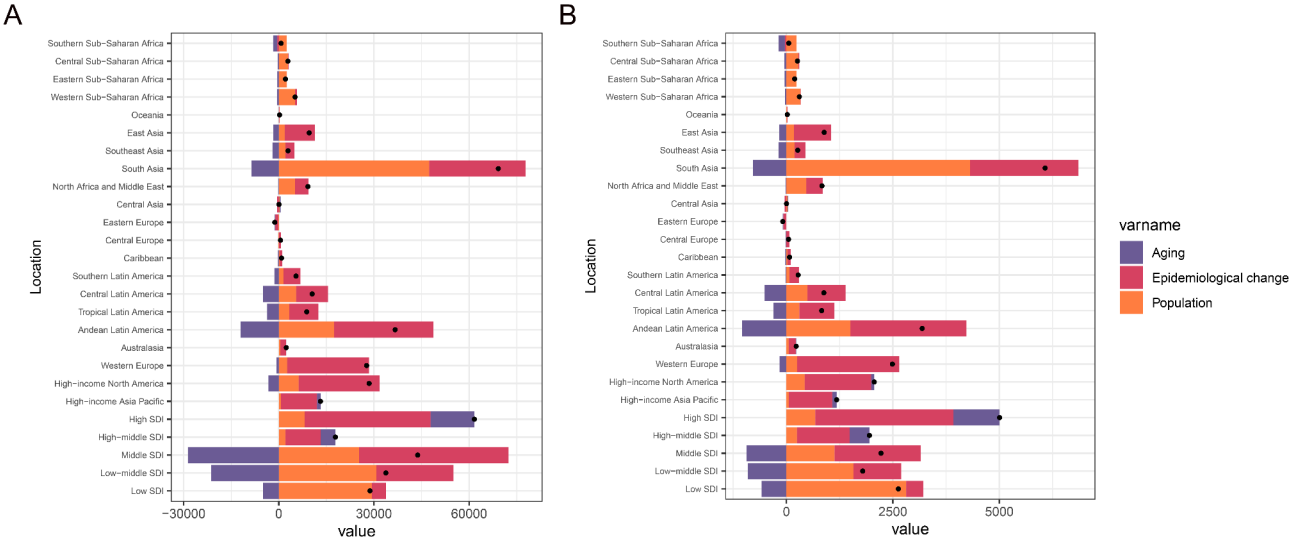

Fig. 3 Population-level changes in ageing, population growth, and epidemiologic factors for prevalence (**A**) and YLDs (**B**) across various SDI and GBD regions from 1990 to 2021. Black dots represent the overall change from all three components. Positive values indicate a positive contribution, whereas negative values indicate a negative contribution. Abbreviations: GBD, Global Burden of Disease; HF, heart failure; ILD, interstitial lung disease; SDI, Socio-demographic Index; YLDs, years lived with disability

relationship is attributed to age-related genomic instability, telomere attrition, impaired autophagy, and mitochondrial dysfunction, which collectively facilitate the onset and progression of IPF [39–43]. The ongoing trend of global population ageing, coupled with improvements in the diagnosis and treatment of ILD, has substantially contributed to the 32-year rise in the prevalence of ILD-associated HF [44, 45].

Projections indicate that by 2050, individuals aged 65 years and older will constitute 20% of the global population, with 80% of this demographic residing in LMICs [44]. However, delayed diagnoses and insufficient treatment of ILD in LMICs significantly compromise the prognosis and life expectancy of affected individuals. Addressing this challenge requires bolstering diagnostic capabilities in primary care facilities and fostering interdisciplinary collaboration among pulmonologists, radiologists, and other specialists to enhance the management of ILD and its associated HF.

Limitation

This study has several limitations. First, ILD encompasses more than 200 distinct conditions. The primary focus of this analysis is on diagnoses captured by the ICD-10, specifically interstitial pulmonary disease (J84.9), pulmonary sarcoidosis (D86.2), and sarcoidosis (D86.9), which do not

