

## Does deforestation drive visceral leishmaniasis transmission? A causal analysis

Cleber Vinicius Brito dos Santos, Anaiá da Paixão Sevá, Guilherme Loureiro Werneck and Cláudio José Struchiner

### Article citation details

*Proc. R. Soc. B* **288**: 20211537.

<http://dx.doi.org/10.1098/rspb.2021.1537>

### Review timeline

Original submission: 22 February 2021

1st revised submission: 6 July 2021

2nd revised submission: 30 July 2021

Final acceptance: 30 July 2021

Note: Reports are unedited and appear as submitted by the referee. The review history appears in chronological order.

## Review History

### RSPB-2021-0444.R0 (Original submission)

#### Review form: Reviewer 1

##### Recommendation

Accept with minor revision (please list in comments)

**Scientific importance: Is the manuscript an original and important contribution to its field?**

Excellent

**General interest: Is the paper of sufficient general interest?**

Excellent

**Quality of the paper: Is the overall quality of the paper suitable?**

Good

**Is the length of the paper justified?**

Yes

**Should the paper be seen by a specialist statistical reviewer?**

Yes

**Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.**

No

**It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.**

**Is it accessible?**

Yes

**Is it clear?**

Yes

**Is it adequate?**

Yes

**Do you have any ethical concerns with this paper?**

No

### **Comments to the Author**

The work is of relevant interest and in general it is well written, but there are some adjustments that need to be made: in the second paragraph of the introduction, lines 43 to 48, when the authors describe the etiology and areas of occurrence of visceral leishmaniasis, there is a need to improve the logical sequence. I suggest starting with the countries where LV occurs and which are the most affected. Comment on the two species of Leishmania (*L. donovani* and *L. infantum*) that cause VL, and their respective epidemiological pictures: anthroponotic and zoonotic: and where they occur. After, channel the information to Brazil.

Line 57: reference [17]. I think the correct reference for this information is [18].

Lines 59-60. The beginning of the expansion of VL in São Paulo state coincided with the construction of the Bolivia-Brazil gas pipeline in 1998, In accordance with the cited reference [14], the beginning of the expansion of VL in São Paulo state partially coincided with .... in the period between 1997-1999.

Line 171: include class 20,001 - 50,000,

Line 321. Please check the reference [58], as the article is about cutaneous leishmaniasis.

References:

18, 34, 46 and 69 - Please include the website and access date.

## **Review form: Reviewer 2**

### **Recommendation**

Major revision is needed (please make suggestions in comments)

**Scientific importance: Is the manuscript an original and important contribution to its field?**

Acceptable

**General interest: Is the paper of sufficient general interest?**

Good

**Quality of the paper: Is the overall quality of the paper suitable?**

Acceptable

**Is the length of the paper justified?**

Yes

**Should the paper be seen by a specialist statistical reviewer?**

No

**Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.**

No

**It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.**

**Is it accessible?**

N/A

**Is it clear?**

N/A

**Is it adequate?**

N/A

**Do you have any ethical concerns with this paper?**

No

#### **Comments to the Author**

Manuscript: Does deforestation drive visceral leishmaniasis transmission? A counterfactual analysis

The manuscript has great relevance for understanding the role of environmental risk factors such as the presence or absence of forests in the spreading of visceral leishmaniasis in Brazil, particularly in São Paulo state. The study is in line with the editorial focus of RSPB. The methodology is interesting, however, some aspects should be improved and elucidated.

#### Major concerns

Why Campina do Monte Alegre was chosen as an example of the network between municipalities in São Paulo state. What are the environmental and epidemiological characteristics of the municipality? In the discussion, why did the authors not correlate the results found with endemic municipalities of the western region? It is well known that the VL in São Paulo state spread mainly in the western region where the environmental changes occurred and the tropical forest was completely devastated. Why did the authors not discuss the absence of Lu Longipalpis, the low levels of CVL, and the rare cases of HVL in the coastal área of São Paulo state, where the Atlantic forest was preserved? Conversely, in the western region on the border of Mato Grosso do Sul, in which deforestation and environmental changes heavily occurred, high levels of vector, CVL, and HVL were found.

The conclusions are not supported by the data presented and the authors should discuss clearly how this data can be helpful to advance our understanding of the topic under study. Public health relevance should be addressed.

#### Minor concerns

The title of the manuscript (A counterfactual analysis) is not related to the objectives, methods, or results. The term: A counterfactual analysis makes no sense and should be changed.

#### INTRODUCTION

The introduction should be shortened and only relevant information included.

