

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Lung cancer mortality in the wake of the changing smoking epidemic: a descriptive study of the global burden in 2020 and 2040
AUTHORS	Weber, Andras; Morgan, Eileen; Vignat, Jerome; Laversanne, Mathieu; Pizzato, Margherita; Runggay, Harriet; Singh, Deependra; Nagy, Péter; Kenessey, István; Soerjomataram, Isabelle; Bray, Freddie

VERSION 1 – REVIEW

REVIEWER	Barclay, Matthew University College London
REVIEW RETURNED	10-Aug-2022

GENERAL COMMENTS	<p>Thank you for inviting me to review this interesting descriptive study of lung cancer mortality globally, which highlights the narrowing gender gap in mortality due to lung cancer. While it does not really bring new information to the table, I found it an interesting read and felt the methods were likely to be suitable. My main concern is that the projections (that assume current age-specific incidence rates remain stable (or change predictably) for 18 years into the future) may be a little unreasonable, and that it will be important to give this some context through comparison with other efforts to project lung cancer mortality. With that said I view the paper as eminently suitable for publication in BMJ Open, with only some minor additions to the discussion.</p> <p>Major comments</p> <p>I would remove the words "case report" from the title, and consider adding "cross-sectional" instead.</p> <p>The results subtitle "Lung cancer mortality – national rankings 2020" might be better rephrased as "Lung cancer mortality compared with mortality from other causes, 2020".</p> <p>The discussion seems to be missing the context of relevant literature on cancer mortality projections. If there are other (perhaps jurisdiction-specific) projections of lung cancer incidence and mortality it would be interesting to discuss how and whether these projections agreed or disagreed with GLOBOCAN</p>
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	<p>projections. For example, I know there is work by Smittenaar and colleagues that produces projections for the UK up to 2035 (doi: 10.1038/bjc.2016.304), while Rahib and colleagues present projections for US lung cancer incidence and mortality up to 2040 (doi:10.1001/jamanetworkopen.2021.4708). There are likely similar studies for other high HDI nations, and it will be interesting to understand if these give similar results to the GLOBOCAN projections. In particular, whether approaches like Smittenaar et al that attempt to measure trends in age-specific incidence as well as demographic changes give similar results to GLOBOCAN projections.</p> <p>Comparisons with other projections of lung cancer mortality will help in adding the key limitation to the discussion of the paper: the fact that the projections are based on existing incidence rates and do not take into account, for example, the impact that any changes in tobacco smoking may have. This is by no means a fatal flaw, but it is important to clearly set out this limitation in the discussion.</p> <p>I note that a major policy recommendation is to focus tobacco control strategies in EU nations on women (discussion, page 7, lines 40-45). I wonder to what extent this is already the case? Looking at the UK plan, I suspect it is not currently a major focus except for reducing smoking in pregnancy, and it would be useful to give this context for a few exemplar nations. It would be useful to understand whether this is something currently being done, that should be continued, or whether this is currently a missing plank in many high-HDI countries tobacco control policies.</p> <p>I have less insight into current tobacco control strategies in lower HDI countries, but again when making recommendations about focus on educational programmes in schools it may be useful to understand the extent to which these already exist. A comprehensive review is likely impossible, but it would be useful context to know if there are lower HDI countries that are already trying to implement this or if there are lower HDI countries that are not.</p> <p>Additionally, the possible role of e-cigarettes is not addressed, even to discuss research into their possible harms or benefits, which seems an odd omission for a modern discussion of tobacco control policies.</p> <p>Minor points</p> <p>Page 6, lines 21-24. It may make sense to use the specific HDI terms rather than synonyms throughout, to avoid possible confusion. In particular, 'transitioning' seems to be being used for both low or medium HDI countries and high or very high HDI countries.</p>
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REVIEWER	Samet, Jonathan University of Colorado Denver
REVIEW RETURNED	24-Aug-2022

