

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of the COVID-19 pandemic on the cost of chronic diseases treatment and care at public hospitals in Wallaga zones, Oromia Regional State, Ethiopia: A hospital-based, cross-sectional study
AUTHORS	Terefa, Dufera; Tesfaye, Edosa; Tolessa, Belachew; Desisa, Adisu; Olani, Wolkite; Fetensa, Getahun; Chego, Melese; Abdisa, Eba; Turi, Ebisa; Bekuma, Tariku Tesfaye; Getachew, Motuma; Tesfaye, Lensa; Tilahun, Temesgen

VERSION 1 – REVIEW

REVIEWER	Mohamoud, Jamal Hassan SIMAD University, 4. Department of Public Health, Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu, Somalia.
REVIEW RETURNED	03-Apr-2023

GENERAL COMMENTS	<p>I thought your text was excellent and will encourage you to keep up the good work while providing you with some suggestions and comments.</p> <p>Comments and suggestion</p> <p>Abstract:</p> <ul style="list-style-type: none">• Before stating the study's objective in the abstract, it is preferable to provide the reader a quick introduction to help them comprehend the topic at hand. <p>Methods and Materials</p> <ul style="list-style-type: none">• It is preferable to list the hospitals where your study was done in the study setting section.• What sample technique was used to select the hospitals is the one question I have.• The ethical section slipped your mind.• How did you estimate the cost of treatment before to the COVID 19 lockout given that you mentioned comparing before and after?• It would be preferable to make recommendations to the hospital administrators and the local government since you suggested in the conclusion section that the healthcare provider arrange a special charge waiver.
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REVIEWER	Olu, Olushayo WHO International
REVIEW RETURNED	05-Apr-2023

GENERAL COMMENTS	<p>General comments</p> <p>Public health shock events such as disease outbreaks often have a significant impact on the delivery of and utilization of healthcare services resulting in dire consequences. COVID-19 is no exception to this rule. The pandemic resulted in significant disruption in healthcare services in most African countries that were already struggling to deliver healthcare even before the pandemic. This study, which is on the cost of Non-Communicable Disease (NCD) follow-up care before and during the pandemic is therefore well timed. While it seems that the study which generated the data for the manuscript is well conducted, there is a lot of room for improvement in its reporting as highlighted in my specific comments below. While the language of the manuscript seems to be fair in general, the authors need to pay significant attention to details to address the several grammatical, typographical and punctuation errors in the document. Furthermore, the authors are advised to be consistent in the use of acronyms; for instance, “CDS” and “CDs) are used interchangeably for “Chronic Disease” which I found confusing.</p> <p>Specific comments</p> <p>Background</p> <p>While your background has most of the required elements, they have been presented in a haphazard manner. You started with NCDs in the first two paragraphs and then jumped to COVID-19 and then back again to NCD. I would suggest that you reorganize the section as follow:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Paragraph 1: NCDs and challenges of managing them in Ethiopia <input type="checkbox"/> Paragraph 2: COVID-19 in Ethiopia and its impact on NCD services delivery and utilization <input type="checkbox"/> Paragraph 3: the gaps in the literature concerning the impact of COVID-19 on NCD that this study seeks to address. You have alluded to this in lines 99 to 101 but you would need to further expatiate on this through a brief literature review. This would then be the justification for your study. <input type="checkbox"/> Paragraph 4: the aims and objectives of this study and research question if appropriate <p>Methods and materials</p> <p>Please reorganize this section as follow:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Study design and setting: what kind of study is this, and when and where was it conducted? A brief description of the study area (Ethiopia, Oromia Region and East/West/Horro Guduru Wallaga zones) would be helpful for the readers to contextualize the findings of your study. <input type="checkbox"/> Sample size and sampling methods <input type="checkbox"/> Data collection <input type="checkbox"/> Data analyses <input type="checkbox"/> Ethical consideration <p>I would suggest that you move the costing methods to the data analyses section. The definition of the study variables should be either boxed or annexed as supplementary materials.</p>
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	<p>Results</p> <p>The presentation of data is also haphazard. I would therefore suggest that you rearrange them under the following headings. Furthermore, the data that you have presented in tables do not need to be presented in detail again in the text to abridge this section:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Sociodemographic/economics characteristics and classification of study participants by NCD condition (tables 1 and 3) <input type="checkbox"/> The overall cost of NCD follow-up before and during the pandemic (table 2) <input type="checkbox"/> The cost of NCD follow-up by disease type (table 4) <p>I would also suggest that you check the tables again as some of the figures and additions do not add up. For instance, in Table 2, a+b+c in the “Median (US\$)” column do not add up as well as the d+e of the same column.</p> <p>Discussion</p> <p>I would suggest that you refrain from repeating the findings which you have already presented in the result section here. You should rather focus on discussing and rationalizing those findings in more details. Furthermore, you need to compare your findings to those of other studies which you have cited and describe/discuss the factors that could have been responsible for these findings/trends in Ethiopia. In this regard, I would suggest that you reorganize this section as follow for better flow and clarity:</p> <ul style="list-style-type: none"> <input type="checkbox"/> Paragraph 1: a very brief statement of the main objective and key findings of this study without mentioning figures. <input type="checkbox"/> Paragraphs 2-5: an exhaustive discussion and rationalization of the key findings of the study. Which factors could have been responsible for your findings <input type="checkbox"/> Paragraph 6: study limitations.
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REVIEWER	Simmering, Jacob The University of Iowa College of Pharmacy
REVIEW RETURNED	17-May-2023