Line 33 -The environmental changes have been involved not only in the emerging but also in the re-emerging of VBD. Replace re-emergence by emerging and re-emerging

Line 54: but by 2018 it had spread to 198 municipalities (30.7%).

Authors must update the data for 2020. Data is available on the websites cited in the manuscript.

Lines 57-59: Since then, São Paulo state has recorded 57 more than 3000 cases of HVL, of which 300 were fatal (17), and the disease is now considered endemic in some municipalities.

Please update the cases in HVL as previously recommended.

Lines 59-63 - The beginning of the expansion of VL in São Paulo state coincided with the construction of the Bolivia-Brazil gas pipeline in 1998, which resulted in the disturbance of forestation in Southeastern? Brazil and the migration of workers from endemic areas (14,16).

Please review the information that is incomplete. The expansion of VL in São Paulo state started previously through the construction of a railroad, a highway, and recently a gas pipeline, linking. There are dozens of papers highlighting the role of these constructions in the spreading of VL in São Paulo state.

See reference 14: Cardim MF, Rodas LA, Dibo MR, Guirado MM, Oliveira AM, Chiaravalloti-Neto F. Introduction and expansion of human American visceral leishmaniasis in the state of Sao Paulo, Brazil, 1999-2011. Rev Saude Publica. 2013 Aug;47(4):691-700.

Line 71- remove the term severely that is not appropriated in this context.

Lines 72-82 - I suggest shortening or removing this information from the Introduction. In the methodology, the authors explained the tools used to obtain the results.

Line 121: Reference 18 - please correct the reference, it is impossible to access the information Paulo S de E de S de S. Dados estatísticos da Leishmaniose Visceral Americana de 1999-2018. 2019.

## METHODS

The most common GDP per capita was 10,001-15,000 Brazilian reais (31.13%). Please transition to US dollars. It is impossible for non-Brazilian individuals to analyze the income cited.

GDP per capita (in Brazilian reais)

## DISCUSSION

Although the authors, due to their brand new methodologies have found important results, the discussion is evasive and lacks objectivity. Why did they not discuss the influence or association of the results of table 1 to table 3 to the spreading of vectors, CVL, and HVL in São Paulo state focusing mainly on the regions where the disease heavily spreading?

Lines 302-321 - In the first paragraph of the discussion, it is advisable to write a short summary of the main results or a short paragraph contextualizing the subject. From lines 302-321, in a long text, the authors repeated some of the information given in the introduction and methodology. The text should be resumed or deleted.

Line 303 - emergence, please, correct to emerging in the entire manuscript.

Line 350 - Last, the connectivity between municipalities may be underrepresented due to the deficiency of data on connectivity other than terrestrial (e.g., via airplane).

This sentence makes no sense since very few municipalities studied and located alongside the gas pipeline have airports.

## List of authors

Santos, Cleber; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social Seva, Anaiá; Universidade Estadual de Santa Cruz, Departamento de Ciência Animal e Agrárias Werneck, Guilherme; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social Struchiner, Cláudio; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social; Fundação Getúlio Vargas, Escola de Matemática Aplicada

Author contributions. CVBS and CJS conceived the study; CVBS and APS collected and managed the data; CVBS performed the data analysis; CVBS, APS, GLW and CJS interpreted and discussed the results; CVBS drafted the manuscript; APS, GLW and CJS revised the manuscript.

There is no correlation between the authors listed and their contributions. Please check and

correct.

## BIBLIOGRAPHY

The bibliography must be checked and completed as previously commented. Example:

34. IBGE IB de G e E-. Cidades e Estados. 2020.

46. Transport

## Decision letter (RSPB-2021-0444.R0)

26-May-2021

Dear Mr Santos:

I am writing to inform you that your manuscript RSPB-2021-0444 entitled "Does deforestation drive visceral leishmaniasis transmission? A counterfactual analysis" has, in its current form, been rejected for publication in Proceedings B.

This action has been taken on the advice of referees, who have recommended that substantial revisions are necessary. With this in mind we would be happy to consider a resubmission, provided the comments of the referees are fully addressed. However please note that this is not a provisional acceptance.

The resubmission will be treated as a new manuscript. However, we will approach the same reviewers if they are available and it is deemed appropriate to do so by the Editor. Please note that resubmissions must be submitted within six months of the date of this email. In exceptional circumstances, extensions may be possible if agreed with the Editorial Office. Manuscripts submitted after this date will be automatically rejected.

