The prevalence and burden of interstitial lung diseases in the USA

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To the Editor:

Interstitial lung diseases (ILDs) are a heterogeneous group of diseases (*i.e.* idiopathic interstitial pneumonias, autoimmune ILDs, environmental exposure-related ILDs, sarcoidosis) but share several common clinical and pathophysiological features [1, 2]. ILDs are associated with significant morbidity, mortality and increased financial burden [3, 4].

In the past two decades, there has been significant progress in the diagnosis and treatment of ILDs. However, comprehensive epidemiological data remains limited. Since mortality rates do not give a complete picture of the burden of disease, the World Health Organization assesses the overall burden of disease using disability-adjusted life years (DALYs), a time-based measure that combines years of life lost due to premature mortality and years of healthy life lost due to disability. The objective of this study is to report current estimates and trends of ILD prevalence, DALYs and deaths in the USA.

The data for this study was derived from the Global Burden of Disease (GBD) 2019 study published by the Institute for Health Metrics and Evaluation. The methods used in this study have previously been reported in detail [5]. In brief, the GBD study analyses epidemiologic data using statistical modelling and provides estimates of disease prevalence and burden.

This research study is a secondary analysis of the GBD study results. Data were obtained from the Global Health Data Exchange GBD results online tool [6]. The abbreviation ILD used in our study refers to combined data of both ILDs and pulmonary sarcoidosis. We extracted the crude and age-standardised rates from 2010 to 2019 stratified by sex and age group. Age-standardised rates were based on the GBD global reference population.

In 2019, in the USA, there was an estimated 654 841 (95% uncertainty interval (UI) 566 536–745 855) cases of ILDs, 429 786 (95% UI 283 468–505 372) DALYs and 21 505 (95% UI 12 237–26 667) deaths from ILDs.

In 2019, the crude prevalence of ILDs per 100 000 was 179.7 in males and 218.9 in females (table 1). The age-standardised prevalence of ILDs per 100 000 was 121.3 (95% UI 105.7–136.5) in males and 131.4 (95% UI 114.8–148.3) in females. The overall crude prevalence increased 19.1% from 2010 to 2019, however, the age-standardised prevalence rate was stable.

In 2019, the crude DALYs from ILDs per 100 000 was 142.4 in males and 118.2 in females. The age-standardised DALYs from ILDs per 100 000 was 93.3 (95% UI 58.9–110.3) in males and 69.3 (95% UI 45.1–82.2) in females. The overall crude DALYs rate increased 15.8% from 2010 to 2019 (21% in males and 10.2% in females). The age-standardised DALYs rate have been stable since 2010.

In 2019, the crude deaths from ILDs per 100 000 was 7.3 in males and 5.9 in females. The age-standardised deaths from ILDs per 100 000 was 4.6 (95% UI 2.5–5.7) in males and 2.9 (95% UI 1.5–3.6) in females. The crude death rates increased 18.1% compared to 2010. The percent increase was higher in males compared to females (25.7% *versus* 10.2%). The age-standardised death rates were stable.

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Interstitial lung diseases (ILDs) are a significant contributor to disability and deaths in the USA. The prevalence and deaths from ILDs have increased but when adjusted for age, have been stable since 2010. https://bit.ly/3IDlZrg

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TABLE 1 Prevalence, disability-adjusted life years (DALYs) and mortality rates due to interstitial lung diseases in the USA

