PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A review of drug recalls and quality of pharmaceutical products in Nepal
AUTHORS	Neupane, Astha; Bastakoti, Maheshwor; Tamang, Sabita; Giri, Basant

VERSION 1 – REVIEW

REVIEWER	Naughton, Bernard University of Oxford Said Business School
REVIEW RETURNED	19-Jul-2021

GENERAL COMMENTS	This was a clearly written paper which was easy to understand. This article may be useful as a tool to raise awareness of the issue of SF medicines in Nepal. It has also been written for a general audience, which is a positive in my opinion. Please find below my comments listed according to authors line numbering system. My comments are provided to help the authors to improve the overall quality of the paper. Of course, I do not expect the authors to take all of my comments on board, and I welcome any logical counterarguments or corrections to my remarks. Abstract Title: This study title concerns the incidences of poor-quality medicine in Nepal. In my opinion, using this studies data to estimate the prevalence or incidence of national medicine quality is inappropriate because these recalls only reflect poor quality medicines identified by the regulator. Therefore, the title should contain the specific boundary conditions of the study. Perhaps a tittle of ' The Recall of Poor Quality Pharmaceutical Products in Nepal' may be more suitable? Line 34: Participants. As this study does not contain participants. I suggest that the authors include a line that says 'This study did not contain participants. However, data was collected from 72 drug recalls and 4 research papers', or something similar to that effect. Line 41: What is the value in comparing different classes of drugs and how often they were recalled using statistics? What does that tell us? It certainly doesn't convincingly support an argument that one group of medicines is more likely to be poor quality than another, does it? Instead, I think it would be best to use descriptive statistics throughout and to explain why this data cannot be compared. Line 50: 'The substandard and/or falsified drugs….threaten health of population'. That is not a conclusion of this study. The conclusions should be based on the data from the study i.e. the conclusions should focus on drug recalls.

	Line 52: Also, you do not know that cases of SF medicines are increasing more generally within Nepal as the data presented in this study is a specific subset of poor quality medicines i.e. recalls by the regulator. The studies boundary conditions need to be more specific and the conclusions should be contained within these boundary conditions. Line 53-55: I agree with this statement, but it seems to be contrary to lines line 52. Strengths and limitations of this study: I do not believe that it is appropriate to say that SF medicines have increased significantly. Recalls have increased but we don't know if that's because the regulator is providing more resources to identify them, or because the problem is worsening. There could be several reasons. It doesn't mean that there are more SF medicines in circulation in Nepal more generally. It only means the regulator has found more. Line 72-76: The authors include statistics about the prevalence of poor quality medicine. However, this data is slightly misleading. Please read the paper by McManus & Naughton 2020 in BMJ Global health https://gh.bmj.com/content/5/8/e002393 which describes the limitations of sampling studies and systematic reviews to provide estimates. I think this paper and others by Mackey et al 2018 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2696502 add value and balance to the use of poor quality medicine prevalence estimates. Line 78: Should this be 'a major producer' instead of 'the major producer'. Line 92-94: From my understanding, you found that drug recalls increased in Nepal. I am not convinced that your study shows that low quality drugs in general have increased, and I cannot see how an increase in drug recalls equates to a 'significant increase' in SF medicines more generally. Methodology: There was a study conducted by Almuzaini et al in 2013 which looked at a similar issue in the UK https://bmjopen.bmj.com/content/3/7/e002924 . They used a more thorough and detailed methodology. Why have the authors not used that approach or even referenced it? Good papers usually appreciate the existing, relevant literature, in the field. To see this paper left out is unusual. You do not have to use the approach my Almuzaini but I would expect you to provide a statement regarding why you chose not to use it i.e. identify its limitations. That would build upon the Almuzaini methodology and propel the field forward. Results Line 134-136: It is fine to say that recalls increased significantly but why is that important and does it tell us anything new or interesting? Discussion Line 219-270: I found these lines and much of the discussion in general to be largely unrelated to the study's findings. I suggest the authors either provide a better explanation regarding why the information contained in the discussion is related to the study findings, or perhaps consider significantly reducing this text. In my view, the

	discussion should be based upon the study findings and literature which contributes to the study findings. Conclusion Line 333-335: I do not think that this is a conclusion of your study. Line 340-341: Is this a conclusion? The idea of a systematic review to understand the prevalence of SF medicines, as mentioned previously, is contested and has its limitations. I suggest you discuss this in the body of your article before making it a conclusion.