Please find below the comments made by the referees, not including confidential reports to the Editor, which I hope you will find useful. If you do choose to resubmit your manuscript, please upload the following:

- 1) A 'response to referees' document including details of how you have responded to the comments, and the adjustments you have made.
- 2) A clean copy of the manuscript and one with 'tracked changes' indicating your 'response to referees' comments document.
- 3) Line numbers in your main document.
- 4) Data - please see our policies on data sharing to ensure that you are complying (<https://royalsociety.org/journals/authors/author-guidelines/#data>).

To upload a resubmitted manuscript, log into <http://mc.manuscriptcentral.com/prsb> and enter your Author Centre, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Resubmission." Please be sure to indicate in your cover letter that it is a resubmission, and supply the previous reference number.

Sincerely,  
Professor Gary Carvalho  
mailto: [proceedingsb@royalsociety.org](mailto:proceedingsb@royalsociety.org)

Associate Editor  
Board Member: 1

#### Comments to Author:

Thank you for submitting your manuscript “Does deforestation drive visceral leishmaniasis transmission? A counterfactual analysis” to Proceedings B. I have now received two reviews on the manuscript. While both reviewers see important advances that the study provides for understanding environmental drivers of disease risk, several concerns have been raised that should all be addressed. In particular, both reviewers note several ways that the writing can be edited to improve clarity for readers and to better contextualize these findings and their implications. For example, reviewer 2 highlight the convention of the first paragraph in the discussion to summarize the main results and their implications. Like the reviewer, I’m also confused about the meaning of a “counterfactual analysis”.

#### Reviewer(s)' Comments to Author:

Referee: 1

##### Comments to the Author(s)

The work is of relevant interest and in general it is well written, but there are some adjustments that need to be made: in the second paragraph of the introduction, lines 43 to 48, when the authors describe the etiology and areas of occurrence of visceral leishmaniasis, there is a need to improve the logical sequence. I suggest starting with the countries where LV occurs and which are the most affected. Comment on the two species of *Leishmania* (*L. donovani* and *L. infantum*) that cause VL, and their respective epidemiological pictures: anthroponotic and zoonotic: and where they occur. After, channel the information to Brazil.

Line 57: reference [17]. I think the correct reference for this information is [18].

Lines 59-60. The beginning of the expansion of VL in São Paulo state coincided with the construction of the Bolivia-Brazil gas pipeline in 1998, In accordance with the cited reference [14], the beginning of the expansion of VL in São Paulo state partially coincided with .... in the period between 1997-1999.

Line 171: include class 20,001 - 50,000,

Line 321. Please check the reference [58], as the article is about cutaneous leishmaniasis.

References:

18, 34, 46 and 69 - Please include the website and access date.

Referee: 2

##### Comments to the Author(s)

Manuscript: Does deforestation drive visceral leishmaniasis transmission? A counterfactual analysis

The manuscript has great relevance for understanding the role of environmental risk factors such as the presence or absence of forests in the spreading of visceral leishmaniasis in Brazil, particularly in São Paulo state. The study is in line with the editorial focus of RSPB. The methodology is interesting, however, some aspects should be improved and elucidated.

##### Major concerns

Why Campina do Monte Alegre was chosen as an example of the network between municipalities in São Paulo state. What are the environmental and epidemiological characteristics of the municipality? In the discussion, why did the authors not correlate the results found with endemic municipalities of the western region? It is well known that the VL in São Paulo state spread mainly in the western region where the environmental changes occurred and the tropical forest was completely devastated. Why did the authors not discuss the absence of Lu Longipalpis, the low levels of CVL, and the rare cases of HVL in the coastal área of São Paulo state, where the Atlantic forest was preserved? Conversely, in the western region on the border of Mato Grosso do Sul, in which deforestation and environmental changes heavily occurred, high levels of vector, CVL, and HVL were found.

The conclusions are not supported by the data presented and the authors should discuss clearly how this data can be helpful to advance our understanding of the topic under study. Public health relevance should be addressed.

### Minor concerns

The title of the manuscript (A counterfactual analysis) is not related to the objectives, methods, or results. The term: A counterfactual analysis makes no sense and should be changed.

### INTRODUCTION

The introduction should be shortened and only relevant information included.

Line 33 –The environmental changes have been involved not only in the emerging but also in the re-emerging of VBD. Replace re-emergence by emerging and re-emerging

Line 54: but by 2018 it had spread to 198 municipalities (30.7%).

Authors must update the data for 2020. Data is available on the websites cited in the manuscript.