GENERAL COMMENTS	<p>Methods and Statistical Comments:</p> <ol style="list-style-type: none"> 1. What is “bottom-up costing?” Is this simply total costs (direct + indirect)? 2. I do not understand the power analysis. $(1.96^2 * 30.89^2) / (0.05^2 * 48.99^2) * 1.05$ does equal 642 but I am I don’t see any hypothesis being defined here? I am also unfamiliar with this arrangement to calculate required sample size – power is not defined or included in the equation at any point. What is the expected pre-COVID distribution? What is the expected post-COVID distribution? What is the desired study power? 3. What is the “systematic sampling method” used to sample patients at each hospital? 4. “Average participant age was 43.29 (16.5%) years” Is the 16.5 the SD? Why does it have a percent sign? Are the +/- values the SD or CIs – this notation is unclear. Table 1 seems like it should be stratified by before/during COVID. 5. For costs, since the distribution is so skewed, a median and IQR would be nice to see. 6. Why are Z scores reported when the tests are non-parametric?
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	<p>7. For costs, what happens to people who don't report costs? Are they zeros? The average cost conditional on having a cost seems like a poor estimate. If at t=0, 100% of people have a cost of \$2 the average cost is \$2. If at t=1, 99% of people have a cost of \$0 and 1% has a cost of \$5, this estimate would say cost went up (from 2 to 5 dollars) but really 99% of people went from paying 2 to 0 dollars.</p> <p>8. Only 58.7% of patients had an increase in spending after vs before but the median cost increased by 30%. This seems like a pretty large increase since if exactly 50% of patients had an increase in spending the median increase would be 0%. Is this the median cost among those with a cost?</p> <p>9. Is the patient mix well balanced between the before/after periods? It is unclear that this was considered.</p> <p>10. Are these costs in nominal or real terms? Nominal spending (spending that is not adjusted for inflation) may show an increase in spending that is entirely driven by inflation. It seems like there was a very large increase in prices due to inflation during the study period (https://www.reuters.com/article/ethiopia-economy-inflation-idAFL8N35F41Q) that needs to be accounted for when doing the analysis.</p> <p>General Comments:</p> <ol style="list-style-type: none"> 1. The background on COVID-19 is probably unnecessary. Readers will be familiar with the pandemic. Removing this background will make the introduction shorter and more clear. 2. Manuscript needs some copy-editing. There are frequent spaces before periods and the paragraphs need to be clearly denoted with white space or indentation. Study variable section text is bolded. 3. In the inclusion and exclusion criteria "Patients whose age was less than 15-years old and without accompanying patients..." should likely be "accompanying parents." 4. Suggest rephrasing line 201 to "Regarding the educational status of the participants, 137 (22.6%) were illiterate" or "... 137 (22.6%) were unable to read and write."
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REVIEWER	McCormick, Natalie Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology
REVIEW RETURNED	10-Jun-2023

GENERAL COMMENTS	<p>Thank you for preparing this manuscript on the impact of COVID-19 on the direct and indirect costs of cost of chronic diseases in a region of Ethiopia. It is interesting to look at the spillover effects of COVID-19 on other chronic diseases. Please see some comments and queries below, which focus on the analytical aspects of this manuscript:</p> <p><p>1. Introduction, page 4, lines 100-101: I suggest a more conservative statement about the prior literature, such as "there has been little emphasis" or "there have been few investigations" on impact of the pandemic on illness costs of chronic disease follow-up care from a patient perspective.</p> <p>2. Methods, page 7, lines 165-167: How were these chronic diseases selected for inclusion? Some, though not all, were mentioned in the Introduction.</p>
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	<p>3. Methods, page 8: Estimates of mean costs are preferred over median costs for health policy decisions. At this point I advise adding mean cost estimates to Tables 2 and 4 and including them alongside median costs in key areas of the manuscript.</p> <p>4. Discussion, page 19: You acknowledge that you did not include the income losses for patients who were unemployed. It would help to also mention the absence of data on patients who had income before the pandemic but not afterwards. To provide readers with additional context, could you also please mention here the proportion of Ethiopian workers who may have been in these situations?</p> <p>5. It would help to provide a copy of the questionnaire in the Supplement.</p>
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VERSION 1 – AUTHOR RESPONSE

*Reviewer 1 comments;

I thought your text was excellent and will encourage you to keep up the good work while providing you with some suggestions and comments.

