

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The burden of tobacco in Nepal: a systematic analysis from the Global Burden of Disease Study 1990-2017
AUTHORS	Shrestha, Gambhir; Phuyal, Prabin; Gautam, Rabin; Mulmi, Rashmi; Pradhan, Praniil

VERSION 1 – REVIEW

REVIEWER	Pokharel, Yashashwi Health Foundation Nepal, America Nepal Medical Foundation, Nepal, CV research
REVIEW RETURNED	24-Jan-2021

GENERAL COMMENTS	<p>Comments to the Authors</p> <p>The manuscript entitled, “The burden of tobacco in Nepal: a systematic analysis from the Global Burden of Disease Study 1990-2017” by Shrestha et al try to portray the smoking prevalence in 1990 vs 2015/2017 and also corresponding tobacco attributable death and DALY. While I am very appreciative of the effort by the authors for this important topic, several clarifications are needed to improve the content, interpretation and flow of the manuscript. These are outlined below. I hope the authors find them helpful and I encourage them to continue the important work. Thank you.</p> <p>Major Comments</p> <ol style="list-style-type: none">1. If tobacco use prevalence decreased over time, please explain the paradox of increasing tobacco-use related deaths over the same time period. The authors say, “One plausible explanation for this pattern could be the population growth in Nepal, 29 million in 2019 compared with 18.9 million in 1990” as one explanation.” This seems to be at odds, because it’s the proportion of deaths that is increasing and not necessarily absolute numbers of death.2. Perhaps it is more informative to show the prevalence of tobacco use each year from 1990 to 2015/2017 – for example as a bar graph (similar to what you have for Figure 1 now). This will also give some sense of the effect of Tobacco Control and Regulatory Bill from 2011? I suggest doing same for death and DALYs.3. The authors found decreasing trend for age-standardized death and DALY. This should be the main message as when standardized for age, tobacco related deaths and DALY decreased, mirroring the decreasing tobacco prevalence over the study period.4. Title of Figure 3 says the death is attributable to tobacco. I can’t decipher how diabetes or even TB related death is attributable to tobacco?
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	<p>5. The authors draw conclusion from crude rates. As authors know there are lots of potential confounders. For example, during the study period, there was massive increase in air pollution in most metro in the country. While I understand the authors may not have detail data to account for all confounders, they should recognize the limitations in the manuscript.</p> <p>6. The first two sentence of the first paragraph of the Discussion section hints to the limitations of the tobacco use related data in Nepal. Perhaps one of the most important messages is that there is a need for a robust and reliable data representative of all regions in Nepal. Even if there are effective tobacco cessation policies, without a robust and reliable data it will be difficult to understand the effects of such policies. There is important role of academia, government, industry and the international partners in such effort.</p> <p>7. In the limitations section, it will be helpful if the authors expand on the actual limitations of the GBD study itself.</p> <p>8. In the first sentence of the manuscript's conclusion authors say, "This study is one of the first studies in Nepal to show the effect of using tobacco on mortality and DALY" The study shows association and not effect. Please modify accordingly.</p> <p>Minor Comments</p> <ol style="list-style-type: none"> 1. Please correct English and grammar-related errors. 2. What does tobacco use, including any form, mean? In Methods section, please specify what kind of tobacco were used, eg., smoking, chewing tobacco, second-hand exposure etc. 3. Seeing the 3% DALY increase in conclusion of abstract without seeing it in the results section appears odd. Please show it in the results section of the abstract too. 4. The introduction section in the manuscript can be shortened without missing any major information. 5. Can you please show the latest data for the same year? For some parameters it is for 2015 and for other it is for 2017? If it has to be this way, please provide explanation. 6. How is NCD defined? 7. Is neoplasm defined as both benign and malignant or just malignancy? 8. The title of the strobe document at the end of the manuscript "Depression among Inmates in a Regional Prison of Eastern Nepal: A Cross-Sectional Study" is confusing.
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REVIEWER	Allebeck, Peter Karolinska Institutet
REVIEW RETURNED	26-Jan-2021