Lines 57-59: Since then, São Paulo state has recorded 57 more than 3000 cases of HVL, of which 300 were fatal (17), and the disease is now considered endemic in some municipalities.

Please update the cases in HVL as previously recommended.

Lines 59-63 - The beginning of the expansion of VL in São Paulo state coincided with the construction of the Bolivia-Brazil gas pipeline in 1998, which resulted in the disturbance of forestation in Southeastern? Brazil and the migration of workers from endemic areas (14,16). Please review the information that is incomplete. The expansion of VL in São Paulo state started previously through the construction of a railroad, a highway, and recently a gas pipeline, linking. There are dozens of papers highlighting the role of these constructions in the spreading of VL in São Paulo state.

See reference 14: Cardim MF, Rodas LA, Dibo MR, Guirado MM, Oliveira AM, Chiaravalloti-Neto F. Introduction and expansion of human American visceral leishmaniasis in the state of Sao Paulo, Brazil, 1999-2011. Rev Saude Publica. 2013 Aug;47(4):691-700.

Line 71- remove the term severely that is not appropriated in this context.

Lines 72-82 – I suggest shortening or removing this information from the Introduction. In the methodology, the authors explained the tools used to obtain the results.

Line 121: Reference 18 - please correct the reference, it is impossible to access the information Paulo S de E de S de S. Dados estatísticos da Leishmaniose Visceral Americana de 1999-2018. 2019.

### METHODS

The most common GDP per capita was 10,001–15,000 Brazilian reais (31.13%). Please transition to US dollars. It is impossible for non-Brazilian individuals to analyze the income cited.

GDP per capita (in Brazilian reais)

### DISCUSSION

Although the authors, due to their brand new methodologies have found important results, the discussion is evasive and lacks objectivity. Why did they not discuss the influence or association of the results of table 1 to table 3 to the spreading of vectors, CVL, and HVL in São Paulo state focusing mainly on the regions where the disease heavily spreading?

Lines 302-321 – In the first paragraph of the discussion, it is advisable to write a short summary of the main results or a short paragraph contextualizing the subject. From lines 302-321, in a long text, the authors repeated some of the information given in the introduction and methodology. The text should be resumed or deleted.

Line 303 – emergence, please, correct to emerging in the entire manuscript.

Line 350 - Last, the connectivity between municipalities may be underrepresented due to the deficiency of data on connectivity other than terrestrial (e.g., via airplane).

This sentence makes no sense since very few municipalities studied and located alongside the gas pipeline have airports.

List of authors

Santos, Cleber; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social Seva, Anaiá; Universidade Estadual de Santa Cruz, Departamento de Ciência Animal e Agrárias Werneck, Guilherme; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social Struchiner, Cláudio; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social; Fundação Getúlio Vargas, Escola de Matemática Aplicada

Author contributions. CVBS and CJS conceived the study; CVBS and APS collected and managed the data; CVBS performed the data analysis; CVBS, APS, GLW and CJS interpreted and discussed the results; CVBS drafted the manuscript; APS, GLW and CJS revised the manuscript. There is no correlation between the authors listed and their contributions. Please check and correct.

## BIBLIOGRAPHY

The bibliography must be checked and completed as previously commented. Example:

34. IBGE IB de G e E-. Cidades e Estados. 2020.
46. Transport

## Author's Response to Decision Letter for (RSPB-2021-0444.R0

See Appendix A.

## RSPB-2021-1537.R0

### Review form: Reviewer 2 (Luiz Euribel Prestes-Carneiro)

#### **Recommendation**

Accept as is

#### **Scientific importance: Is the manuscript an original and important contribution to its field?**

Good

#### **General interest: Is the paper of sufficient general interest?**

Good

#### **Quality of the paper: Is the overall quality of the paper suitable?**

Good

#### **Is the length of the paper justified?**

Yes

#### **Should the paper be seen by a specialist statistical reviewer?**

No

#### **Do you have any concerns about statistical analyses in this paper? If so, please specify them explicitly in your report.**

No



**It is a condition of publication that authors make their supporting data, code and materials available - either as supplementary material or hosted in an external repository. Please rate, if applicable, the supporting data on the following criteria.**

**Is it accessible?**

Yes

**Is it clear?**

Yes

**Is it adequate?**

Yes

**Do you have any ethical concerns with this paper?**

No

#### **Comments to the Author**

The authors filled most of the issues raised in my comments. The manuscript is suitable for publication in the revised format.