REVIEWER	Hodges, Sarah University of Warwick, Department of History
REVIEW RETURNED	27-Jul-2021

GENERAL COMMENTS	The greatest strength of this article is its approach: it uses original data collected from the Nepali Drug Development Administration (DDA) regarding recalled pharmaceutical products in Nepal during the period 2010-2020 in order to speculate about the overall quality of pharmaceuticals in Nepal. There is additional data in terms of a systematic review, but it was less clear what the aim of incorporating this data was, and how and why it served as an instructive counterpoint for the Nepali DDA recall data. Another great strength of the research design is Nepal itself: it is literally sandwiched between two of the world's largest pharma producers: India and Nepal. Although they don't really have data to show that Indian and Chinese pharmaceuticals dominate in Nepal, the pharmaceutical geopolitics are nevertheless tantalizing to contemplate. I am familiar with the scholarship that they use to claim that India produces poor quality drugs, and would add that it is not based on solid evidence (and indeed the 35% of the world's counterfeit drugs factoid has been heavily criticized and indeed disavowed by the WHO). Nevertheless, analysing recall data strike me as a potentially very robust starting point for understanding pharmaceutical quality on a national level. However, the authors draw a number of inferences unsupported by clear evidence that they infelicitously refer to as 'conclusions'. In particular, they write that 'substandard and/or falsified drugs that do not meet regulatory standards and quality threaten the health of population putting patients' life in danger leading to socio-economic hardship" is not supported by their data. They explain that the largest pool of recalled drugs were 'unregistered.' This means that the paperwork was not correct. This also means (based on their presentation of data) that there was no pharmacological evaluation of this, the largest category of recalled drugs. Problems with paperwork constitute a violation, but it is a very different claim from a claim of safety. It is certainly the case that the 'drug security' paradigm that has come to dominate pharmaco-vigilance since the early 2000s has focused scholarly and policy attention on intellectual property and other paperwork violations, at the expense of chemical analyses of safety. Nevertheless, surely there is nothing to be gained by reproducing this evidence-free conflation in our scholarship. Additionally, there is interesting data that describes how different kinds of recalled drugs were found in Nepal's government hospitals because of peculiar procurement practices. Another interesting bit of data pointed to physicians' and pharmacists' idiosyncratic dispensing as undermining drugs quality / value for

	money. However intriguing this data is, however, it does not suggest that these drugs in and of themselves constitute a health danger (as the authors claim in the conclusion). Rather, that there are non-standard practices among health professionals. This, too, strikes me as better belonging in a different article different to the one under review. I also found the hand sanitizer data interesting, but inapposite. Unless I am mistaken, hand sanitizer is neither an essential drug (of Nepal or anywhere) nor is it a pharmaceutical at all. This data belongs in a different article.

REVIEWER	Joda, Arinola University of Lagos, Clinical Pharmacy & Biopharmacy Department, Faculty of Pharmacy
REVIEW RETURNED	13-Aug-2021

GENERAL COMMENTS	I would suggest that the title be amended to read 'Assessment of Pattern of Drug Recalls and Quality of Pharmaceutical Products in Nepal. I felt constrained to convert this article to an editable format and so I used an online pdf2doc app to convert it so I could document corrections, comments and other issues I had with the article. On the whole the study is good and information made available contributes significantly to knowledge. However, I will not be able to live with myself if I eventually see this article in print with corrections I should have made not addressed because nobody eventually pointed them out to the author and there was no way to get this done using the closed ended options provided in the review template. I would also like to add to the editor that options should be provided for some elaboration on the review questions to enable more information to be shared. In a lot of cases a simple yes or no does not tell the full story, no, not by a long shot.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Mr. Bernard Naughton, University of Oxford Said Business School, Oxford University Hospitals NHS Foundation Trust
Comments to the Author:
Dear Authors,

This was a clearly written paper which was easy to understand. This article may be useful as a tool to raise awareness of the issue of SF medicines in Nepal. It has also been written for a general audience, which is a positive in my opinion. Please find below my comments listed according to authors line numbering system. My comments are provided to help the authors to improve the overall quality of the paper. Of course, I do not expect the authors to take all of my comments on board, and I welcome any logical counterarguments or corrections to my remarks.