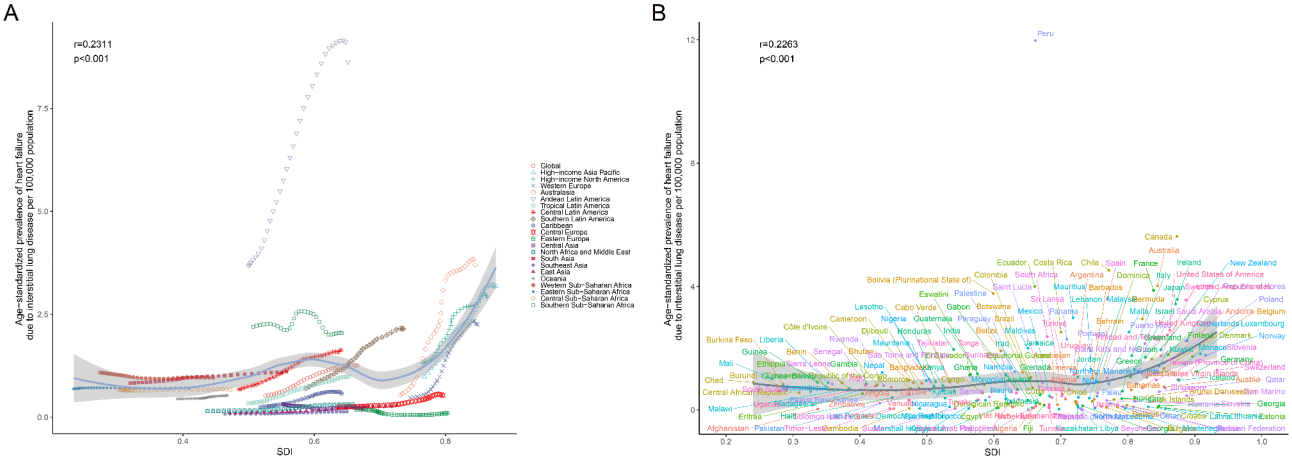

Fig. 4 (**A**) Trends in the age-standardized prevalence of ILD-associated HF across 21 regions by SDI from 1990 to 2021; (**B**) Trends in the age-standardized prevalence of ILD-associated HF across 204 countries by SDI from 1990 to 2021. Abbreviations: HF, heart failure; ILD, interstitial lung disease; SDI, Socio-demographic Index

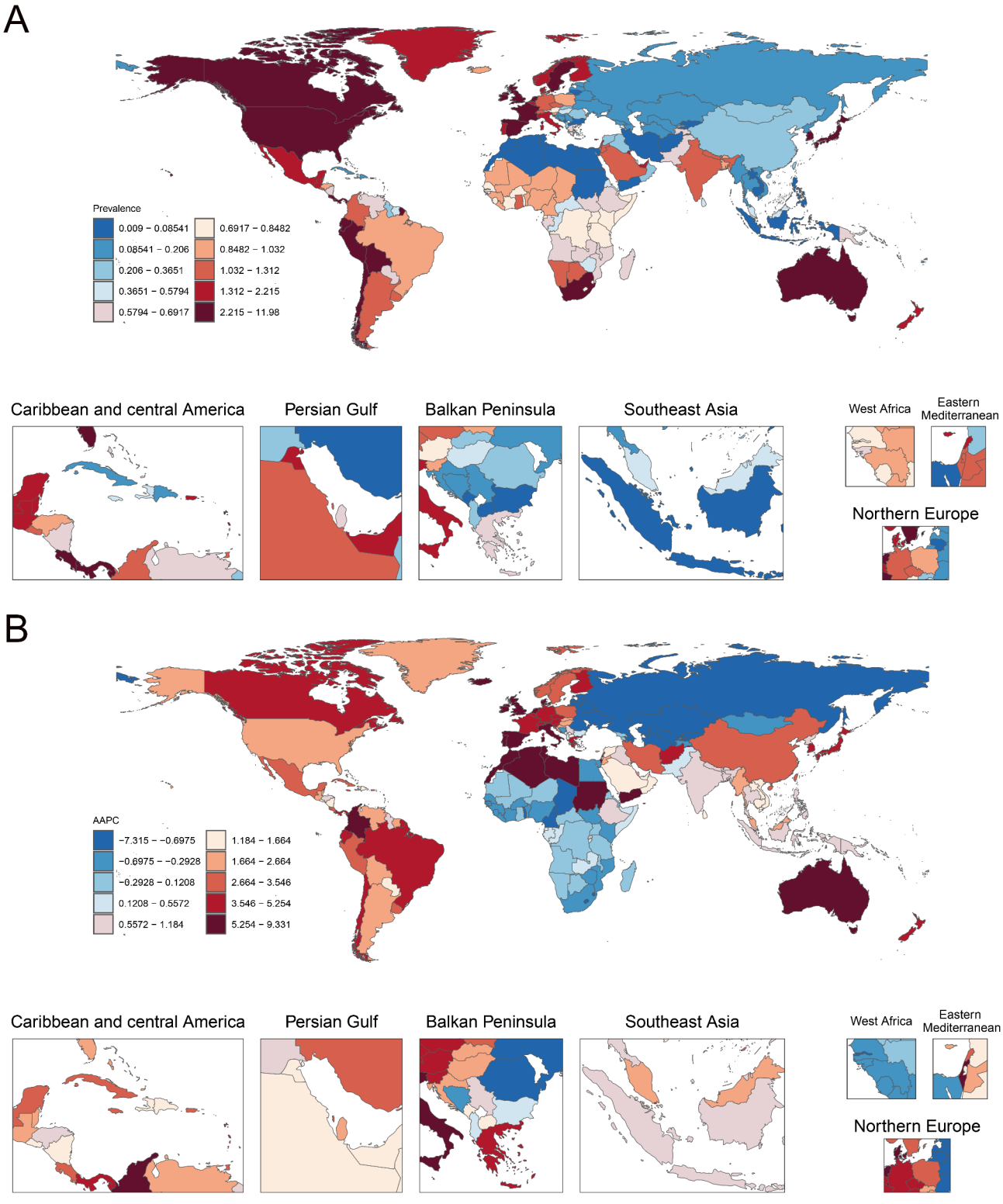

Fig. 5 Global trends in the burden of ILD-associated HF. (**A**) Age-standardized prevalence rate of ILD-associated HF across 204 countries in 2021; (**B**) AAPC in prevalence rates across 204 countries from 1990 to 2021. Abbreviations: AAPC, average annual percent change; HF, heart failure; ILD, interstitial lung disease

