Peer Review File

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Reviewer A

General Comments:
This manuscript presents a comprehensive analysis of the disease burden and future projections of interstitial lung disease (ILD) and pulmonary sarcoidosis (PS) in China from 1992 to 2021. The authors utilized large-scale data from the Global Burden of Disease Study and applied multiple statistical models, including Joinpoint regression, age-period-cohort (APC) analysis, and Bayesian APC modeling. The topic is timely and relevant, especially given the aging population in China and the increasing global burden of respiratory diseases.

However, the manuscript would benefit from several major revisions to improve clarity, methodological transparency, and language quality.

Major Comments:
1. Justification of Statistical Models
Please provide more explanation about why the three models (Joinpoint, APC, and Bayesian APC) were chosen and how their results complement each other. A comparison or discussion of their relative strengths would help readers better understand your approach.
Reply:
We have added more explanation on line 111-116 “Its core strength lies in its ability to detect statistically significant inflection points—time periods where the trend in prevalence or mortality rate changes direction or magnitude. This is particularly valuable in public health research, as it can highlight the potential impact of health policies, clinical guidelines, environmental exposures, or technological advancements(11).”, line 129-131 “This granularity is essential in understanding underlying epidemiological mechanisms and targeting interventions to specific age groups or cohorts.”, and line 148-150 “It is particularly advantageous for projecting age-standardized rates while accounting for uncertainty in parameter estimation.”

2. Prediction Accuracy and Uncertainty
While the future trends are clearly described, the prediction uncertainty (e.g., 95% uncertainty intervals) is not always shown in the figures. Please consider adding uncertainty bands and explaining their interpretation.
Reply:
We have added uncertainty bands the Figure 5, and explailine 89-93 “Uncertainty intervals (UIs) were generated for every metric using the 25th and 975th ordered 1000 draw values of the posterior distribution(10). The 95 % UI is the actual probability distribution around the true parameter value, i.e. 95 % of the possible values of the parameter are within the 95 % UI(11).”

3. Definition and Separation of ILD and PS
It is sometimes unclear whether pulmonary sarcoidosis is treated as part of ILD or a separate category. Please clearly define this relationship at the beginning and maintain consistent terminology throughout the text.
Reply:
We have defined the ILD and PS clearly, and we change the terminology throughout the text.

4. Figures and Supplementary Materials
Many figures, such as Figure 3 and Figure 4, are complex and difficult to interpret. Please improve the figure legends and provide clearer references to them in the main text. If possible, simplify the visual presentation or guide the reader more directly through the findings.
Reply:
We have added the clearer references to Figure 3 and Figure 4 in line 195-218. And we add some explanation in the Figure 3 and Figure 4 (Line 435-450).

Reviewer B

I have reviewed the manuscript titled "Disease burden of Interstitial Lung Disease from 1992 to 2021 and prediction of future disease burden trend in China."
I agree with the authors' assertion that age is a risk factor for increased incidence and mortality of ILD. However, several points require improvement.

I believe the manuscript would benefit from major revisions, as outlined below.

Major Comment:
Please clarify the rationale for separating pulmonary sarcoidosis from other forms of ILD.
Reply:
We have explained the reason in line 101-103 "Although pulmonary sarcoidosis is classified as a form of ILD, the Global Burden of Disease (GBD) database distinguishes pulmonary sarcoidosis as a separate category alongside ILD."

Minor Comments:
Although the authors focus on age, gender, and time period, it is important to note that ILD is often complicated by life-threatening comorbidities such as lung cancer, secondary pneumothorax, and pulmonary hypertension. I recommend briefly addressing this point in the Discussion section. The following article may be helpful to cite in that context and could serve as a reference for future perspectives:
• Kashizaki F, Matsumoto S, Miyasaka A, Tsuchiya N, Osada R, Kaneko M, Yumoto K, Chen H, Konishi K, Koizumi H, Takahashi K, Kaneko T. Effectiveness of upfront triple oral combination therapy with additional pirfenidone in a patient with severe pulmonary hypertension associated with lung diseases. Respirol Case Rep. 2024 Aug 26;12(8): e70010. doi: 10.1002/rcr2.70010. eCollection 2024 Aug.
Reply:
We have added discussion about comorbidities in line 238-241 "ILD and PS places a considerable burden on both patients and the healthcare system. It is frequently associated with serious complications such as pulmonary hypertension and secondary pneumothorax. The average medical cost per patient exceeds 3,700 euros."