*Reviewer 2 Comments;

General comments

Public health shock events such as disease outbreaks often have a significant impact on the delivery of and utilization of healthcare services resulting in dire consequences. COVID-19 is no exception to this rule. The pandemic resulted in significant disruption in healthcare services in most African countries that were already struggling to deliver healthcare even before the pandemic. This study, which is on the cost of Non-Communicable Disease (NCD) follow-up care before and during the pandemic is therefore well timed. While it seems that the study which generated the data for the manuscript is well conducted, there is a lot of room for improvement in its reporting as highlighted in my specific comments below. While the language of the manuscript seems to be fair in general, the authors need to pay significant attention to details to address the several grammatical, typographical and punctuation errors in the document. Furthermore, the authors are advised to be consistent in the use of acronyms; for instance, “CDS” and “CDs) are used interchangeably for “Chronic Disease” which I found confusing.

#Response to general comments:

•“CDS” and “CDs” was corrected throughout the manuscript document.

Specific comments

Background

While your background has most of the required elements, they have been presented in a haphazard manner. You started with NCDs in the first two paragraphs and then jumped to COVID-19 and then back again to NCD. I would suggest that you reorganize the section as follow:

- Paragraph 1: NCDs and challenges of managing them in Ethiopia
- Paragraph 2: COVID-19 in Ethiopia and its impact on NCD services delivery and utilization
- Paragraph 3: the gaps in the literature concerning the impact of COVID-19 on NCD that this study seeks to address. You have alluded to this in lines 99 to 101 but you would need to further expatiate on this through a brief literature review. This would then be the justification for your study.
- Paragraph 4: the aims and objectives of this study and research question if appropriate

#Responses to this section:

•We have reorganized and re-phrased the paragraphs and flow of ideas with in that as per the constructive suggestions given for us.

Methods and materials

Please reorganize this section as follow:

- Study design and setting: what kind of study is this, and when and where was it conducted? A brief description of the study area (Ethiopia, Oromia Region and East/West/Horro Guduru Wallaga zones) would be helpful for the readers to contextualize the findings of your study.
- Sample size and sampling methods
- Data collection
- Data analyses
- Ethical consideration

I would suggest that you move the costing methods to the data analyses section. The definition of the study variables should be either boxed or annexed as supplementary materials.

Responses to this section:

•Correction has been made for each questions and suggestions raised under the method section as per requested.

Results

The presentation of data is also haphazard. I would therefore suggest that you rearrange them under the following headings. Furthermore, the data that you have presented in tables do not need to be presented in detail again in the text to abridge this section:

- Sociodemographic/economics characteristics and classification of study participants by NCD condition (tables 1 and 3)
- The overall cost of NCD follow-up before and during the pandemic (table 2)
- The cost of NCD follow-up by disease type (table 4)

I would also suggest that you check the tables again as some of the figures and additions do not add up. For instance, in Table 2, a+b+c in the “Median (US\$)” column do not add up as well as the d+e of the same column.

#Responses to this section:

- Tables 1 and 3 were merged as table 1 accordingly. Also, table 2 as its and table 4 as 3 were re-adjusted
- Errors in adding up were also corrected.

Discussion

I would suggest that you refrain from repeating the findings which you have already presented in the result section here. You should rather focus on discussing and rationalizing those findings in more details. Furthermore, you need to compare your findings to those of other studies which you have cited and describe/discuss the factors that could have been responsible for these findings/trends in Ethiopia. In this regard, I would suggest that you reorganize this section as follow for better flow and clarity:

- Paragraph 1: a very brief statement of the main objective and key findings of this study without mentioning figures.
- Paragraphs 2-5: an exhaustive discussion and rationalization of the key findings of the study. Which factors could have been responsible for your findings
- Paragraph 6: study limitations.

#Responses to this section:

- We have tried to address points raised under discussion section here.
- However, study limitations section was moved to the part after the abstract as per the guideline or been guided.