GENERAL COMMENTS	This manuscript presents a one-year snapshot of lung cancer mortality globally. The general patterns described are well known and could be gleaned from GloboCan. The straightforward description provided in this paper might be useful to some, but does not bring new insights. The forward projections to 2040 are
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	<p>based on assumed scenarios of constant percentages of increase or decrease, admittedly unrealistic. Could the authors address what are the more likely scenarios in different HDI contexts?</p> <p>The abstract indicates that the findings will be discussed in relation to past tobacco control initiatives. Some perspective on global trends would improve the manuscript, perhaps drawing on the Global Tobacco Control Report and the Tobacco Atlas.</p> <p>Any revision should provide a stronger foundation for interpreting the results and using them to consider lung cancer prevention strategies.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Matthew Barclay, University College London

Comments to the Author:

Thank you for inviting me to review this interesting descriptive study of lung cancer mortality globally, which highlights the narrowing gender gap in mortality due to lung cancer. While it does not really bring new information to the table, I found it an interesting read and felt the methods were likely to be suitable. My main concern is that the projections (that assume current age-specific incidence rates remain stable (or change predictably) for 18 years into the future) may be a little unreasonable, and that it will be important to give this some context through comparison with other efforts to project lung cancer mortality.

With that said I view the paper as eminently suitable for publication in BMJ Open, with only some minor additions to the discussion.

We thank the reviewer for their interest in our manuscript and for their comment. We have provided further context to the prediction analysis in the Discussion, page 7.

Major comments

I would remove the words "case report" from the title, and consider adding "cross-sectional" instead.

We thank the reviewer for their comment and we have made amendments – for the subtitle, we agree the present case report is incorrect, but would prefer “descriptive study”.

The results subtitle “Lung cancer mortality – national rankings 2020” might be better rephrased as “Lung cancer mortality compared with mortality from other causes, 2020”.

Thank you for the comment, we agree and corrected the mentioned subtitle.

The discussion seems to be missing the context of relevant literature on cancer mortality projections. Thank you for the comment. We agree with the reviewers’ comment that the paper would be improved by including the context of relevant literature on cancer mortality projections. We have included the additional relevant literature in the Discussion on page 7.

If there are other (perhaps jurisdiction-specific) projections of lung cancer incidence and mortality it would be interesting to discuss how and whether these projections agreed or disagreed with GLOBOCAN projections. For example, I know there is work by Smittenaar and colleagues that produces projections for the UK up to 2035 (doi: 10.1038/bjc.2016.304), while Rahib and colleagues present projections for US lung cancer incidence and mortality up to 2040 (doi:10.1001/jamanetworkopen.2021.4708). There are likely similar studies for other high HDI nations, and it will be interesting to understand if these give similar results to the GLOBOCAN projections. In

particular, whether approaches like Smittenaar et al that attempt to measure trends in age-specific incidence as well as demographic changes give similar results to GLOBOCAN projections.

Thank you for the valuable remark. All GLOBOCAN estimations for 2020 and projections until 2040 broken down by populations, cancer types and regions can be found on the GLOBOCAN website ("Cancer Tomorrow," n.d.). We collected all the values belonging to the reviewer's useful proposal and displayed in the table below.

Table: Number of lung cancer deaths by sex and sources

Source	Year	Year	Change in %	
Smittenaar et al. (Smittenaar et al., 2016)	2014	2035		
Male	19,563	22,226	+14%	
Female	16,331	19,604	+20%	
GLOBOCAN UK	2020	2040		
0% change in rates per year scenario	Male	19,109	27,142	+42%
Female	17,409	23,014	+32%	
Rahib et al. (Rahib et al., n.d.)	2020	2040		
Male	69,000	29,000	-58%	
Female	61,000	34,000	-44%	
GLOBOCAN US	2020	2040		
0% change in rates per year scenario	Male	73,009	108,049	+48%
Female	65,216	92,350	+42%	