Thank you so much. Your comments and feedbacks have helped to improve the quality of the paper. Really appreciated.

Abstract

Title: This study title concerns the incidences of poor-quality medicine in Nepal. In my opinion, using this studies data to estimate the prevalence or incidence of national medicine quality is inappropriate because these recalls only reflect poor quality medicines identified by the regulator. Therefore, the title should contain the specific boundary conditions of the study. Perhaps a tittle of ' The Recall of Poor Quality Pharmaceutical Products in Nepal' may be more suitable?

We have revised the title as "*Pattern of drug recalls and quality of pharmaceutical products in Nepal".*

Thank you for the suggestion.

Line 34: Participants. As this study does not contain participants. I suggest that the authors include a line that says 'This study did not contain participants. However, data was collected from 72 drug recalls and 4 research papers', or something similar to that effect.

The sentence has been revised incorporating your suggestion.

Line 41: What is the value in comparing different classes of drugs and how often they were recalled using statistics? What does that tell us? It certainly doesn't convincingly support an argument that one group of medicines is more likely to be poor quality than another, does it? Instead, I think it would be best to use descriptive statistics throughout and to explain why this data cannot be compared.

It is a common practice to report classes of substandard and counterfeited drugs in journal articles. We believe that it is important to understand the classes of drugs that are more counterfeited and recalled. Therefore, we also looked at the pattern of recalls for different classes of drugs. It helps to understand which types of drugs are being recalled more or less.

Line 50: 'The substandard and/or falsified drugs….threaten health of population'. That is not a conclusion of this study. The conclusions should be based on the data from the study i.e. the conclusions should focus on drug recalls.

The sentence has been deleted.

Line 52: Also, you do not know that cases of SF medicines are increasing more generally within Nepal as the data presented in this study is a specific subset of poor quality medicines i.e. recalls by the regulator. The studies boundary conditions need to be more specific and the conclusions should be contained within these boundary conditions.

Instead of writing *increase in substandard and fake drugs*, we have now rephrased as *increase in the recalls of substandard and fake drugs* to better describe our work. (*see* second sentence of Conclusion section of abstract)

Line 53-55: I agree with this statement, but it seems to be contrary to lines line 52.

Line 52 has been rephrased as *increase in the recalls of substandard and fake drugs.*

Strengths and limitations of this study: I do not believe that it is appropriate to say that SF medicines

have increased significantly. Recalls have increased but we don't know if that's because the regulator is providing more resources to identify them, or because the problem is worsening. There could be several reasons. It doesn't mean that there are more SF medicines in circulation in Nepal more generally. It only means the regulator has found more.

We agree with your views. We had clearly mentioned in conclusion section (page 17). But looks like in some places it created confusion. We have now rephrased the narration to make it clear just like in rephrased line 52.

Line 72-76: The authors include statistics about the prevalence of poor quality medicine. However, this data is slightly misleading. Please read the paper by McManus & Naughton 2020 in BMJ Global health https://gh.bmj.com/content/5/8/e002393 which describes the limitations of sampling studies and systematic reviews to provide estimates. I think this paper and others by Mackey et al 2018 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2696502 add value and balance to the use of poor quality medicine prevalence estimates.
We note the concerns raised by MacManus and Naughton regarding sample collection methods and systematic review process. We also agree that there are some disagreements in these topics among researchers. Our work involved analyzing drug recall notices in this manuscript. We have cited previously published papers regarding prevalence of poor-quality medicines that may have used different methodology than suggested by MacManus and Naughton. In future studies involving sample collection and systematic review, we will consider the points raised ManManus and Naughton. Thank you for the suggestion.

Line 78: Should this be 'a major producer' instead of 'the major producer'.
Corrected

Line 92-94: From my understanding, you found that drug recalls increased in Nepal. I am not convinced that your study shows that low quality drugs in general have increased, and I cannot see how an increase in drug recalls equates to a 'significant increase' in SF medicines more generally.

