Reviewer A

The authors used data from the GBD to conduct this study. It was undeniable that there were many studies of disease burden like this one, including asthma. Therefore, the value of this study should be assessed from two perspectives.

Comment 1: Firstly, I think the authors should highlight in the introduction and discussion section how the burden of disease in the regions mentioned in this study differs from that in other regions of the world. I think this is a central part of the study, not just the process involved in analyzing the data. In short, the current manuscript was inadequate in its elaboration of this aspect.

Reply: We appreciate your valuable comment. We agree and have described the differences of burden among regions in the Introduction and Discussion section of the revised manuscript. As the reviewer said, it is important to discuss the difference of disease burden between regions mentioned in our study and other regions of the world. Although the focus of this article is mainly to describe and analyze the burden between the three East Asian countries, the comparison with other regions (i.e. Europe, America) should also be a central part. This may provide a deeper understanding of differences in the burden of asthma associated with geographical specificity.

Changes in the text:

Introduction S- The deaths of asthma have declined to varying degrees in all regions of the world, with the largest decline occurring in the high-income Asia Pacific region. And Oceania has the highest ASDALR, while East Asia has the lowest. East Asia is at a low level of asthma burden globally. (see Page 5-6, line 77-80)

Discussion S- This study systematically summarized the burden of asthma, its temporal trend and risk factors in China, South Korea and Japan from 1990 to 2019, as well as the predictions until 2030. The burden of asthma continued to decline in the world, but the incident cases, deaths and DALYs in South Korea were still high. (see Page 15, line 239-241)

Discussion S - The disease burden of asthma in the entire Asian region is at a low level from a global perspective. (see Page 15, line 244-245)

Discussion S - Compared to high-income countries in North America, South Korea, and Japan seem to have good asthma control. (see Page 15, line 249-250)

Discussion S - Although the burden of asthma has increased to some extent in North America and South Latin America, ASDALR has also significantly decreased. (see Page 15, line 252-254)

Comment 2: Second, the authors did an analysis of risk factors for asthma, which is commendable, but the statistical methods section is not sufficiently developed.

Reply: Thank you for pointing this out. Based on your suggestion, we have added more

details on the statistical analysis of risk factors in the revised manuscript. The revised content is as follow.

Changes in the text:　The risk factors for asthma were estimated based on the comparative risk assessment framework of the GBD Study 2019. We extracted data on major risk factors related to asthma, such as tobacco, metabolic factors, and environmental/occupational factors, and described the risk factor composition of ASIR and ASDALR between different genders. (see Page 8 line 118-121)

Comment: In summary, I think this study was acceptable in terms of design and processing, but I think the authors should have highlighted the geographical specificity mentioned in the manuscript and even more should have compared and described it in the discussion section in relation to other studies.

Reviewer B

Comment 1: 9.95 not -0.59, -76.30 not -5.22, -50.87 not -2.89.

Reply: We thank you for your comment. We have carefully reviewed the authenticity of the data based on your suggestions. There may be some misunderstanding between us regarding the values of AAPC (average annual percentage change) and PC (percentage change). The suggested data you provide is calculated using the formula: (a-b)/b ， where a refers to 2019 numbers, b represents 1990 numbers. Indeed, our original data is calculated using Joinpoint software for AAPC, average annual percentage change, and 95% CI. The natural logarithm of rate was assumed to be linear along with time; that is $Y = \alpha + \beta X + \varepsilon$, where Y refers to ln (rate), X represents year, and ε is the error, β represents the trend of the period segment. AAPC was calculated as $[(\text{Exp }(\beta)-1)] \times 100$, and its 95% CI was estimated by the linear model. Thus, the results of AAPC in the current version of the manuscript were correct. We hope that the reviewers can understand the expression of our original text.

Reference:

1. Clegg LX, Hankey BF, Tiwari R, et al. Estimating average annual per cent change in trend analysis. Stat Med. 2009; 28: 3670–3682.

2. Statistical Methodology and Applications Branch SRP, National Cancer Institute, Joinpoint Regression Program, Version 4.9.1.0. 2022.

Changes in the text: N/A

Comment 2: No test of statistical significance but 95% CI or UI.

Reply: Thank you for pointing this out. Although GBD 2019 raw data has indirect statistical P values, our manuscript has not directly used this statistical method. Based on your comment, we have deleted the sentences about the statistically significant.