*Reviewer 3 Comments;

Methods and Statistical Comments:

1. What is “bottom-up costing?” Is this simply total costs (direct + indirect)?
2. I do not understand the power analysis. $(1.96^2 * 30.89^2) / (0.05^2 * 48.99^2) * 1.05$ does equal 642 but I am I don't see any hypothesis being defined here? I am also unfamiliar with this arrangement to calculate required sample size – power is not defined or included in the equation at any point. What is the expected pre-COVID distribution? What is the expected post-COVID distribution? What is the desired study power?

3. What is the “systematic sampling method” used to sample patients at each hospital?
4. “Average participant age was 43.29 (16.5%) years” Is the 16.5 the SD? Why does it have a percent sign? Are the +/- values the SD or CIs – this notation is unclear. Table 1 seems like it should be stratified by before/during COVID.
5. For costs, since the distribution is so skewed, a median and IQR would be nice to see.
6. Why are Z scores reported when the tests are non-parametric?
7. For costs, what happens to people who don't report costs? Are they zeros? The average cost conditional on having a cost seems like a poor estimate. If at t=0, 100% of people have a cost of \$2 the average cost is \$2. If at t=1, 99% of people have a cost of \$0 and 1% has a cost of \$5, this estimate would say cost went up (from 2 to 5 dollars) but really 99% of people went from paying 2 to 0 dollars.
8. Only 58.7% of patients had an increase in spending after vs before but the median cost increased by 30%. This seems like a pretty large increase since if exactly 50% of patients had an increase in spending the median increase would be 0%. Is this the median cost among those with a cost?
9. Is the patient mix well balanced between the before/after periods? It is unclear that this was considered.
10. Are these costs in nominal or real terms? Nominal spending (spending that is not adjusted for inflation) may show an increase in spending that is entirely driven by inflation. It seems like there was a very large increase in prices due to inflation during the study period (<https://www.reuters.com/article/ethiopia-economy-inflation-idAFL8N35F41Q>) that needs to be accounted for when doing the analysis.

#Responses to this section:

1. Bottom-up costing is not just simply adding direct and indirect cost to get the total cost. Rather, it is a patient based approach that can estimate total average cost per case, which is by the prevalence of the illness to get an estimate of the total direct cost.
2. This is because, to calculate the sample size for population mean using mean and standard deviation we have to calculate/take “ ϵ^2 ” by considering 5% of the mean and we have cited in this regard especially in calculating the cost data to estimate the sample size for economic costs of a certain programs. Also, as our participants from whom we have collected the data were similar, we haven't considered the sample size independently as expected pre-COVID and post-COVID distribution.
3. To sample patients at each study hospital, systematic random sampling technique was used.
4. 16.5 is the SD and +/- values the SD, but re-modified in the way It has to be clear. Table 1 was mentioned as such because the socio-demographic variables been mentioned there has no significant difference before and during COVID-19 and that is why we have stated in that way.
5. We have re-considered a median and IQR as per the constructive suggestion given.
6. For continues cost data, the normality distribution was checked and the data was not normally distributed and we used Related-samples Wilcoxon signed rank test and at $p < 0.05$ to declare level of significance of median cost difference. Wilcoxon all came up with statistically comparable techniques for analyzing ranked cost data and Wilcoxon provided a different version of this statistic, which can be converted into a Z score and can, therefore, be compared against critical values of the normal distribution.
7. In fact, there are complexities in estimating cost data's in cost of illness analysis in which there might be cases with zero health care costs. This phenomenon can skew outcomes, making the use of an “average” cost inaccurate. For this, there are methods for dealing with these skewed health care costs.
8. This means that, 348 out of 593 (58.7%) patients incurred significantly higher costs during the pandemic compared to before the pandemic. The median cost was corrected.
9. In fact, we have operationalized under the operational definition what by mean before the pandemic and during the pandemic and clarify this for our participants during data collection while the data collectors collect the data. Also, the nature of our tool clearly indicates that.
10. Since we have considered the current monetary value, costs are in nominal terms.

General Comments

1. The background on COVID-19 is probably unnecessary. Readers will be familiar with the pandemic. Removing this background will make the introduction shorter and more clear.
2. Manuscript needs some copy-editing. There are frequent spaces before periods and the paragraphs need to be clearly denoted with white space or indentation. Study variable section text is bolded.
3. In the inclusion and exclusion criteria "Patients whose age was less than 15-years old and without accompanying patients..." should likely be "accompanying parents."
4. Suggest rephrasing line 201 to "Regarding the educational status of the participants, 137 (22.6%) were illiterate" or "... 137 (22.6%) were unable to read and write."

#Responses to this section:

1. In fact, it was unnecessary as readers are familiar with COVID-19, but to highlight its impact on cost of chronic disease follow up care. Also, we have minimized unnecessary things related with COVID-19 as well and had taken things that related with our current study.
2. Spaces before periods, space or indentation, bolded texts were corrected accordingly.
3. Accompanying patients was corrected as "accompanying parents."
4. Corrected as; 137 (22.6%) were illiterate.