We have rephrased *increase of low-quality drugs to increase in recalls of low-quality drugs*.

Methodology: There was a study conducted by Almuzaini et al in 2013 which looked at a similar issue in the UK https://bmjopen.bmj.com/content/3/7/e002924 . They used a more thorough and detailed methodology. Why have the authors not used that approach or even referenced it? Good papers usually appreciate the existing, relevant literature, in the field. To see this paper left out is unusual. You do not have to use the approach my Almuzaini but I would expect you to provide a statement regarding why you chose not to use it i.e. identify its limitations. That would build upon the Almuzaini methodology and propel the field forward.

We somehow missed this paper by Almuzaini in our earlier version of the manuscript. Now we have cited their paper. Thank you for pointing this out.

Results
Line 134-136: It is fine to say that recalls increased significantly but why is that important and does it tell us anything new or interesting?

Increase in drug recalls is important as it may tell that the regulating agency has become more vigilant or there may be increasing awareness among public about the fake drugs. It is a new thing in Nepal.

Discussion
Line 219-270: I found these lines and much of the discussion in general to be largely unrelated to the study's findings. I suggest the authors either provide a better explanation regarding why the information contained in the discussion is related to the study findings, or perhaps consider significantly reducing this text. In my view, the discussion should be based upon the study findings and literature which contributes to the study findings.

We agree with your opinion that discussion should be based on the study findings and literature which contributes to the study findings. In the discussion section we aimed to provide explanation of our work with taking reference to other related works on drug quality. We believe that the discussion section in our manuscript is needed to fully understand the results of our work and why we carried out this work.

Conclusion
Line 333-335: I do not think that this is a conclusion of your study.

These lines are removed.

Line 340-341: Is this a conclusion? The idea of a systematic review to understand the prevalence of SF medicines, as mentioned previously, is contested and has its limitations. I suggest you discuss this in the body of your article before making it a conclusion.

We are referring not to systematic literature review but to original research on drug quality. The sentence has been rephrased as: Therefore, more studies are needed ……

Reviewer: 2
Prof. Sarah Hodges, University of Warwick
Comments to the Author:
The greatest strength of this article is its approach: it uses original data collected from the Nepali Drug Development Administration (DDA) regarding recalled pharmaceutical products in Nepal during the period 2010-2020 in order to speculate about the overall quality of pharmaceuticals in Nepal. There is additional data in terms of a systematic review, but it was less clear what the aim of incorporating this data was, and how and why it served as an instructive counterpoint for the Nepali DDA recall data.

Dear Dr. Hodges,

Thank you so much reading our manuscript and providing your comments.

We wanted to put together all the available information on the drug quality. Therefore, we combined both recalled data made available by the Government and academic research data published in journals.

Another great strength of the research design is Nepal itself: it is literally sandwiched between two of the world's largest pharma producers: India and Nepal. Although they don't really have data to show that Indian and Chinese pharmaceuticals dominate in Nepal, the pharmaceutical geopolitics are nevertheless tantalizing to contemplate. I am familiar with the scholarship that they use to claim that India produces poor quality drugs, and would add that it is not based on solid evidence (and indeed the 35% of the world's counterfeit drugs factoid has been heavily criticized and indeed disavowed by the WHO).

Nevertheless, analysing recall data strike me as a potentially very robust starting point for understanding pharmaceutical quality on a national level. However, the authors draw a number of inferences unsupported by clear evidence that they infelicitously refer to as 'conclusions'. In particular, they write that 'substandard and/or falsified drugs that do not meet regulatory standards and quality threaten the health of population putting patients' life in danger leading to socio-economic hardship" is not supported by their data.

The sentence you have mentioned has been deleted.

They explain that the largest pool of recalled drugs were 'unregistered.' This means that the paperwork was not correct. This also means (based on their presentation of data) that there was no pharmacological evaluation of this, the largest category of recalled drugs. Problems with paperwork constitute a violation, but it is a very different claim from a claim of safety. It is certainly the case that the 'drug security' paradigm that has come to dominate pharmaco-vigilance since the early 2000s has focused scholarly and policy attention on intellectual property and other paperwork violations, at the expense of chemical analyses of safety. Nevertheless, surely there is nothing to be gained by reproducing this evidence-free conflation in our scholarship.