## **Decision letter (RSPB-2021-1537.R0)**

27-Jul-2021

Dear Mr Santos

I am pleased to inform you that your Review manuscript RSPB-2021-1537 entitled "Does deforestation drive visceral leishmaniasis transmission? A counterfactual analysis" has been accepted for publication in Proceedings B.

The referee(s) do not recommend any further changes. Therefore, please proof-read your manuscript carefully and upload your final files for publication. Because the schedule for publication is very tight, it is a condition of publication that you submit the revised version of your manuscript within 7 days. If you do not think you will be able to meet this date please let me know immediately.

To upload your manuscript, log into <http://mc.manuscriptcentral.com/prsb> and enter your Author Centre, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, upload a new version through your Author Centre.

Before uploading your revised files please make sure that you have:

1) A text file of the manuscript (doc, txt, rtf or tex), including the references, tables (including captions) and figure captions. Please remove any tracked changes from the text before submission. PDF files are not an accepted format for the "Main Document".

2) A separate electronic file of each figure (tiff, EPS or print-quality PDF preferred). The format should be produced directly from original creation package, or original software format. Please note that PowerPoint files are not accepted.

3) Electronic supplementary material: this should be contained in a separate file from the main text and the file name should contain the author's name and journal name, e.g. `authorname_procb_ESM_figures.pdf`

All supplementary materials accompanying an accepted article will be treated as in their final form. They will be published alongside the paper on the journal website and posted on the online figshare repository. Files on figshare will be made available approximately one week before the accompanying article so that the supplementary material can be attributed a unique DOI. Please see: <https://royalsociety.org/journals/authors/author-guidelines/>

#### 4) Data-Sharing and data citation

It is a condition of publication that data supporting your paper are made available. Data should be made available either in the electronic supplementary material or through an appropriate repository. Details of how to access data should be included in your paper. Please see <https://royalsociety.org/journals/ethics-policies/data-sharing-mining/> for more details.

If you wish to submit your data to Dryad (<http://datadryad.org/>) and have not already done so you can submit your data via this link

<http://datadryad.org/submit?journalID=RSPB&manu=RSPB-2021-1537> which will take you to your unique entry in the Dryad repository.

If you have already submitted your data to dryad you can make any necessary revisions to your dataset by following the above link.

5) For more information on our Licence to Publish, Open Access, Cover images and Media summaries, please visit <https://royalsociety.org/journals/authors/author-guidelines/>.

Once again, thank you for submitting your manuscript to Proceedings B and I look forward to receiving your final version. If you have any questions at all, please do not hesitate to get in touch.

Sincerely,  
Professor Gary Carvalho  
<mailto:proceedingsb@royalsociety.org>

Associate Editor  
Board Member  
Comments to Author:

I appreciate the effort that the authors have made to address points raised by the reviewers. The manuscript is much improved. However, there are a few additional minor points that I would like addressed. Notably, the title has not been amended, as initially suggested by one of the reviewers and myself. The reference to a counterfactual analysis is simply not something that many readers will understand, and it's important that readers are able to understand the topic from the title. I would like the title amended (e.g., to something like "The effects of deforestation on visceral leishmaniasis transmission and disease") and the reference to a counterfactual analysis removed from the abstract. There are also a few minor grammatical errors in the introduction regarding transmission and disease. Pathogens and parasites are transmitted amongst hosts, not diseases (on line 45, change to "the two most common species of causative parasites" and also amend line 48). Also, line 80 change to "in most studies, data are assumed...".

Reviewer(s)' Comments to Author:

Referee: 2

Comments to the Author(s).

The authors filled most of the issues raised in my comments. The manuscript is suitable for publication in the revised format.

Sincerely,  
Proceedings B  
mailto: [proceedingsb@royalsociety.org](mailto:proceedingsb@royalsociety.org)

## Decision letter (RSPB-2021-1537.R1)

30-Jul-2021

Dear Mr Santos

I am pleased to inform you that your manuscript entitled "Does deforestation drive visceral leishmaniasis transmission? A causal analysis" has been accepted for publication in Proceedings B.

You can expect to receive a proof of your article from our Production office in due course, please check your spam filter if you do not receive it. PLEASE NOTE: you will be given the exact page length of your paper which may be different from the estimation from Editorial and you may be asked to reduce your paper if it goes over the 10 page limit.

If you are likely to be away from e-mail contact please let us know. Due to rapid publication and an extremely tight schedule, if comments are not received, we may publish the paper as it stands.

If you have any queries regarding the production of your final article or the publication date please contact [procb\\_proofs@royalsociety.org](mailto:procb_proofs@royalsociety.org)

Your article has been estimated as being 9 pages long. Our Production Office will be able to confirm the exact length at proof stage.