Reviewer C

This manuscript provides insight on the burden of ILD in China but the timeframe from 1992-2021 raises concern of the validity of the diagnosis of ILD in such cases.

Comment: There have been several guidelines published within the last 10 years which have substantially shifted the standard of diagnosis of ILD rendering the findings of this study perhaps irrelevant.

Reply:

We sincerely thank the reviewer for the insightful comments regarding the diagnostic validity of interstitial lung disease (ILD) over the study period (1992–2021), and we fully acknowledge that diagnostic standards and clinical practice have evolved significantly over the past decade. However, we respectfully offer the following clarifications to support the rationale for our chosen timeframe and the continued relevance of our findings:

(1) Longitudinal case definition consistency: GBD 2021 uses fixed ICD-10 codes (J84.0–J84.9, D86.0–D86.9) across all study years. Historical data were systematically re-analyzed using uniform case definitions to ensure comparability (GBD 2021 methodology, Ref 10).

(2) Correction for under-ascertainment: GBD employs DisMod-MR 2.1, a Bayesian meta-regression tool, to model and correct for temporal variations in diagnostic sensitivity (e.g., lower detection rates in the 1990s vs. post-2010). This minimizes bias from improved diagnostics over time.

(3) Joinpoint analysis validation: Our model identified significant prevalence surges during 2005–2010 and 2019–2021 (APC = 5.50% and 2.54%, respectively), aligning with known periods of guideline updates and increased screening. This consistency supports the robustness of trend analysis.

(4) Value of Historical Trends for Public Health Planning

Understanding how ILD burden has evolved over a 30-year period provides critical insight for forecasting future needs and guiding health policy, particularly in regions, which is economically underdeveloped and facing a rapidly aging population. While recent guidelines are essential for clinical accuracy, public health planning requires broader historical context to allocate nursing and medical resources appropriately, especially when regional disparities exist.

Comment: In addition, the standard of care has changed in the last 10 years which makes it difficult to use these findings to generalize to the population today.

Reply:

We agree that therapeutic advances may alter disease outcomes. However, our study examines epidemiological burden (incidence, mortality) rather than treatment efficacy, and its conclusions remain relevant for three reasons:

(1) Mortality trends reflect care advancements: The 2.5% decline in age-standardized mortality rate (ASMR) observed in our data (1992–2021) aligns with global improvements in ILD management (Ref 4, 19). The rise in crude mortality (0.26 to 0.54/100,000) is primarily attributable to population aging—a finding robust to therapy changes.

(2) Projections account for period effects: Our Bayesian APC model incorporates temporal trends (e.g., healthcare access improvements) into forecasts. The predicted ASMR decline for 2021–2030 (Fig 5b) inherently accommodates ongoing therapeutic progress.

(3) Core drivers persist: Aging and environmental exposures (e.g., occupational hazards) remain dominant risk factors (RR > 3.0 for age 65–75 in APC analysis). These are unaffected by treatment standards and validate the study's public health relevance.

(4) We have added limitation about this study in discussion in line 306-311 "In addition, this study relies on GBD data, which standardizes historical records to ensure comparability across decades. Nevertheless, changes in diagnostic guidelines and therapies (e.g., antifibrotics) may affect temporal trends. The GBD corrects for under-diagnosis in early years, but residual bias cannot be excluded. Despite this, our models capture the fundamental drivers of ILD burden—

age demographics and environmental exposures—which remain relevant for public health planning. Future studies should integrate clinical data to refine subtype-specific burdens."