	Prevalence (95% UI)			DALYs rates (95% UI)			Mortality rates (95% UI)		
	2010	2019	Change, %	2010	2019	Change, %	2010	2019	Change, %
Overall	167.7 (151.0–183.7)	199.7 (172.7–227.4)	19.1 (12.1–26.1)	112.4 (75.7–132.0)	130.1 (86.4–154.1)	15.8 (11.5–20.2)	5.5 (3.3–6.7)	6.6 (3.7–8.1)	18.1 (13.0–23.6)
Sex									
Male	147.4 (132.8–161.4)	179.7 (155.1–205.0)	21.9 (14.7–29.2)	117.7 (74.7–137.8)	142.4 (88.1–169.2)	21.0 (14.7–27.3)	5.8 (3.2–6.9)	7.3 (4.0–9.0)	25.7 (18.0–33.2)
Female	187.4 (169.1–204.8)	218.9 (189.4–249.1)	16.8 (10.0–24.3)	107.3 (67.7–128.4)	118.2 (74.2–141.8)	10.2 (5.8–14.7)	5.3 (2.6–6.6)	5.9 (2.9–7.4)	10.2 (4.5–15.5)
Age, years									
50–54	192.7 (143.7–247.6)	197.1 (134.8–272.5)	2.3 (−9.1–15.0)	103.2 (77.2–122.2)	99.5 (74.6–117.6)	−3.6 (−9.7–2.5)	2.2 (1.6–2.5)	2.1 (1.5–2.5)	−4.7 (−11.6–1.1)
55–59	254.2 (195.5–330.0)	262.4 (186.5–367.5)	3.2 (−8.9–15.9)	148.0 (106.3–173.8)	147.5 (105.6–177.6)	−0.3 (−6.5–5.7)	3.8 (2.5–4.3)	3.7 (2.5–4.4)	-0.8 (−7.3–5.7)
60–64	340.3 (257.5–453.8)	357.5 (255.0–504.3)	5.1 (−6.4–16.2)	221.8 (153.5–257.8)	224.6 (155.8–264.7)	1.3 (−4.9–7.7)	6.7 (4.3–7.7)	6.8 (4.4–7.9)	0.7 (−5.6–8.0)
65–69	464.6 (345.3–604.9)	500.5 (345.9–696.0)	7.7 (−6.4–20.9)	336.9 (216.8–397.4)	339.1 (219.8–404.6)	0.7 (−5.1–6.0)	12.4 (7.5–14.5)	12.4 (7.4–14.7)	−0.2 (−6.0–5.5)
70–74	645.0 (482.8–854.1)	694.7 (481.0–985.1)	7.7 (−5.2–22.1)	486.9 (301.4–584.1)	503.9 (308.0–614.0)	3.5 (−2.3–10.0)	22.2 (12.7–26.4)	22.9 (12.7–28.1)	3.0 (−3.4–10.2)
75–79	844.1 (649.6–1085.2)	909.9 (655.9–1245.3)	7.8 (−3.4–20.7)	639.2 (389.1–778.4)	654.2 (392.7–810.0)	2.4 (−2.8–8.3)	37.1 (20.7–45.1)	37.7 (20.8–47.1)	1.8 (−3.9–8.3)
80–84	981.0 (785.7–1189.4)	1061.5 (788.3–1398.8)	8.2 (−4.6–21.7)	730.1 (430.9–912.1)	759.5 (437.6–980.3)	4.0 (−2.0–11.5)	55.3 (29.5–69.7)	57.3 (29.6–75.2)	3.6 (−3.3–12.4)
>85	929.7 (784.2–1072.2)	993.2 (797.2–1202.4)	6.8 (−1.7–15.3)	719.2 (403.5–937.5)	747.4 (399.8–991.7)	3.9 (−2.7–11.1)	82.1 (41.0–109.4)	87.6 (41.2–120.1)	6.7 (−2.0–15.5)

The prevalence, DALYs and mortality rates are presented as crude rates per 100 000 people with corresponding 95% uncertainty intervals (UIs). These were based on 1000 runs of the models for each quantity of interest, with the mean considered as the point estimate, and the 2.5th and 97.5th percentiles considered as the 95% UI. All ages were included for the overall rates, and male and female rates. Non-fatal estimates were obtained from systematic reviews, surveys, administrative health records, registries and disease surveillance systems. The specific data sources used for quantifying non-fatal outcomes are available online in the Global Burden of Disease Results Tool [6]. Non-fatal data were analysed using DisMod-MR version 2.1, a Bayesian meta-regression tool that adjusts data points for variations in study methods among different data sources. Fatal estimates were obtained from vital registration data (death records from the National Center for Health Statistics and population counts from the US Census Bureau). The single cause of death was determined using the *International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification*. Causes of death data were analysed using the Cause of Death Ensemble Model with corrections for changes in coding practices for underlying causes of death [7]. DALYs were calculated as the sum of years of life lost (YLL) and years of healthy life lost due to disability (YLD) for each cause. For each disease, the YLD is derived from the multiplication of the incidence by the duration of disability and a weight factor. To account for the co-occurrence of disease and injury outcomes, the YLD was corrected for comorbidity, assuming a multiplicative rather than additive function of disability weights. The YLL due to premature death was estimated by multiplying the death number for a given age and sex by the standard life expectancy. One DALY is equal to the loss of 1 year of healthy life from the combined impacts of death and disability. Since our study utilised existing data without patient identifiers, it did not require institutional review board approval. The Global Burden of Disease study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting recommendations.