### Data Accessibility section

Please remember to make any data sets live prior to publication, and update any links as needed when you receive a proof to check. It is good practice to also add data sets to your reference list.

### Open Access

You are invited to opt for Open Access, making your freely available to all as soon as it is ready for publication under a CCBY licence. Our article processing charge for Open Access is £1700.

Corresponding authors from member institutions

(<http://royalsocietypublishing.org/site/librarians/allmembers.xhtml>) receive a 25% discount to these charges. For more information please visit <http://royalsocietypublishing.org/open-access>.

### Paper charges

An e-mail request for payment of any related charges will be sent out shortly. The preferred payment method is by credit card; however, other payment options are available.

### Electronic supplementary material:

All supplementary materials accompanying an accepted article will be treated as in their final form. They will be published alongside the paper on the journal website and posted on the online figshare repository. Files on figshare will be made available approximately one week before the accompanying article so that the supplementary material can be attributed a unique DOI.

You are allowed to post any version of your manuscript on a personal website, repository or preprint server. However, the work remains under media embargo and you should not discuss it with the press until the date of publication. Please visit <https://royalsociety.org/journals/ethics-policies/media-embargo> for more information.

Thank you for your fine contribution. On behalf of the Editors of the Proceedings B, we look forward to your continued contributions to the Journal.

Sincerely,  
Proceedings B  
[mailto: proceedingsb@royalsociety.org](mailto:proceedingsb@royalsociety.org)

## Appendix A

### AUTHORS RESPONSE TO DECISION LETTER FOR (RSPB-2021-0444):

#### Does deforestation drive visceral leishmaniasis transmission? A counterfactual analysis

#### RESPONSES TO THE REVIEWERS' COMMENTS

We would like to thank the reviewers for putting in the time and effort to provide us with valuable comments. We have revised our manuscript accordingly and feel the reviewers' Comments have helped us to improve the manuscript considerably. The responses have been embedded after the reviewer comment in green (R:...)

#### REFEREE: 1

##### Comments to the Author(s)

The work is of relevant interest and in general it is well written, but there are some adjustments that need to be made.

Dear reviewer, thank you for your helpful comments. We improved the manuscript according to all of your suggestions. The responses have been embedded after the reviewer comment in green (R:...)

1. in the second paragraph of the introduction, lines 43 to 48, when the authors describe the etiology and areas of occurrence of visceral leishmaniasis, there is a need to improve the logical sequence. I suggest starting with the countries where VL occurs and which are the most affected. Comment on the two species of *Leishmania* (*L. donovani* and *L. infantum*) that cause VL, and their respective epidemiological pictures: anthroponotic and zoonotic: and where they occur. After, channel the information to Brazil.

R: Thank you for your relevant comments and detailed information, We followed the reviewer's suggestion and modified the text accordingly..

2. Line 57: reference [17]. I think the correct reference for this information is [18].

R: Thanks. The reference has been changed.

3. Lines 59-60. The beginning of the expansion of VL in São Paulo state coincided with the construction of the Bolivia-Brazil gas pipeline in 1998, In accordance with the cited reference [14], the beginning of the expansion of VL in São Paulo state partially coincided with .... in the period between 1997-1999.

R: We apologize for that. The text has been modified.

4. Line 171: include class 20,001 - 50,000

R: Corrected.

5. Line 321. Please check the reference [58], as the article is about cutaneous leishmaniasis.

R: We thank the reviewer for the comment. We inserted an appropriate reference. Since the discussion has changed, the correspondent reference [58] is now [67]:

Saccaro NL, Mation LF, Sakowski PAM. (2016). Impacts of deforestation on the incidence of diseases in the Brazilian Amazon. Discussion paper / Institute for Applied Economic Research (IPEA).- Brasília : Rio de Janeiro. Available from [https://www.econstor.eu/bitstream/10419/220300/1/dp\\_212.pdf](https://www.econstor.eu/bitstream/10419/220300/1/dp_212.pdf).

6. References: 18, 34, 46 and 69 - Please include the website and access date.

R: The website and access dates have been inserted. Since we modified the text, the reference [69] is now [70]

## REFEREE: 2

Comments to the Author(s)

Manuscript: Does deforestation drive visceral leishmaniasis transmission? A counterfactual analysis

The manuscript has great relevance for understanding the role of environmental risk factors such as the presence or absence of forests in the spreading of visceral leishmaniasis in Brazil, particularly in São Paulo state. The study is in line with the editorial focus of RSPB. The methodology is interesting, however, some aspects should be improved and elucidated.