*Reviewer 4 Comments;

Thank you for preparing this manuscript on the impact of COVID-19 on the direct and indirect costs of cost of chronic diseases in a region of Ethiopia. It is interesting to look at the spillover effects of COVID-19 on other chronic diseases. Please see some comments and queries below, which focus on the analytical aspects of this manuscript:

1. Introduction, page 4, lines 100-101: I suggest a more conservative statement about the prior literature, such as "there has been little emphasis" or "there have been few investigations" on impact of the pandemic on illness costs of chronic disease follow-up care from a patient perspective.
2. Methods, page 7, lines 165-167: How were these chronic diseases selected for inclusion? Some, though not all, were mentioned in the Introduction.
3. Methods, page 8: Estimates of mean costs are preferred over median costs for health policy decisions. At this point I advise adding mean cost estimates to Tables 2 and 4 and including them alongside median costs in key areas of the manuscript.
4. Discussion, page 19: You acknowledge that you did not include the income losses for patients who were unemployed. It would help to also mention the absence of data on patients who had income before the pandemic but not afterwards. To provide readers with additional context, could you also please mention here the proportion of Ethiopian workers who may have been in these situations?
5. It would help to provide a copy of the questionnaire in the Supplement

#Responses to this section:

1. Corrected as per the suggestion.
2. Exactly, some of the chronic diseases, HIV, stroke and epilepsy, were not been mentioned under the introduction section. This is because we have considered that under introduction section to highlight chronic diseases in general, not specific diseases. But, under the method section, operational definition part, we have considered specifically these diseases because by considering the situation of the study setting to measure these diseases in our way.
3. As per the suggestion, mean cost was included alongside the median costs.
4. Our intention was about not considering income losses for patients who were unemployed. This did not mean that, we haven't considered employed workers. If we consider Ethiopian workers situation, It could be beyond what we want to emphasize and could be out of scope. Even, lack evidences for this.
5. The questionnaire was supplemented accordingly.

VERSION 2 – REVIEW

REVIEWER	Mohamoud, Jamal Hassan SIMAD University, 4. Department of Public Health, Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu, Somalia.
REVIEW RETURNED	29-Jul-2023

GENERAL COMMENTS	<p>Although well-written, this essay might use some refinement, particularly in the background and outcomes.</p> <p>Background As a background, it's preferable to identify your problem first rather than explaining the worldwide issue so that the readers can assist in understanding what your research problem is. You have to clarify why it is crucial to concentrate on the Impact of COVID-19 Pandemic on the Cost of Treating Chronic Diseases rather than Communicable Diseases. I have a few questions need to know.</p> <ul style="list-style-type: none"> • What is your research gap in your study? • What is your contextual prospective of your study? <p>Methodology sections</p> <ul style="list-style-type: none"> • How do you choose these hospitals? I mean what was your sample technique used to select the study area? • You employed systematic sampling methods; therefore, what was your sample interval ("K") and how evenly distributed was your sample size among hospitals ("sample distribution")? • I have an inquiry about the study variables and I want to know what your dependent variable was. • How do you measure the data from before the COVID-19 pandemic? You indicated in the data analysis section that you will analyze the impact of the COVID-19 pandemic on the cost of chronic treatment before and during the COVID-19 pandemic. It seems that this is causing recall bias? <p>Results: I believe there are some missing data in Table 2, such as the fact that only 501 of each group "before and during the COVID-19 pandemic" were analysed despite the sample size being 601. If the data are not normally distributed, should we use the IQR instead of the mean in data analysis since you mentioned that the data were normally distributed and that you used to analyze the median rather than just the mean? So the question is, why do you use "Mean and IQR" both?</p> <p>Conclusion: It is preferable to specify which patient population—for instance, hypertension or diabetes patients—has the greatest impact on the price of ongoing care as a result of the COVID-19 pandemic. So the comment should be included in the results and conclusion.</p>
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REVIEWER	Simmering, Jacob The University of Iowa College of Pharmacy
REVIEW RETURNED	30-Aug-2023