We agree with you that the ‘unregistered’ drugs did not go through quality evaluation. They might be good quality or might be bad quality. In either case, distribution of unregistered or unlicensed drugs without the approval from the concerned authority is illegal and it poses safety concern to the consumers.

Additionally, there is interesting data that describes how different kinds of recalled drugs were found in Nepal's government hospitals because of peculiar procurement practices. Another interesting bit of data pointed to physicians' and pharmacists' idiosyncratic dispensing as undermining drugs quality / value for money. However intriguing this data is, however, it does not suggest that these drugs in and of themselves constitute a health danger (as the authors claim in the conclusion). Rather, that there are non-standard practices among health professionals. This, too, strikes me as better belonging in a different article different to the one under review.

The sentence from conclusion has been deleted.

I also found the hand sanitizer data interesting, but inapposite. Unless I am mistaken, hand sanitizer is neither an essential drug (of Nepal or anywhere) nor is it a pharmaceutical at all. This data belongs in a different article.

Nepal’s department of drug administration (DDA) is responsible for making guideline on the composition and use of hand sanitizers. The manufacturers need to get DDA’s approval. [Even though this regulation started only after the COVID-19]. Therefore, we included this data.

Reviewer: 3
Dr. Arinola Joda, University of Lagos
Comments to the Author:
I would suggest that the title be amended to read
'Assessment of Pattern of Drug Recalls and Quality of Pharmaceutical Products in Nepal.

I felt constrained to convert this article to an editable format and so I used an online pdf2doc app to convert it so I could document corrections, comments and other issues I had with the article. On the whole the study is good and information made available contributes significantly to knowledge. However, I will not be able to live with myself if I eventually see this article in print with corrections I should have made not addressed because nobody eventually pointed them out to the author and there was no way to get this done using the closed ended options provided in the review template.

I would also like to add to the editor that options should be provided for some elaboration on the review questions to enable more information to be shared. In a lot of cases a simple yes or no does not tell the full story, no, not by a long shot.

Dear Dr. Joda,

Thank you for reading manuscript. We are sorry that you got trouble while making comments.

VERSION 2 – REVIEW

REVIEWER	Naughton, Bernard University of Oxford Said Business School
REVIEW RETURNED	16-Nov-2021

GENERAL COMMENTS	Reviewer: 1 Dr Bernard Naughton, University of Dublin, Trinity College Comments to the Author: Dear Authors, This was a clearly written paper which was easy to understand. This article may be useful as a tool to raise awareness of the issue of SF medicines in Nepal. It has also been written for a general audience, which is a positive in my opinion. Please find below my comments listed according to authors line numbering system. My comments are provided to help the authors to improve the overall quality of the paper. Of course, I do not expect the authors to take all of my comments on board, and I welcome any logical counterarguments or corrections to my remarks. Thank you so much. Your comments and feedbacks have helped to improve the quality of the paper. Really appreciated. Thank you. Abstract Title: This study title concerns the incidences of poor-quality medicine in Nepal. In my opinion, using this studies data to estimate the prevalence or incidence of national medicine quality is inappropriate because these recalls only reflect poor quality medicines identified by the regulator. Therefore, the title should contain the specific boundary conditions of the study. Perhaps a tittle of ‘ The Recall of Poor Quality Pharmaceutical Products in Nepal’ may be more suitable? We have revised the title as “Pattern of drug recalls and quality of pharmaceutical products in Nepal”.

