PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Screening, diagnosis and care cascade for viral hepatitis B and C in Yaoundé, Cameroon: a qualitative study of patients and health providers coping with uncertainty and unbearable costs
AUTHORS	Chabrol, Fanny; Noah Noah, Dominique; Tchoumi, Eric Pascal; Vidal, Laurent; Kuaban, Christopher; Carrieri, Maria Patrizia; Boyer, Sylvie

VERSION 1 – REVIEW

REVIEWER	C John Clements University of Melbourne Australia
REVIEW RETURNED	15-Aug-2018

GENERAL COMMENTS	This article uses established sociological methodologies to explore dimensions of treatment for hepatitis B and C in Cameroon. It is an important study to publish in the medical literature as it demonstrates the human side of recent therapeutic interventions. While the introduction of antiviral agents in the treatment of HIV and hepatitis have been revolutionary, they become ineffective and almost irrelevant if patients cannot afford them and if the system fails to provide the necessary support. I would like to have seen in the article a brief description of the health system in Cameroon relating to funding – what percentage of patients have private funding, and does the government provide any sort of financial safety net for the poor? Also, it would be interesting to know the literacy level, and if there is health education material available to assist in information-sharing. There are several references to counselling, but it would be important to know if there is a pool of staff trained in counselling – I suspect not. How could this skill be improved and expanded? The use of English is very good with only a few points that could be improved. References 3, 15, 20 and 21 are incomplete (use of “et al” is inappropriate).

REVIEWER	Sonjelle Shilton, Francesco Marinucci, Elena Ivanova Reipold Foundation for Innovative new Diagnostics Switzerland
REVIEW RETURNED	03-Oct-2018

GENERAL COMMENTS	The manuscript provides valuable knowledge regarding the state of patient perceptions of their experiences seeking HCV and HBV diagnosis and care in Yaoundé. However the manuscript would be strengthened by addressing and clarifying aspects of the study relating to data collection, methods, and analysis. General comments

	As the interviews were focused not only on the screening portion but also the diagnosis and care pathway, the authors should consider changing the title to “Screening, diagnosis and care cascade for viral hepatitis… “ to reflect more accurately the study results and conclusions. In Conclusion section of the Abstract, please consider the wording of the finding that “Free or reasonably-priced access to hepatitis treatments can only be effective and efficient at reducing the hepatitis disease burden if the whole package of pre-therapeutic check-up and treatment is standardized, simplified and subsidized by national comprehensive policies orientated towards universal health care”. The study points out that complicated and expensive diagnostic procedures and algorithms are also a major barrier to continuation of the hepatitis care cascade, however the wording of the finding is only implicit on this aspect. Perhaps explicit mention that the diagnostic algorithm needs to be simplified would help to highlight this fact. Methods section does not describe when the consenting of patients happened. Please clarify, was it during the authorization of the recording or before. Please clarify the inclusion criteria for the health care worker interviews as well as the consenting process for those Analysis section seems to be only describing the analysis of the patient interviews. Please give more details on the analysis of the health care workers interviews. Please clarify if the coding done was inductive coding only, or a mix of both inductive and deductive In Observations section in Findings, there is no detail on the methods of observation, please expand on how the observations were conducted, was there a standardized tool or check list. Was there an average time of observation and split of number of observations at the two hospitals? Did this split have any bearing on the analysis given the differences in clientele and (possibly their socio economic status, and for example where the HIV care patients only at Hospital Central?) between to the two hospitals. In Discussion, the authors state that the study identified “lack of simple, reliable, and low-cost diagnostic tests” as one of the major barriers for patients with HBV and HCV. However, the Findings section mentions only price for testing as a barrier while complexity of testing algorithms is not reflected. If there is any specific data or quotes related to complexity of testing algorithm, please include them in Findings section. It would be also helpful to describe what the standard of care entails for HBV and HCV screening and diagnosis. The authors mentioned the average national monthly salary for which a reference/ source is needed. If the figure is reliable it is recommended to express the OOP in the Discussion section as Catastrophic health expenditure (CHE) i.e. when out-of-pocket (OOP) payments for health services consume such a large portion of a household’s available income and the household may be pushed into poverty as a result. On p. 17, the authors are saying “More specifically, our results highlight the urgent need for a comprehensive national programme in Cameroon for the screening, care and treatment of HBV and HCV. Screening uptake and access to a subsidized pre-therapeutic package could be enhanced through technological innovations and point-of-care devices at a reduced cost [18]”. Please consider the point that there is no evidence that direct costs of POC test would be much lower than cost of centralized HCV test. However, indirect costs, e.g. the OOP related to transport, will be lower.

	As it is the Conclusion section is incomplete if there is no mentioning on the urgency of simplified and standardized testing algorithms as way to reduce the overall costs. Standardized algorithm for testing would be beneficial as it could eliminate the use of unnecessary and expensive tests (such as re-testing with EIA after RDT screening which is unnecessary if high-quality RDT are used and QA programmes are implemented at screening sites, use of FIBRO test instead of APRI for liver staging, as well as the unneeded HCV RNA VL at 4 weeks and 8 week during treatment). The authors should mention the importance of aligning the national algorithms with the WHO testing guidelines (2017). Minor comments: typo on p.4 HBC instead of HBV On top of p. 5 in the sentence "Currently, the country has no national viral hepatitis program or national guidelines on screening, care and treatment for these infections", please add "diagnosis" after "screening".