GENERAL COMMENTS	<p>Reading the authors' responses:</p> <ol style="list-style-type: none"> 1. I still have no idea what bottom-up costing is. 2. A power analysis only makes sense when a hypothesis is defined. It is the power to reject H0 when HA is true. There is no
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	<p>hypothesis being tested here and the answer does not address that question. If there is no hypothesis test, there is no power. So what is this power test? What is is related to?</p> <p>3. This is addressed.</p> <p>4. This is addressed.</p> <p>5. This is addressed.</p> <p>6. This is addressed.</p> <p>7. What are these methods? Are they applied here? This is not just skew but selection - I think this is beyond the scope of most statistical methods to correct.</p> <p>8. This seems addressed.</p> <p>9. I do not understand this answer. It does not address my question or concern.</p> <p>10. Prices need to be analyzed in real terms otherwise inflation, which was large during the study period, is an omitted confounding variable.</p>
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REVIEWER	McCormick, Natalie Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology
REVIEW RETURNED	04-Aug-2023

GENERAL COMMENTS	<p>Thank you for the improvements made, including the addition of estimated mean costs in Tables 2 & 3. However, I feel a few more items should be addressed:</p> <p>1. It still isn't clear if there was a specific list if chronic diseases that were eligible for inclusion, although several references are made in the text to the "selected CDs". Was it the ones listed in the Operational Definitions box? If so, this box should be referenced early-on in the text.</p> <p>2. Could you please note in the Limitations that this study did not include the costs experienced by patients who were employed before the pandemic but then lost their jobs?</p> <p>3. I did not see a copy of the questionnaire.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer 1	
<p>Although well-written, this essay might use some refinement, particularly in the background and outcomes. See file attached</p> <p>Background</p>	<p>Background:</p> <ul style="list-style-type: none"> ✓ It was amended. ✓ It is crucial to concentrate on the Impact of COVID-19 Pandemic on the Cost of Treating Chronic Diseases

As a background, it's preferable to identify your problem first rather than explaining the worldwide issue so that the readers can assist in understanding what your research problem is.

You have to clarify why it is crucial to concentrate on the Impact of COVID-19 Pandemic on the Cost of Treating Chronic Diseases rather than Communicable Diseases. I have a few questions need to know.

- What is your research gap in your study?
- What is your contextual prospective of your study?

Methodology sections

- How do you choose these hospitals? I mean what was your sample technique used to select the study area?
- You employed systematic sampling methods; therefore, what was your sample interval ("K") and how evenly distributed was your sample size among hospitals ("sample distribution")?
- I have an inquiry about the study variables and I want to know what your dependent variable was.
- How do you measure the data from before the COVID-19 pandemic? You indicated in the data analysis section that you will analyze the impact of the COVID-19 pandemic on the cost of chronic treatment before and during the COVID-19 pandemic. It seems that this is causing recall bias?

Results:

I believe there are some missing data in Table 2, such as the fact that only 501 of each group "before and during the COVID-19 pandemic" were analysed despite the sample size being 601.

If the data are not normally distributed, should we use the IQR instead of the mean in data

rather than Communicable Diseases particularly in this study because during COVID-19 pandemic the lock-down of many services has translated into reduced access, a decrease in referrals, and reduced hospitalizations of patients with non-COVID-19 pathology including Chronic Diseases patients as we have mentioned under the background section. But, there were chronic disease patients who have mandatory follow up care at health facilities in which they have to routinely visit health facilities which might have greater impact on the cost of the patient visits. However, despite an individual might have communicable diseases and seek health services they might not routinely follow the health facilities during this era as CD patients and this is why we have focused on the chronic disease in particular.

- ✓ As it has been mentioned under the background section there was nothing which was known about costs of chronic disease follow-up care from a patient perspective during COVID 19 pandemic especially in Ethiopian context and the study area in particular despite there were chronic disease patients who have mandatory follow up care at health facilities in which they have to routinely visit health facilities which might have greater impact on the cost of the patient visits in a such low resource settings.

Methodology sections:

- ✓ **We have used simple random sampling technique to select the study hospital. This was mentioned under "Sample Size and Sampling Methods" section.**
- ✓ Simple random sampling technique was used from the registration book to sample patients at each study hospitals as per their proportion to select 642 participants.
- ✓ In this study we did not conducted regression analysis to show the dependence of one variable on the other variable for which the presence of dependent variable is mandatory. Just we have conducted the median difference to show the impact of the pandemic on cost