	Thank you for the suggestion. In light of the editorial policy for article titles I suggest that you change the title to 'A review of drug recalls and quality of pharmaceutical products in Nepal' as mentioned above. Line 34: Participants. As this study does not contain participants. I suggest that the authors include a line that says 'This study did not contain participants. However, data was collected from 72 drug recalls and 4 research papers', or something similar to that effect. The sentence has been revised incorporating your suggestion. Accepted Line 41: What is the value in comparing different classes of drugs and how often they were recalled using statistics? What does that tell us? It certainly doesn't convincingly support an argument that one group of medicines is more likely to be poor quality than another, does it? Instead, I think it would be best to use descriptive statistics throughout and to explain why this data cannot be compared. It is a common practice to report classes of substandard and counterfeited drugs in journal articles. We believe that it is important to understand the classes of drugs that are more counterfeited and recalled. Therefore, we also looked at the pattern of recalls for different classes of drugs. It helps to understand which types of drugs are being recalled more or less. I accept your preference to keep the data regarding different drug classes, I suggest that you make it clear that this article is about recalled drugs and not an estimate of medicine quality in Nepal. The data doesn't tell us which medicines are counterfeited it tells us which have been recalled. Line 50: 'The substandard and/or falsified drugs….threaten health of population'. That is not a conclusion of this study. The conclusions should be based on the data from the study i.e. the conclusions should focus on drug recalls. The sentence has been deleted. Accepted Line 52: Also, you do not know that cases of SF medicines are increasing more generally within Nepal as the data presented in this study is a specific subset of poor quality medicines i.e. recalls by the regulator. The studies boundary conditions need to be more specific and the conclusions should be contained within these boundary conditions. Instead of writing increase in substandard and fake drugs, we have now rephrased as increase in the recalls of substandard and fake drugs to better describe our work. (see second sentence of Conclusion section of abstract) Accepted

	Line 53-55: I agree with this statement, but it seems to be contrary to lines line 52. Line 52 has been rephrased as increase in the recalls of substandard and fake drugs. I believe 'Falsified' is the more widely accepted term, rather than Fake. I suggest you change the term and ensure the terminology is consistent throughout the paper. Strengths and limitations of this study: I do not believe that it is appropriate to say that SF medicines have increased significantly. Recalls have increased but we don't know if that's because the regulator is providing more resources to identify them, or because the problem is worsening. There could be several reasons. It doesn't mean that there are more SF medicines in circulation in Nepal more generally. It only means the regulator has found more. We agree with your views. We had clearly mentioned in conclusion section (page 17). But looks like in some places it created confusion. We have now rephrased the narration to make it clear just like in rephrased line 52. Accepted Line 72-76: The authors include statistics about the prevalence of poor quality medicine. However, this data is slightly misleading. Please read the paper by McManus & Naughton 2020 in BMJ Global health https://gh.bmj.com/content/5/8/e002393 which describes the limitations of sampling studies and systematic reviews to provide estimates. I think this paper and others by Mackey et al 2018 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2696502 add value and balance to the use of poor quality medicine prevalence estimates. We note the concerns raised by MacManus and Naughton regarding sample collection methods and systematic review process. We also agree that there are some disagreements in these topics among researchers. Our work involved analyzing drug recall notices in this manuscript. We have cited previously published papers regarding prevalence of poor-quality medicines that may have used different methodology than suggested by MacManus and Naughton. In future studies involving sample collection and systematic review, we will consider the points raised ManManus and Naughton. Thank you for the suggestion. Accepted Line 78: Should this be 'a major producer' instead of 'the major producer'. Corrected This amendment hasn't been made. I suggest that you remove 'the major producers and change to 'major producers' this softens the language.