Thank you for your valuable comments and detailed observations through the manuscript.. We improved the manuscript according to your suggestions. The responses have been embedded after the reviewer comment in green (R:...)

Major concerns

1. Why Campina do Monte Alegre was chosen as an example of the network between municipalities in São Paulo state. What are the environmental and epidemiological characteristics of the municipality?

R: We randomly chose the municipality of Campina do Monte Alegre. There is no particular characteristic that influenced such choice. Just remembering, figure 1C is simply a pictorial example to the reader of what constitutes a network; all 645 municipalities of São Paulo have their own network based on the neighbourhood matrix.

2. In the discussion, why did the authors not correlate the results found with endemic municipalities of the western region? It is well known that the VL in São Paulo state spread mainly in the western region where the environmental changes occurred and the tropical forest was completely devastated. Why did the authors not discuss the absence of Lu Longipalpis, the low levels of CVL, and the rare cases of HVL in the coastal área of São Paulo state, where the Atlantic forest was preserved? Conversely, in the western region on the border of Mato Grosso do Sul, in which deforestation and environmental changes heavily occurred, high levels of vector, CVL, and HVL were found.

R: We apologize for not providing additional details in the original manuscript on these issues. We have modified the text, and new information has been added to better describe the VL dynamics and its relation to the deforestation process in Sao Paulo state (lines 327-335).

3. The conclusions are not supported by the data presented and the authors should discuss clearly how this data can be helpful to advance our understanding of the topic under study. Public health relevance should be addressed.

R: We thank the reviewer for the comment. Our results point to a significant effect of deforestation on the surge of VL (as presented in Table 3), and when we compare a hypothetical scenario where the state-wide deforestation dropped (50% to 0%), vector, CVL and HVL occurrences reduced by 11%, 6.67% and 29.87% respectively (figure 5). So, given that deforestation is a causal factor for VL occurrence, we conclude that to control disease transmission properly, decision-makers must take deforestation into account and find viable solutions for the trade-off (economic development vs. deforestation). In fact it was missing the reinforcement of our main results and also the link with our proposal to solve issues associated with VL occurrence and public health relevance. Thus, we have improved the conclusion, as your suggestion. (lines 321-326 and 409-419).

#### Minor concerns

4. The title of the manuscript (A counterfactual analysis) is not related to the objectives, methods, or results. The term: A counterfactual analysis makes no sense and should be changed.

R: The objective of our study was to estimate the causal effects of deforestation on VL. To this end, we simulate what would have happened, if we changed the current deforestation status (the factual) to hypothetical deforestation prevalence scenarios (the counterfactuals) and comparing the potential outcomes (VL occurrence or absence) under the simulations. We have now made explicit in the main text that our analysis reflects the contrast between potential outcomes (counterfactuals) and hope to have clarified this issue. (lines 211 to 215).

#### INTRODUCTION

5. The introduction should be shortened and only relevant information included.

R: We thank the reviewer for the recommendation. We shortened the intro; by now, there are 756 words, compared to 820 as in the previous version.

6. Line 33 –The environmental changes have been involved not only in the emerging but also in the re-emerging of VBD. Replace re-emergence by emerging and re-emerging

R: The text has been modified by inserting “re-emergence” (line 33). Our English editing consultant advised that the correct term in this context is “emergence and reemergence”, so we keep in that way.

7. Line 54: but by 2018 it had spread to 198 municipalities (30.7%).

Authors must update the data for 2020. Data is available on the websites cited in the manuscript.

R: The data was updated. Unfortunately, the more recent data concerning the presence of *Lutzomyia longipalpis* in the Sao Paulo state dates to 2019:

[https://www.saude.sp.gov.br/resources/cve-centro-de-vigilancia-epidemiologica/areas-de-vigilancia/doencas-de-transmissao-por-vetores-e-zoonoses/dados/leish/lv\\_mapas.pdf](https://www.saude.sp.gov.br/resources/cve-centro-de-vigilancia-epidemiologica/areas-de-vigilancia/doencas-de-transmissao-por-vetores-e-zoonoses/dados/leish/lv_mapas.pdf)

8. Lines 57-59: Since then, São Paulo state has recorded 57 more than 3000 cases of HVL, of which 300 were fatal (17), and the disease is now considered endemic in some municipalities.

Please update the cases in HVL as previously recommended.

R: We also updated data related to HVL cases, but as previously mentioned, the more recent and reliable information dates to 2019.