<p>analysis since you mentioned that the data were normally distributed and that you used to analyze the median rather than just the mean? So the question is, why do you use "Mean and IQR" both?</p> <p>Conclusion:</p> <p>It is preferable to specify which patient population—for instance, a hypertension or diabetes patient—has the greatest impact on the price of ongoing care as a result of the COVID-19 pandemic. So the comment should be included in the results and conclusion.</p>	<p>of treatment and follow up care of chronic disease patients.</p> <ul style="list-style-type: none"> ✓ Despite it might have recall bias as it was mentioned under the limitation of the study section, the cost data was collected from the patient that they have incurred before (which mean within four months period of follow up). <p>Results:</p> <ul style="list-style-type: none"> ✓ This is not missing data, rather here we have estimated the income lost for the study participants and only 501 of the participants have an income to analyze the Income lost. ✓ Under the Data Analysis section: We have mentioned as; the normality distribution of treatment cost data was checked, and it was not normally distributed. AS a result, non-parametric tests were used to analyze the median cost for each cost category, as well as a 2-paired sample Wilcoxon sign rank test to compare the costs incurred before and during the pandemic lock-down, with the level of significance of the median cost difference set at $p < 0.05$. <p>Because of this scientific evidence and justification we have used the median cost rather than the mean cost from the beginning and then after we have been recommended to add the mean cost as estimates of mean costs are preferred over median costs for health policy decisions. Also, we have used mean and standard deviation, median and IQR together not mean with IQR as it has been mentioned in the tables and the text too.</p> <p>Conclusion:</p> <ul style="list-style-type: none"> ✓ Hypertensive patient had the greatest impact on the cost of ongoing care as a result of the COVID-19 pandemic.
<p>Reviewer 2</p>	
<p>Reviewer 3</p>	

<p>1. I still have no idea what bottom-up costing is.</p> <p>2. A power analysis only makes sense when a hypothesis is defined. It is the power to reject H0 when HA is true. There is no hypothesis being tested here and the answer does not address that question. If there is no hypothesis test, there is no power. So what is this power test? What is related to?</p> <p>3. This is addressed.</p> <p>4. This is addressed.</p> <p>5. This is addressed.</p> <p>6. This is addressed.</p> <p>7. What are these methods? Are they applied here? This is not just skew but selection - I think this is beyond the scope of most statistical methods to correct.</p> <p>8. This seems addressed.</p> <p>9. I do not understand this answer. It does not address my question or concern.</p> <p>10. Prices need to be analyzed in real terms otherwise inflation, which was large during the study period, is an omitted confounding variable.</p>	<p>1. Bottom-up approach or "patient-based" approach is a cost of illness estimation method. In a bottom-up approach, the cost estimation can be stratified into two steps. The first step is to measure and quantify the health inputs employed and the second step is to estimate the unit costs of the inputs used to produce and confer specific medical and health care services. The bottom-up approach often multiplies the unit cost of a particular treatment by the average amount of utilization of the treatment to get an average cost estimate of the treatment. The method is repeated for each type of care to obtain a total average cost per case, which is then multiplied by the prevalence of the illness to get an estimate of the total direct cost. Bottom-up costing is not just simply adding direct and indirect cost to get the total cost.</p> <p>2. In fact, we have not tested a hypothesis in this study, which in the other term means that there is no power really as it has been suggested. However, to calculate the sample size for population mean using mean cost and standard deviation taken from a certain study findings in cost of illness studies, we have to take/consider 5% of the mean cost and power of two(square it; "€2") in calculating the cost data to estimate the sample size for economic costs of a certain programs. For this as evidence we have cited in this regard.</p> <p>7. One of the approaches for dealing with these complexities is log-transform the cost data. This can only be done if costs are non-zero because you can't log-transform a zero value. That is why we have not applied it here.</p> <p>9. If I did not miss understood, the patients well balanced between the before/after periods. Because, we have clearly stated and clarified when we say before the pandemic and during the pandemic period means. Then, the data collectors have clarified this for the patients during data collection while collecting the data. Additionally, the nature of our tool clearly indicates that period.</p>
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	10. I accept the suggestion that; the Prices were analyzed in real terms.
Reviewer 4	
<p>Thank you for the improvements made, including the addition of estimated mean costs in Tables 2 & 3. However, I feel a few more items should be addressed:</p> <p>1. It still isn't clear if there was a specific list of chronic diseases that were eligible for inclusion, although several references are made in the text to the "selected CDs". Was it the ones listed in the Operational Definitions box? If so, this box should be referenced early-on in the text.</p> <p>2. Could you please note in the Limitations that this study did not include the costs experienced by patients who were employed before the pandemic but then lost their jobs?</p> <p>3. I did not see a copy of the questionnaire.</p>	<p>1.The Operational Definitions box was referenced</p> <p>2. I have noted as per suggestion as; This study did not include the costs experienced by patients who were employed before the pandemic but then lost their jobs.</p> <p>3.The questionnaire was supplemented accordingly on the online system. Also, if possible I will send by email.</p>

VERSION 3 – REVIEW

REVIEWER	Mohamoud, Jamal Hassan SIMAD University, 4. Department of Public Health, Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu, Somalia.
REVIEW RETURNED	26-Sep-2023