	Line 92-94: From my understanding, you found that drug recalls increased in Nepal. I am not convinced that your study shows that low quality drugs in general have increased, and I cannot see how an increase in drug recalls equates to a 'significant increase' in SF medicines more generally. We have rephrased increase of low-quality drugs to increase in recalls of low-quality drugs. I have recently published a paper which links directly into this point. To ensure that your paper links into existing conversations in the literature, I suggest you read the paper and reference it https://journals.sagepub.com/doi/full/10.1177/23992026211052272 .Essentially it describes medicine recall in the UK over the past few years and it says that work like my own, Almuzaini et al, and yours etc could be used to estimate medicine quality if researchers had access to suitable numerators and denominators. By adding your work to the existing conversation about using recall data to estimate medicine quality, your paper may be more impactful. There are also others out there who have provided similar studies in different countries e.g.Saudi Arabia https://fjps.springeropen.com/track/pdf/10.1186/s43094-020-00112-3.pdf Please make sure that you acknowledge similar work, reference their contributions and contribute to the conversation regarding drug recall data and medicine quality, to help move thinking forward. Methodology: There was a study conducted by Almuzaini et al in 2013 which looked at a similar issue in the UK https://bmjopen.bmj.com/content/3/7/e002924 . They used a more thorough and detailed methodology. Why have the authors not used that approach or even referenced it? Good papers usually appreciate the existing, relevant literature, in the field. To see this paper left out is unusual. You do not have to use the approach my Almuzaini but I would expect you to provide a statement regarding why you chose not to use it i.e. identify its limitations. That would build upon the Almuzaini methodology and propel the field forward. We somehow missed this paper by Almuzaini in our earlier version of the manuscript. Now we have cited their paper. Thank you for pointing this out. Thank you, but I suggest you explain why you used your approach. For me its important to acknowledge previous work in the area and add to the methodological conversation. This section should reference previous methodologies used for assessing medicine recalls e.g. Almuzaini https://pubmed.ncbi.nlm.nih.gov/23883882/ Naughton and Akgul https://journals.sagepub.com/doi/full/10.1177/23992026211052272 AlQuadeib https://fjps.springeropen.com/track/pdf/10.1186/s43094-020-00112-3.pdf and others who have done similar studies. Take this as an opportunity to justify your approach in light of other approaches. Just a few more sentences here would make the choice of methodology much stronger. Results

	Line 134-136: It is fine to say that recalls increased significantly but why is that important and does it tell us anything new or interesting? Increase in drug recalls is important as it may tell that the regulating agency has become more vigilant or there may be increasing awareness among public about the fake drugs. It is a new thing in Nepal. Then be clear that you have observed changes in drug recalls but further studies are required to understand why there has been a change in these medicine recall numbers. Discussion Line 219-270: I found these lines and much of the discussion in general to be largely unrelated to the study's findings. I suggest the authors either provide a better explanation regarding why the information contained in the discussion is related to the study findings, or perhaps consider significantly reducing this text. In my view, the discussion should be based upon the study findings and literature which contributes to the study findings. We agree with your opinion that discussion should be based on the study findings and literature which contributes to the study findings. In the discussion section we aimed to provide explanation of our work with taking reference to other related works on drug quality. We believe that the discussion section in our manuscript is needed to fully understand the results of our work and why we carried out this work. I suggest the text is reduced further as suggested to improve overall clarity and make it more succinct. Conclusion Line 333-335: I do not think that this is a conclusion of your study. These lines are removed. Accepted Line 340-341: Is this a conclusion? The idea of a systematic review to understand the prevalence of SF medicines, as mentioned previously, is contested and has its limitations. I suggest you discuss this in the body of your article before making it a conclusion. We are referring not to systematic literature review but to original research on drug quality. The sentence has been rephrased as: Therefore, more studies are needed …… I suggest you read the recent paper by Naughton and Akgul https://journals.sagepub.com/doi/full/10.1177/23992026211052272 this might help to improve your recommendations for how to move the contributions from this paper forward and how in the future recall data could be used to estimate national medicine quality. Other suggestions to improve the paper:

	Line 30: change from ‘during January 2010’ to ‘from January 2010 to December 2020’ Line 45: change to …’and drugs which failed several laboratory tests’ Line 47: change form did not include number to ‘did not include the number of samples tested’ Line 48/49: Please review the grammar here Line 56: Please review the grammar here ‘the health of the population of today and future’ Line 80: I think you can improve this section by connecting in with other literature. I suggest here that you situate your study within a body of research and link it to existing arguments to ensure the paper is building on existing work. I suggest this section is changed to describe Ozawa, the WHO and McManus &Naughton’s estimated medicine quality rates, acknowledge that each study presents different results which demonstrates that estimating poor quality medicine rates is difficult, while referencing relevant arguments in the literature, from Mackey https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2696502 , and Mcmanus & Naughton. https://gh.bmj.com/content/5/8/e002393 In doing so, this would provide a more balanced and objective view of international medicine quality estimates. Line 133/134: I am not sure this level of statistical analysis is useful. I will revert to the journals statistical experts. The same can be said for line 150-151

VERSION 2 – AUTHOR RESPONSE

In light of the editorial policy for article titles I suggest that you change the title to ‘A review of drug recalls and quality of pharmaceutical products in Nepal’ as mentioned above.