comprehensively represent the spectrum of conditions [13]. Second,. the diagnoses of ILD and HF are derived from data obtained through disease registries, medical records, and population health surveys across diverse

countries and regions. The database lacks standardized diagnostic criteria and robust differential diagnostic protocols. Global inconsistencies in healthcare infrastructure and national policy frameworks further compromise the uniform application of the ICD. In resource-constrained settings, this systemic weakness may manifest as coding errors, incomplete diagnostic or imaging documentation, and clinical misclassification—for instance, diagnostic confusion between ILD and chronic obstructive pulmonary disease (COPD). Notably, standardized ICD implementation faces heightened challenges in regions outside WHO member states, where coding compliance is neither mandated nor systematically monitored. These multilayered issues collectively amplify geographic disparities in disease ascertainment and reporting accuracy. Third, current estimates of ILD-associated HF severity rely heavily on modeling approaches that infer functional impairment from clinical diagnoses and healthcare cost data in medical records. This methodology risks generating conclusions misaligned with actual clinical observations, as real-world diagnostic heterogeneity and socioeconomic confounders are insufficiently captured in such models. Although the original epidemiological data standards remain a limitation and source of uncertainty in GBD analyses, and GBD data analyses cannot fully replace high-quality primary data, they ensure that populations or causes with little or no data are not excluded from critical benchmarking used for burden estimation [12]. Furthermore, the GBD 2021 Diseases and Injuries Collaborators have been continuously improving the reliability of collected data by strengthening data collection systems [12]. Finally, the retrospective nature of the GBD database introduces a potential lag in its applicability for guiding timely decision-making.

Conclusions

Over the past 32 years, the prevalence and YLDs associated with ILD-associated HF have exhibited a consistent upward trajectory, with older populations experiencing the most pronounced increases. This trend aligns with the global ageing of the population, as the proportion of ILD patients with HF aged over 65 years has risen in most regions during this period. The prevalence of ILD-associated HF demonstrates a positive correlation with SDI. Despite global projections suggesting a decline in the prevalence of ILD-associated HF over the next 28 years, targeted health policies tailored to regional contexts remain essential to further enhance the diagnosis and treatment of patients with ILD and ILD-associated HF.

Abbreviations

AAPC	Average annual percent change
APC	Annual percentage change
ASPR	Age-standardized prevalence rate
ASRs	Age-standardized rates
BAPC	Bayesian age-period-cohort
CRDs	Chronic respiratory diseases
CTD	Connective tissue diseases
GBD	Global Burden of Disease Study
GHDx	Global Health Data Exchange
HF	Heart failure
IIPs	Idiopathic interstitial pneumonias
IPF	Idiopathic pulmonary fibrosis
LMICs	Low- and middle-income countries
PH	Pulmonary hypertension
PAP	Pulmonary arterial pressure
SDI	Socio-demographic Index
UI	Uncertainty interval
YLDs	Years lived with disability

Supplementary Information

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Supplementary Table 1: YLDs of ILD-associated HF cases and rates in 1990 and 2021. **Supplementary Table 2**: Joinpoint regression analysis of sex-specific age-standardized prevalence rates for ILD-associated HF globally from 1990 to 2021. **Supplementary Table 3**: Trends in subtypes of ILD-associated HF across various age groups. **Supplementary Table 4**: Prevalence of ILD-associated HF in 1990 and 2021 across 204 countries

Supplementary Figure 1: Trends in all-age cases and age-standardized prevalence and YLD rates of ILD-associated HF by sex from 1990 to 2021. (**A**) Prevalence number and rate; (**B**) YLD number and rate. Abbreviations: HF, heart failure; ILD, interstitial lung disease; YLDs, years lived with disability

Supplementary Figure 2: Trend of age-standardized prevalence rates by Joinpoint regression, 1990–2021

Supplementary Figure 3: Trends in age-standardized prevalence rates globally, 1990–2050

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Author contributions

RL Lu designed the study and drafted the manuscript. Q Huang and TT Yu analyzed documents and interpreted the data. Corresponding authors XP Hong and DZ Liu read and revised the manuscript. All authors contributed to the final manuscript. All authors have read and approved the final submitted version.

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Data availability

A repository of the datasets generated or analyzed during the current study period is available at (http://ghdx.healthdata.org/gbd-results-tool).

Declarations

Ethics approval and consent to participate

Data from this GBD database are publicly available, and further permission from IHME is not required.

Competing interests

The authors declare no competing interests.

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