GENERAL COMMENTS	Firstly, I want to express my gratitude to the authors for submitting their manuscript. I've reviewed the corrections that were made based on my input, and I have one comment to add. When conducting data analysis, especially in cases where there are outliers present, it might be advisable to analysis the Interquartile Range (IQR) rather than relying solely on the median.
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REVIEWER	Simmering, Jacob The University of Iowa College of Pharmacy
REVIEW RETURNED	13-Sep-2023

GENERAL COMMENTS	R3.7. While a log transform is not possible due to zeros, this doesn't answer the question. First, the initial response states that the average is inaccurate and their are statistical methods for deal with this skew in health care costs. Then these responses state that it in inappropriate/not possible to apply these methods to this
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	<p>sample due to the presence of zeros. The change in the mean cost conditional on having a cost doesn't tell us about changes in costs over time.</p> <p>R3.10. The paper doesn't discuss how the costs is converted to real terms. Additional, conversion out of the Ethiopian currency to USD for analysis using a single exchange rate seems problematic. It is not clear to me why the analysis should not be done in Ethiopian currency units exclusively. Converting using a single or even a series of exchange rates and doing the analysis in a different currency introduces the potential for macroeconomic confounding. The currency needs to be converted to real terms using Ethiopian inflation data.</p>
REVIEWER	McCormick, Natalie Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology
REVIEW RETURNED	07-Oct-2023
GENERAL COMMENTS	<p>Thank you for these responses, including noting the limitation regarding patients who were employed before the pandemic but then lost their jobs. It is also now clearer which chronic diseases were eligible for inclusion and I have no further queries.</p> <p><p>While I still don't see a copy of the questionnaire, that could be a system issue, so I simply recommend the publishers make the survey available to readers if this manuscript is accepted for publication.</p>

VERSION 3 – AUTHOR RESPONSE

Reviewer 1	
<p>Comments to the Author:</p> <p>Firstly, I want to express my gratitude to the authors for submitting their manuscript. I've reviewed the corrections that were made based on my input, and I have one comment to add. When conducting data analysis, especially in cases where there are outliers present, it might be advisable to analysis the Interquartile Range (IQR) rather than relying solely on the median.</p>	<ul style="list-style-type: none"> As it has been mentioned in the tables and the text too, we have used median and IQR together rather than relying solely on the median.
Reviewer 3	
<p>Comments to the Author:</p> <p>R3.7. While a log transform is not possible due to zeros, this doesn't answer the question. First, the initial response states that the average is inaccurate and there are statistical methods for deal with this skew in health care costs. Then</p>	<p>R3.7;</p> <ul style="list-style-type: none"> I am really sorry for this. I mean that, despite there being approaches for dealing with skewed outcomes that could be due to zero health care costs or extraordinarily large health care costs,

<p>these responses state that it is inappropriate/not possible to apply these methods to this sample due to the presence of zeros. The change in the mean cost conditional on having a cost doesn't tell us about changes in costs over time.</p> <p>R3.10. The paper doesn't discuss how the costs is converted to real terms. Additional, conversion out of the Ethiopian currency to USD for analysis using a single exchange rate seems problematic. It is not clear to me why the analysis should not be done in Ethiopian currency units exclusively. Converting using a single or even a series of exchange rates and doing the analysis in a different currency introduces the potential for macroeconomic confounding. The currency needs to be converted to real terms using Ethiopian inflation data.</p>	<p>log-transform can only be done if costs are non-zero because we can't log-transform a zero value, which could skew the outcome, and that is why we have not applied it here. So, as it is beyond the scope of most statistical methods to correct this, we have used multiple-part analysis to determine average costs for such complexities in cost data.</p> <p>R3.10;</p> <ul style="list-style-type: none"> • In our analysis, the cost data was first converted to real terms by adjusting market prices to reflect true costs using Ethiopian inflation data as it has been indicated in the costing approach under the data analysis section. • Additionally, from the beginning, the analysis was done in Ethiopian currency units exclusively, then by considering different currency might introduces the potential for macroeconomic confounding conversion out of the Ethiopian currency(average currency) to USD for analysis using Ethiopian inflation data was done because we have compared our finding with others findings internationally.
<p>Reviewer 4</p>	
<p>Comments to the Author:</p> <p>Thank you for these responses, including noting the limitation regarding patients who were employed before the pandemic but then lost their jobs. It is also now clearer which chronic diseases were eligible for inclusion and I have no further queries.</p> <p>While I still don't see a copy of the questionnaire that could be a system issue, so I simply recommend the publishers make the survey available to readers if this manuscript is accepted for publication.</p>	<ul style="list-style-type: none"> • The questionnaire was supplemented accordingly as per suggested. If it was necessary I will share it via email for the confirmation.