GENERAL COMMENTS	<p>While a descriptive national study, and thus perhaps limited international interest, it is still interesting to follow the development in a country with very high smoking prevalence, and that has implemented ambitious policy measured.</p> <p>Although data can be found by anyone in the GBD database, this is well packaged.</p> <p>The method should be described better, the sources used in the GBD study should be clarified, the measure of prevalence described (SIR or prevalence or both). A short summary of DALY estimation, referring rather to IHME and publications, rather than WHO for definition of the concept.</p> <p>Results are too detailed in both text and tables. The absolute numbers are less interesting, and tables should be be restricted to</p>
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	<p>age standardised data. Also tables do not need to list all figures on cause specific deaths and dalys. Tables become very clumsy and not reader friendly. The graphs give a good description of distribution by causes. Also the text can summarize shortly the distribution by causes.</p> <p>The development over time should better be visualized in a graph, and not only the beginning and the end of the period. This would enable comparison by year when measures were introduced.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1

6. Reviewer’s comment: If tobacco use prevalence decreased over time, please explain the paradox of increasing tobacco-use related deaths over the same time period. The authors say, “One plausible explanation for this pattern could be the population growth in Nepal, 29 million in 2019 compared with 18.9 million in 1990” as one explanation.” This seems to be at odds, because it’s the proportion of deaths that is increasing and not necessarily absolute numbers of death.

Authors’ reply: Thank you for picking up such an important point. We have now included only the age-standardized deaths and DALYs, which are also in decreasing trend. We have added, “In contrary to an overall decrease in the prevalence of tobacco use and age-standardized deaths and DALYs in both males and females in recent decades, the total deaths and DALYs were higher in 2017 compared with 1990.” (revised manuscript page number 15).

7. Reviewer’s comment: Perhaps it is more informative to show the prevalence of tobacco use each year from 1990 to 2015/2017 – for example as a bar graph (similar to what you have for Figure 1 now). This will also give some sense of the effect of Tobacco Control and Regulatory Bill from 2011? I suggest doing same for death and DALYs.

Authors’ reply: We have now shown the trend of prevalence of tobacco, deaths, and DALYs by year in figures 2 and 3.

8. Reviewer’s comment: The authors found decreasing trend for age-standardized death and DALY. This should be the main message as when standardized for age, tobacco related deaths and DALY decreased, mirroring the decreasing tobacco prevalence over the study period.

Authors’ reply: We agree upon it and have added it in the revised manuscript (Revised manuscript page number 15)

9. Reviewer’s comment: Title of Figure 3 says the death is attributable to tobacco. I can’t decipher how diabetes or even TB related death is attributable to tobacco?

Authors’ reply: This is according to GBD data. DM and TB low less contribute less on deaths attributable to tobacco. May we give the reason for it as tobacco smoking is a well-known risk factor of TB mycobacteria infection. Thus, the rate of active TB disease increases with tobacco smoking, which is believed to be the reason for increased mortality due to tuberculosis attributable to tobacco smoking. (<https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/411801> <https://academic.oup.com/aje/article/187/9/1846/4964691?login=true>). Tobacco smoking is also a well-known risk factor for diabetes and active tobacco smoking can aggravate the microvascular and macrovascular complications due to diabetes, thus increases the risk of mortality and morbidity among patients with diabetes.

(<https://www.sciencedirect.com/science/article/abs/pii/S0033062003000112> ,

<https://www.ahajournals.org/doi/full/10.1161/CIRCULATIONAHA.115.017926>)

10. Reviewer’s comment: The authors draw conclusion from crude rates. As authors know there are lots of potential confounders. For example, during the study period, there was massive increase in air pollution in most metro in the country. While I understand the authors may not have detail data to account for all confounders, they should recognize the limitations in the manuscript.

Authors' reply: Yes, we agree. We have incorporated the suggestions in the limitation part recognizing air pollution as one of the confounders in this study (revised manuscript page number 17).

11. Reviewer's comment: The first two sentence of the first paragraph of the Discussion section hints to the limitations of the tobacco use related data in Nepal. Perhaps one of the most important messages is that there is a need for a robust and reliable data representative of all regions in Nepal. Even if there are effective tobacco cessation policies, without a robust and reliable data it will be difficult to understand the effects of such policies. There is important role of academia, government, industry and the international partners in such effort.

Authors' reply: Thank you for a nice suggestion. We have incorporated it in the conclusion part (Revised manuscript page number 18).

12. Reviewer's comment: In the limitations section, it will be helpful if the authors expand on the actual limitations of the GBD study itself.

Authors' reply: The limitations of the study are rewritten explaining the actual limitations of the GBD study (Revised manuscript page number 17).