In 2019, the crude and age-standardised case fatality rates in males were 4.0% (95% UI 2.6–4.4) and 3.8% (95% UI 2.4–4.2), respectively. In females, the crude and age-standardised case fatality rates were 2.7% (95% UI 1.5–3.0) and 2.2% (95% UI 1.3–2.5), respectively.

The age-specific prevalence of ILDs was noted to increase with increasing age, reaching the highest prevalence in the 80–84 years age group. In 2019, the prevalence in this age group per 100 000 in males was 1167 and in females was 983.5. The prevalence of ILDs was slightly lower in males until age 75 years and was higher compared to females in those over age 75 years. The age-specific DALYs rates and death rates also increased with increasing age in both males and females. However, the increase in DALYs rates and death rates were proportionally higher in males compared to females and therefore the difference widened with increasing age (data not shown).

In this study we provide a comprehensive report of the overall prevalence, burden and trends of ILDs in the USA. Our study shows that ILDs remain a significant cause of death and disability in the USA. In 2019, ILDs were present in 0.21% of the population and contributed to 0.39% of the total DALYs and 0.73% of the total deaths. Since 2010 the crude prevalence, DALY rates and death rates of ILDs in the USA have been increasing, but the age-standardised rates have been stable. Crude rates are reflective of the present disease state and are useful for policymakers and physicians, whereas age-standardised estimates allow comparison over time, adjusting for the differences in the age distribution of the population. This finding suggests that the increase in overall prevalence is primarily due to the increasing average age in the US population. Since smoking is a risk factor for idiopathic pulmonary fibrosis (IPF) and several other ILDs, the decline in smoking rates in the USA likely played a significant role in the stable age-standardised prevalence that was noted [8].

In our study, when stratified by age and gender, the prevalence of ILDs was similar for males and females until age 75 years. However, in those older than age 75 years, the prevalence trended toward higher rates in males than females. In addition, the DALYs and deaths seem to increase at a proportionally higher rate for males compared to females over the age of 65 years. This is likely due to a higher percentage of IPF patients among the older age group of patients with ILDs [9, 10]. In 2019, according to the US Centers for Disease Control and Prevention Wonder Underlying Cause of Death Database [11], the crude mortality rate from pulmonary fibrosis per 100 000 was 5.1 (95% CI 5.0–5.2) in males and 3.7 (95% CI 3.6–3.8) in females. Based on this, pulmonary fibrosis contributed to 69.8% of the deaths from ILDs in males and 62.7% in females. The percentage of ILD decedents with pulmonary fibrosis increased with age and was 59.4%, 74.2% and 79.4% in the 65–74 years age group, 75–84 years age group and those 85 years and older, respectively (data not shown).

The general limitations of the GBD study have been reported previously [7]. The limitations of our study include variability in the case definitions used to report ILDs, leading to potential misdiagnosis and under-diagnosis. The majority of data used to estimate prevalence is derived from hospital records and insurance claims which can be unreliable. Attributable risk factor analysis is not currently available for ILDs in the GBD data. The underlying aetiology of ILDs and stratification based on race are also not available in this data set.

This study provides comprehensive national estimates of the prevalence, mortality and DALY due to ILDs. Although age-standardised morbidity and mortality from ILDs have remained stable in the USA, the ILD ranking as the cause of death and DALY has worsened. Among the level three causes, ILD was ranked as 54th in DALYs in 2019, 58th in 2010 and 74th in 1990. Similarly, ILD was ranked 30th among causes of deaths in 2019, compared to 32nd in 2010 and 41st in 1990 [6]. This suggests that the allocation of resources to understand the risk factors for ILDs and to address the burden of disease remains inadequate. Increasing the awareness of the disease, expanding the availability of diagnostic equipment in less-developed areas and improving access to ILD specialised centres are crucial for early diagnosis and intervention.

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