Briefly based on the main theories and history of the global smoking epidemic, in very high HDI countries men's lung cancer mortality should clearly decrease, while women's should increase or stagnate recently (or later decrease in vanguard countries) in the near future (Lopez et al., 1994). Obviously, some countries might differ from the general model (Janssen et al., 2020). Moreover, rapidly ageing population age structures can have impact on these non-standardized figures as well. According to the comparison (Table), only Rahib et. al. meet somewhat these conditions and as far as we experienced none of the forecasts took into account the changing smoking prevalence in the past as a key determinant of lung cancers. However, our results provide a solution to this problem by presenting possible scenarios, on a greater geographical (by HDI level) scale, so it is somewhat generalizing. For men, death rates with annually decreasing age-specific rates are more typical (-3%, -2%, -1%), while for women these are more likely to increase (1%, 2%, 3%) or stagnate (0%) (or moderately decrease in pioneering countries with advanced stage in anti-tobacco strategies, such as the USA) in the future, in case of very high HDI countries.

Comparisons with other projections of lung cancer mortality will help in adding the key limitation to the discussion of the paper: the fact that the projections are based on existing incidence rates and do not take into account, for example, the impact that any changes in tobacco smoking may have. This is by no means a fatal flaw, but it is important to clearly set out this limitation in the discussion.

Thank you for the comment. We agree with the reviewer's comment that it would be helpful to compare with other research on lung cancer projections and include these comparisons in the updated manuscript, page 7-8. We also highlight in the discussion that our own projections do not take into account changes in tobacco smoking patterns and are based on population ageing and growth.

I note that a major policy recommendation is to focus tobacco control strategies in EU nations on women (discussion, page 7, lines 40-45). I wonder to what extent this is already the case? Looking at the UK plan, I suspect it is not currently a major focus except for reducing smoking in pregnancy, and it would be useful to give this context for a few exemplar nations. It would be useful to understand whether this is something currently being done, that should be continued, or whether this is currently a missing plank in many high-HDI countries tobacco control policies.

We thank the reviewer for their comment and agree that it would be important to clarify where and what tobacco control strategies are already ongoing and where there is a need to be implemented to reduce smoking in women. Examining the most recent and official guidelines of the European tobacco control (The European report on tobacco control policy - Review of implementation of the Third Action Plan for a Tobacco-free Europe 1997–2001 (World Health Organization Regional Office for Europe, n.d.) and European Strategy for Tobacco Control, 2002 (World Health Organization, 2002)), both documents draw attention to the particularly vulnerable situation of women in terms of smoking, but not recommend any targeted measures for them. In the publication: Women and the tobacco epidemic. Challenges for the 21st century by Dr Jonathan Samet and Dr Soon-Young Yoon (Jonathan Samet and Soon-Young Yoon, 2001) there is much more to learn about this. For instance, in Sweden, some policies, such as those directed at health promotion, have been implemented in a gender-specific way. Pregnant women have been identified as a focus, but also young women. Furthermore, Scotland also has gender-specific programs, such as the Women, Low Income, and Smoking Project. From these reports it appears that tobacco control programs in some EU countries are currently ongoing, should be continued and expand to as many countries as possible. We include this clarification in the Discussion on page 8.

I have less insight into current tobacco control strategies in lower HDI countries, but again when making recommendations about focus on educational programs in schools it may be useful to understand the extent to which these already exist. A comprehensive review is likely impossible, but it would be useful context to know if there are lower HDI countries that are already trying to implement this or if there are lower HDI countries that are not.

We thank the reviewer for highlighting the need to examine where such recommendations are already being undertaken. We have found that according to Dai et al., Brazil is an exemplar nation where reductions in smoking prevalence were observed after the ratification of the WHO Framework Convention on Tobacco Control (FCTC) in 2005, through the implementation of a national ban on tobacco advertising, a national comprehensive smoke-free policy, large pictorial health warnings on cigarette packages, and continuous raises in taxes and prices of tobacco products. (Dai et al., 2022). We include Brazil as an example for other lower HDI countries of programs that are already being implemented on page 8.

Additionally, the possible role of e-cigarettes is not addressed, even to discuss research into their possible harms or benefits, which seems an odd omission for a modern discussion of tobacco control policies.

Thank you for the comment. We agree with the reviewer that the role of e-cigarettes would be worth mentioning and have included this in our Discussion on page 8.