The title has been changed as suggested.

I did not receive a copy of the Prisma checklist. Please attach as part of this revision.

The Prisma checklist has been re-submitted.

I accept your preference to keep the data regarding different drug classes, I suggest that you make it clear that this article is about recalled drugs and not an estimate of medicine quality in Nepal. The data doesn’t tell us which medicines are counterfeited it tells us which have been recalled.

Title of the article has been rephrased as suggested and necessary changes have also been made in the main text.

I believe ‘Falsified’ is the more widely accepted term, rather than Fake. I suggest you change the term and ensure the terminology is consistent throughout the paper.

Fake has been replaced by ‘Falsified’.

This amendment hasn’t been made. I suggest that you remove ‘the major producers and change to ’major producers’ this softens the language.

It has been amended as suggested.

I have recently published a paper which links directly into this point. To ensure that your paper links into existing conversations in the literature, I suggest you read the paper and reference it https://journals.sagepub.com/doi/full/10.1177/23992026211052272. Essentially it describes medicine recall in the UK over the past few years and it says that work like my own, Almuzaini et al, and yours etc could be used to estimate medicine quality if researchers had access to suitable numerators and denominators. By adding your work to the existing conversation about using recall data to estimate medicine quality, your paper may be more impactful. There are also others out there who have provided similar studies in different countries e.g.Saudi Arabia https://fjps.springeropen.com/track/pdf/10.1186/s43094-020-00112-3.pdf

Please make sure that you acknowledge similar work, reference their contributions and contribute to the conversation regarding drug recall data and medicine quality, to help move thinking forward.

Thank you, but I suggest you explain why you used your approach. For me its important to acknowledge previous work in the area and add to the methodological conversation. This section should reference previous methodologies used for assessing medicine recalls e.g. Almuzaini https://pubmed.ncbi.nlm.nih.gov/23883882/ Naughton and Akgul https://journals.sagepub.com/doi/full/10.1177/23992026211052272 AlQuadeib https://fjps.springeropen.com/track/pdf/10.1186/s43094-020-00112-3.pdf and others who have done similar studies.

Take this as an opportunity to justify your approach in light of other approaches. Just a few more sentences here would make the choice of methodology much stronger. Then be clear that you have observed changes in drug recalls but further studies are required to understand why there has been a change in these medicine recall numbers. I suggest the text is reduced further as suggested to improve overall clarity and make it more
succinct. I suggest you read the recent paper by Naughton and Akgul

https://journals.sagepub.com/doi/full/10.1177/23992026211052272

this might help to improve your recommendations for how to move the contributions from this paper forward and how in the future recall data could be used to estimate national medicine quality.

Thank you for your insights. We have added missing references and revised the text, accordingly, see the track change file, especially in the introduction and discussion sections.

Other suggestions to improve the paper:

Line 30: change from ‘during January 2010’ to ‘from January 2010 to December 2020’
Changed

Line 45: change to …’and drugs which failed several laboratory tests’
Corrected

Line 47: change form did not include number to ‘did not include the number of samples tested’
Corrected

Line 48/49: Please review the grammar here
Revised

Line 56: Please review the grammar here ‘the health of the population of today and future’
Rephrased

Line 80: I think you can improve this section by connecting in with other literature. I suggest here that you situate your study within a body of research and link it to existing arguments to ensure the paper is building on existing work. I suggest this section is changed to describe Ozawa, the WHO and McManus &Naughton’s estimated medicine quality rates, acknowledge that each study presents

different results which demonstrates that estimating poor quality medicine rates is difficult, while referencing relevant arguments in the literature, from Mackey https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2696502 , and Mcmanus & Naughton. https://gh.bmj.com/content/5/8/e002393
In doing so, this would provide a more balanced and objective view of international medicine quality estimates.

Last section of introduction has been revised. Please check the main text in track change mode. Thank you for your suggestion. Also added suggested references.

Line 133/134: I am not sure this level of statistical analysis is useful. I will revert to the journals statistical experts. The same can be said for line 150-151

We believe that the statistical analysis is helpful to report the differences.