Changes in the text:　Delete this sentence：p-value < 0.05 was considered statistically significant. (see Page 9, line 134-135)

Comment 3: The table shows a raised global incidence from 3216.32 to 3697.93.

Reply: We thank and agree with the reviewer's careful review. As you said, the global incidence of asthma showed an increasing trend from 1990-2019. To be clearer, we have modified the description of global burden based on your suggestion. The updated content is as follow.

Changes in the text: The incident cases, deaths, and DALYs of asthma showed a decreasing trend in China, South Korea and Japan from 1990–2019. And the incident cases, deaths of the world have a slow upward trend, but DALYs is still declining. (see Page 10, line 139-141)

Comment 4: The UI or CI should be from the small to the large.

Reply: We appreciate and agree with the reviewer's comment. Based on your suggestions, all the UI and CI have been corrected and ranged from the small to the large in the revised manuscript.

Changes in the text: −29.94%–−27.18. (see Page 10, line 146)

Comment 5: These PC are true but differ from those in table 2. The UI or CI should be from the small to the large：Compared with 1990, the changes were -9.95% (-6.95%~-12.08%), -76.30% (-80.32%~-73.77%) and -50.87% (-45.87%~-54.69%) (Table 2).

Reply: Thanks for your suggestions.

- There might be some misunderstandings about the two different values of AAPC and PC, which maybe lead to differences in our results. The main difference between PC and AAPC lies in the differences in calculation methods, which perform more detailed segmented calculations on the data. The data percentage changes in this sentence refer specifically to the changes in the objective values in the table from 1990 to 2019, not the AAPC values.

-We have validated the data based on your comments and modified all the UI or CI in the full text in descending order.

Changes in the text: Compared to 1990, the changes were −9.95% (−12.08%–−6.95%), −76.30% (−80.32–−73.77%), and −50.87% (−54.69–−45.87%) in 2019(Table 2). (see Page 10, line 156-157)

Comment 6: The sentence about both gender burden here is doubled with incorrect PC.

Reply: Thanks for your suggestion. We have carefully validated the authenticity of the data based on your suggestions. There may still have misunderstood due to differences in calculation formulas and methods between AAPC and PC. The data we describe here are AAPC, not just percentage changes.

Changes in the text: N/A.

Comment 7: Figures shows higher incidence number in the younger age group while death appears higher in the older population which is not cleared in the paragraph.

Reply: Thanks for your valuable suggestion. We agree and have added content that the

incidence of asthma in the younger was higher while the deaths appeared higher in the older, as the reviewer mentioned. The modified sentences were as follows.

Changes in the text: The younger have a high incidence in China, but the deaths of the elderly are relatively high. (see Page 11, line 174-175)

Comment 8: Such a fact needs a more confirmatory reference.

Reply: We appreciate your valuable comments. We have further searched the literature to supplement more convincing articles to verify this view based on the comments of the reviewers.

Changes in the text: In addition, the high morbidity of boys is partially due to the fact that the airway of adolescent boys is smaller than that of young girls, which is reversed after puberty (1-3). (see Page 16, line 271-273)

1. Baptist A P, Busse P J. Asthma Over the Age of 65: All's Well That Ends Well[J]. J Allergy Clin Immunol Pract, 2018, 6(3): 764-773.

2.Becklake MR, Kauffmann F. Gender differences in airway behaviour over the human life span. Thorax. 1999;54(12):1119-1138.

3. Wright AL. Epidemiology of asthma and recurrent wheeze in childhood. Clin Rev Allergy Immunol. 2002;22(1):33-44.

Comment 9: Named and numbered reference.

Reply: We thank you for your comments. We have carefully verified the naming rules and revised the format and other details according to the requirements of the journal.

Changes in the text: Baptist et al. (23) confirmed that asthma is a common occurrence among individuals > 65-years-old, and the elderly had a higher incidence and mortality than other age groups. (see Page 16-17, line 281-283)

Comment 10: These 2 figures represent the risk factors for DALY not for deaths as the subtitle present.

Reply: Thank you for your careful review. We apologize for this inaccuracy and have corrected the description of the subtitle in these figures.