13. Reviewer's comment: In the first sentence of the manuscript's conclusion authors say, "This study is one of the first studies in Nepal to show the effect of using tobacco on mortality and DALY" The study shows association and not effect. Please modify accordingly.

Authors' reply: we have modified it as "This study is one of the first studies in Nepal to show the trend of mortality and DALY attributable to tobacco use." (Revised manuscript page number 17).

14. Reviewer's comment: Please correct English and grammar-related errors.

Authors' reply: We have aggressively checked and corrected the English of the manuscript to our best.

15. Reviewer's comment: What does tobacco use, including any form, mean? In Methods section, please specify what kind of tobacco were used, eg., smoking, chewing tobacco, second-hand exposure etc.

Authors' reply: Tobacco use in any form included smoking or smokeless tobacco or both. We have added it in Methods section (Revised Manuscript page number 6).

16. Reviewer's comment: Seeing the 3% DALY increase in conclusion of abstract without seeing it in the results section appears odd. Please show it in the results section of the abstract too.

Authors' reply: We have changed the entire abstract more focusing on the age-standardized findings as per the journal's format. (Revised manuscript page number 2).

17. Reviewer's comment: The introduction section in the manuscript can be shortened without missing any major information.

Authors' reply: We have shortened the introduction part (Revised manuscript page numbers 3 and 4).

18. Reviewer's comment: Can you please show the latest data for the same year? For some parameters it is for 2015 and for other it is for 2017? If it has to be this way, please provide explanation.

Authors' reply: The GBD provides data for only smoking up to the year 2015 while DALYs and Deaths data are available up to 2017 (Now 2019). We have mentioned it in the statistical analysis part (Revised manuscript page number 6).

19. Reviewer's comment: How is NCD defined?

Authors' reply: Non-communicable disease includes all the NCDs including diabetes and kidney diseases, and cancer, which are shown separately in the figure.

20. Reviewer's comment: Is neoplasm defined as both benign and malignant or just malignancy?

Authors' reply: Neoplasms included both benign and malignant tumors, now mentioned in the manuscript (Revised manuscript page number 5).

21. Reviewer's comment: The title of the strobe document at the end of the manuscript "Depression among Inmates in a Regional Prison of Eastern Nepal: A Cross-Sectional Study" is confusing.

Authors' reply: Thank you for picking up this mistake of mine. It is now corrected in the revised document.

Reviewer 2

1. Reviewer's comment: While a descriptive national study, and thus perhaps limited international interest, it is still interesting to follow the development in a country with very high smoking prevalence, and that has implemented ambitious policy measures.

Although data can be found by anyone in the GBD database, this is well packaged.

Authors' reply: Thank you for your encouraging words.

2. Reviewer's comment: The method should be described better, the sources used in the GBD study should be clarified, the measure of prevalence described (SIR or prevalence or both). A short summary of DALY estimation, referring rather to IHME and publications, rather than WHO for definition of the concept.

Authors' reply: We have described detailedly the sources of data in GBD, the calculation of DALYs according to the IHME (Revised manuscript page numbers 5 and 6). The measure of the prevalence of smoking is in the age-standardized form which is mentioned in the revised manuscript (Revised manuscript page numbers 2, 6 and 7).

3. Reviewer's comment: Results are too detailed in both text and tables. The absolute numbers are less interesting, and tables should be restricted to age-standardized data. Also tables do not need to list all figures on cause-specific deaths and DALYs. Tables become very clumsy and not reader-friendly. The graphs give a good description of distribution by causes. Also the text can summarize shortly the distribution by causes.

Authors' reply: We have restricted table 1 to age-standardized data (Revised Table 1). It will be interesting to show the data specific to cause-specific deaths and DALYs. We have shortened the summary of the results in the text. We have summarized the distribution by causes as "27,000 deaths are attributable to tobacco comprising of 90% deaths due to NCDs. Similarly, more than 702,000 DALYs were attributable to tobacco use comprising 89% DALYs for NCDs" (Revised manuscript page number 11).

4. Reviewer's comment: The development over time should better be visualized in a graph, and not only the beginning and the end of the period. This would enable comparison by year when measures were introduced.

Authors' reply: We have added two graphs for showing the prevalence of tobacco smoking (Revised figure 1) and age-standardized deaths and DALYs (Revised Figure 2) by year as suggested.