Minor points

Page 6, lines 21-24. It may make sense to use the specific HDI terms rather than synonyms throughout, to avoid possible confusion. In particular, 'transitioning' seems to be being used for both low or medium HDI countries and high or very high HDI countries.

We thank the reviewer for highlighting this discrepancy which has now been corrected in the updated manuscript.

Reviewer: 2

Dr. Jonathan Samet, University of Colorado Denver

Comments to the Author:

This manuscript presents a one-year snapshot of lung cancer mortality globally. The general patterns described are well known and could be gleaned from GloboCan. The straightforward description provided in this paper might be useful to some, but does not bring new insights. The forward

projections to 2040 are based on assumed scenarios of constant percentages of increase or decrease, admittedly unrealistic.

We thank the reviewer for their insights and appreciate their concerns with the projections' methodology. We have now included a separate paragraph in the discussion section of the updated manuscript to explain the use of the scenarios for predictions.

Could the authors address what are the more likely scenarios in different HDI contexts?

We thank the reviewer for suggesting this very important perspective. In very high HDI countries for men, death rates with annually decreasing age-specific rates are more likely (-3%, -2%, -1%), while for women they are likely to increase (1%, 2%, 3%) or stagnate (0%) or moderately decrease in pioneering countries such as the USA in the future. It appears that generally, as the HDI level decreases, the implemented anti-tobacco strategies also decrease. Consequently, in the case of men, this is likely to increase the number of deaths caused by lung cancer in the future in lower HDI countries. The situation may be similar for women; however, this also depends on the local strength of traditional gender roles. We have added some clarity on this in the text, starting on page 6.

The abstract indicates that the findings will be discussed in relation to past tobacco control initiatives. Some perspective on global trends would improve the manuscript, perhaps drawing on the Global Tobacco Control Report and the Tobacco Atlas. Any revision should provide a stronger foundation for interpreting the results and using them to consider lung cancer prevention strategies.

We thank the reviewer for their comment and agree that including discussions on global trends of tobacco use would be highly relevant and improve the manuscript. We include further discussion around historic global tobacco trends using the advised reports and the impact this could have on future lung cancer incidence and mortality in page 6.

VERSION 2 – REVIEW

REVIEWER	Ashbury, Fredrick PICEPS Consultants, Inc.
REVIEW RETURNED	15-Feb-2023

GENERAL COMMENTS	<p>The authors have attended to reviewers' comments competently and the quality of writing has improved considerably. I believe the journal's copy-edit process will take care of any remaining minor grammatical/sentence structure issues.</p> <p>There is one additional concept that I would like the authors to address, please. A key concern in health promotion/cancer prevention is the extent to which middle-income and lower-income countries have adequate financial and trained resources to deploy these interventions to mitigate risk. I suggest that the authors at least comment on this issue in the discussion section. Lung cancer rates in these countries will continue to persist (even worsen), as tobacco companies will continue to shift and escalate their campaigns to preserve business interests and profits where resistance efforts are weakest.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 3

Dr. Fredrick Ashbury, PICEPS Consultants, Inc.

Comments to the Author:

The authors have attended to reviewers' comments competently and the quality of writing has improved considerably. I believe the journal's copy-edit process will take care of any remaining minor

grammatical/sentence structure issues.

There is one additional concept that I would like the authors to address, please. A key concern in health promotion/cancer prevention is the extent to which middle-income and lower-income countries have adequate financial and trained resources to deploy these interventions to mitigate risk. I suggest that the authors at least comment on this issue in the discussion section. Lung cancer rates in these countries will continue to persist (even worsen), as tobacco companies will continue to shift and escalate their campaigns to preserve business interests and profits where resistance efforts are weakest.

We thank the Reviewer for suggesting this very important perspective and we included this concept into our research between rows 240-244: *“One key concern is the limited financial and trained resources in middle- and lower-income countries, that can hinder health promotion and cancer prevention strategies in these countries. Based on our findings, decreases in lung cancer rates are not likely in these countries until 2040 and presumably tobacco companies are expected to shift and escalate promotional campaigns to preserve business interests and profits where resistance efforts are the weakest [30].”*