Changes in the text: The subtitle of the Figure4（C-D）has been modified to read: age standardised DALY rate (per 100 000).
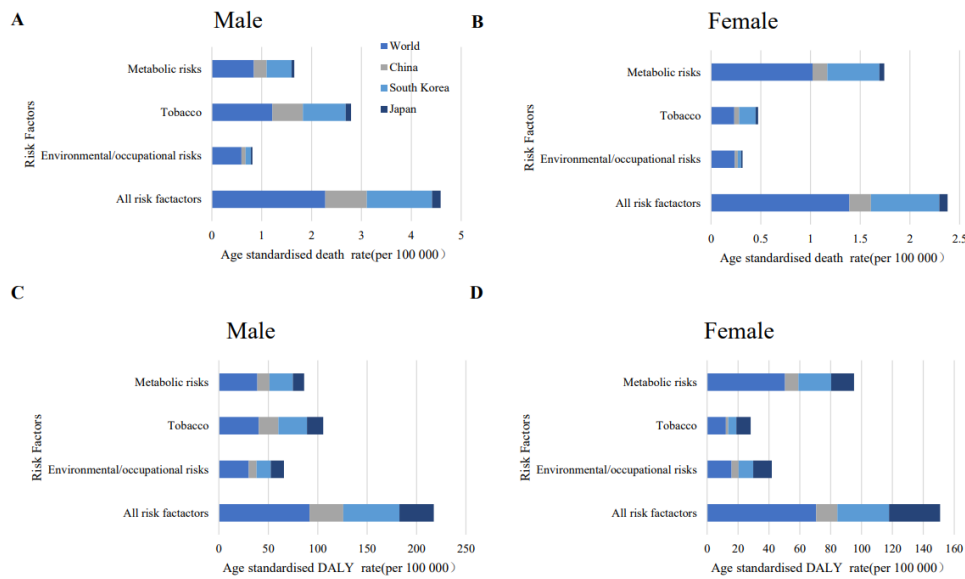
Figure 4 Risk factors distribution of asthma burden in China, South Korea, Japan, and the World. A Risk factors of male for the age-standardised death rate (per 100 000); B Risk factors of female for the age-standardised death rate (per 100 000); C Risk factors of male for the age-standardised DALY rate (per 100 000); D Risk factors of female for the age-standardised DALY rate (per 100 000). DALY: Disability-adjusted life year. Data Source: Global Burden of Disease Study 2019.

Reviewer C

This manuscript analyzed burden of asthma in Asian countries. Burden of asthma is important because asthma is a life-long chronic inflammatory disease. The authors analyzed the estimated incidence of asthma, death, and DALYs. The aim of the study is thought as appropriate and important. However, crude comparison of asthma incidence among the Asian countries, China, South Korea, and Japan, is considered as inappropriate.

First of all, diagnosis of asthma depends on ICD-10 codes. However, medical environment of each country is not same. For example, Korean investigators use additional information to make a diagnosis of asthma with ICD-10 code, such as prescription history of asthma medication. I think temporal change in same country could make a sense, but comparison between countries should be more careful. The accuracy of ICD-10 code in defining the diagnosis would be different according to diseases. I agree that there is no arguing point using ICD-10 code in analysis of cancer (ref.10) or other objective parameters. But, diagnosis of asthma is more complex, and the diagnosis of asthma with ICD-10 code might have limitations according to each countries reimbursement issue of medical cost, cultural variance, low insight of asthma, accessibility to health service, and etc. By supplement this limitation, it would be an

interesting and meaningful investigation.

Reply: We appreciate your valuable suggestions and agree the reviewer's point that the heterogeneity in the diagnosis of asthma among those countries may inevitably exist. Based on your suggestion, this limitation has been discussed in the revised manuscript. Indeed, the diagnosis of asthma is complex, as the reviewer mentioned. A diagnosis based solely on the ICD-10 code may be affected by potential bias due to the differences among countries, such as medical expense reimbursement issues, cultural variance, and insight into asthma, etc. In the setting, the comparison for disease burden of asthma between countries may need to be interpreted cautiously. Therefore, it may be more important to present the temporal change of burden in same country rather than emphasize their differences in the current study.

Changes in the text: And last, the based solely on the ICD-10 code may be affected by potential bias due to the differences among countries, such as medical expense reimbursement issues, cultural variance, and insight into asthma, etc. There may need to careful explain the comparison of asthma disease burden among countries. (see Page 18-19, line 324-327)