9. Lines 59-63 - The beginning of the expansion of VL in São Paulo state coincided with the construction of the Bolivia-Brazil gas pipeline in 1998, which resulted in the disturbance of forestation in Southeastern? Brazil and the migration of workers from endemic areas (14,16). Please review the information that is incomplete. The expansion of VL in São Paulo state started previously through the construction of a railroad, a highway, and recently a gas pipeline, linking. There are dozens of papers highlighting the role of these constructions in the spreading of VL in São Paulo state.

See reference 14: Cardim MF, Rodas LA, Dibo MR, Guirado MM, Oliveira AM, Chiaravalloti-Neto F. Introduction and expansion of human American visceral leishmaniasis in the state of Sao Paulo, Brazil, 1999-2011. Rev Saude Publica. 2013 Aug;47(4):691-700.

R: We agree with the reviewer that the information is incomplete. We removed the term 'beginning', which is incorrect in this context and comment on others constructions (the highway and railroad) linked to VL occurrence and spread in São Paulo (lines 63-66).

10. Line 71- remove the term severely that is not appropriated in this context.

R: The term 'severely' has been removed

11. Lines 72-82 – I suggest shortening or removing this information from the Introduction. In the methodology, the authors explained the tools used to obtain the results.

R: We agree with the reviewer and the paragraph has been modified.

12. Line 121: Reference 18 - please correct the reference, it is impossible to access the information

Paulo S de E de S de S. Dados estatísticos da Leishmaniose Visceral Americana de 1999-2018. 2019.

R: The reference has been corrected. We replaced the link.

## METHODS

13. The most common GDP per capita was 10,001–15,000 Brazilian reais (31.13%). Please transition to US dollars. It is impossible for non-Brazilian individuals to analyze the income cited.

GDP per capita (in Brazilian reais)

R: We have modified text, replacing the GDP per capita quantities from Brazilian *Reais* to US dollars

## DISCUSSION



14. Although the authors, due to their brand new methodologies have found important results, the discussion is evasive and lacks objectivity. Why did they not discuss the influence or association of the results of table 1 to table 3 to the spreading of vectors, CVL, and HVL in São Paulo state focusing mainly on the regions where the disease heavily spreading?

R: Thanks for the suggestion. We modified the text, inserting the path of VL through the state, the deforestation process and its relation with VL, as cited by previous work (lines 327-335).

15. Lines 302-321 – In the first paragraph of the discussion, it is advisable to write a short summary of the main results or a short paragraph contextualizing the subject. From lines 302-321, in a long text, the authors repeated some of the information given in the introduction and methodology. The text should be resumed or deleted.

R: We thank the reviewer for the suggestions. A paragraph has been added in the beginning of the discussion section to summarise the major findings (lines 321-326) and the discussion has been modified to improve clarity and a better contextualization of our findings (lines 327-351).

16. Line 303 – emergence, please, correct to emerging in the entire manuscript.

R: The text has been modified (lines 353 and 367).

17. Line 350 - Last, the connectivity between municipalities may be underrepresented due to the deficiency of data on connectivity other than terrestrial (e.g., via airplane).

This sentence makes no sense since very few municipalities studied and located alongside the gas pipeline have airports.

R: We agree with the reviewer and the text has been removed.

#### List of authors

Santos, Cleber; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social Seva, Anaiá; Universidade Estadual de Santa Cruz, Departamento de Ciência Animal e Agrárias Werneck, Guilherme; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social Struchiner, Cláudio; Universidade do Estado do Rio de Janeiro, Instituto de Medicina Social; Fundação Getúlio Vargas, Escola de Matemática Aplicada

Author contributions. CVBS and CJS conceived the study; CVBS and APS collected and managed the data; CVBS performed the data analysis; CVBS, APS, GLW and CJS interpreted and discussed the results; CVBS drafted the manuscript; APS, GLW and CJS revised the manuscript.

18 There is no correlation between the authors listed and their contributions. Please check and correct.

R: Dear reviewer, thank you for noting this. We have been added all first letters of complete name in the system of manuscript submission. However, the system selects only the authors first and last names. In the case of using only the authors first and last name initials letters seems confusing because there are two CS, that correspond to different authors, (CVBS and CJS). In any form, we will contact the manuscript central to find a solution to this.

#### BIBLIOGRAPHY

19. The bibliography must be checked and completed as previously commented. Example:

34. IBGE IB de G e E-. Cidades e Estados. 2020.

#### 46. Transport

R: We thank the reviewer for the comments. The references were checked and corrected.