VERSION 1 – AUTHOR RESPONSE

Reviewer 1.

This article uses established sociological methodologies to explore dimensions of treatment for hepatitis B and C in Cameroon. It is an important study to publish in the medical literature as it demonstrates the human side of recent therapeutic interventions. While the introduction of antiviral agents in the treatment of HIV and hepatitis have been revolutionary, they become ineffective and almost irrelevant if patients cannot afford them and if the system fails to provide the necessary support.

- I would like to have seen in the article a **brief description of the health system in Cameroon** relating to **funding** – what percentage of patients have **private funding**, and does the government provide any sort of financial safety net for the poor? Also, it would be interesting to know the **literacy level**, and if there is **health education material** available to assist in information-sharing. There are several references to counselling, but it would be important to know if there is **a pool of staff trained in counselling** – I suspect not. How could this skill be improved and expanded?

We have added these important contextual elements on Cameroon health system and human development indicators (see pages 4-5).

"Cameroon is a lower middle income country of Central Africa with a yearly gross domestic product (GDP) of 1354 USD per capita in 2015 and a literacy rate of 80% in young adults (15-24 years) [13]. However, human development indicators remain low: with a human development index of 0.55 in 2018, Cameroon is ranked 151 out of 188 countries, with 38% of the working population earning 3.10 USD (in purchasing power parity) per day or less [14]. The country's health system is mainly funded by private health expenditures through out-of-pocket payments which represent approximately two-thirds of total health expenditures [15]. Social security expenditures on health represent only 2.6% of government health expenditure. In addition, safety nets for the poor are almost non-existent: theoretically, hospitals should have a social service to provide some financial support for the needy, but in reality there is no government funding for this service, and accordingly it is often dysfunctional."

As suggested, we also added some precision on the health education material available to assist counselling sessions and the training of HCP (See last paragraph, page 5) of the setting subsection of the methods:

"However, no specific education material on hepatitis and its prevention, care and treatment has been developed to help effectively carry out pre- and post-test counselling sessions. Specifically, no billboards were available in hospital services and except for hepato-gastroenterologists, other HCP in general have not been trained in counselling on viral hepatitis".

Reviewer 2.

- The manuscript provides valuable knowledge regarding the state of patient perceptions of their experiences seeking HCV and HBV diagnosis and care in Yaoundé. However the manuscript would be strengthened by addressing and clarifying aspects of the study relating to data collection, methods, and analysis. As the interviews were focused not only on the screening portion but also the diagnosis and care pathway, the authors should consider **changing the title** to "**Screening, diagnosis and care cascade for viral hepatitis**… "to reflect more accurately the study results and conclusions.

Thank you for this point. We have revised the title accordingly.

- In **Conclusion** section of the Abstract, please consider the wording of the finding that "Free or reasonably-priced access to hepatitis treatments can only be effective and efficient at reducing the hepatitis disease burden if the whole package of pre-therapeutic check-up and treatment is standardized, simplified and subsidized by national comprehensive policies orientated towards universal health care". The study points out that complicated and expensive diagnostic procedures and algorithms are also a major barrier to continuation of the hepatitis care cascade, however the wording of the finding is only implicit on this aspect. **Perhaps explicit mention that the diagnostic algorithm needs to be simplified** would help to highlight this fact.

Indeed, the sentence was as such too implicit, we have added a precision that the diagnostic algorithm needs to be simplified (See the conclusion of the abstract page 1):

"Free or reasonably-priced access to hepatitis B and C treatments can only be effective and efficient at reducing the hepatitis disease burden if the screening algorithm and the whole pre-therapeutic assessment package are simplified, standardized, and subsidized by comprehensive national policies orientated towards universal health care".

- **Methods** section does not describe when the **consenting of patients** happened. Please clarify, was it during the authorization of the recording or before. Please clarify the **inclusion criteria** for the health care worker interviews as well as the **consenting process** for those.

We have added details on the methods section on how and when the consent of patients was obtained (See second § page 7):

"*Study participation was proposed to patients after their consultation. Those who agreed to share their experiences and perceptions were contacted by phone to make an appointment for an interview outside of the hospital, usually at their home*".

We added the following detail regarding HCP's inclusion criteria (page 6, last §):

"*…mainly gastroenterologists working in infectious disease departments and involved in the consultation of patients affected by viral hepatitis in three reference hospitals of Yaoundé (Hôpital Central, Hôpital Général and CHU), one private clinic in Yaoundé, and one district hospital near Yaoundé*";

And the consenting process was detailed as follows (last § page 7):

Before starting each interview, the purpose and implications of the study participation was explained and consent for participation and audio-recording of the interviews was obtained.

- Analysis section seems to be only describing the analysis of the patient interviews. Please give more details on the **analysis of the health care workers interviews**. Please clarify if the coding done was inductive coding only, or a mix of both **inductive** and **deductive**.

We have added the following to clarify this point (see first paragraph page 8) in the Analysis subsection in the methods):

"Analysis of patients' and HCP interviews was performed using the same inductive method whereby analytical themes were generated by hypothesis and confirmed or re-evaluated by data collection".

- In **Observations** section in **Findings**, there is no detail on the **methods of observation**, please expand on how the observations were conducted, was there a standardized tool or check list. Was there an average time of observation and split of number of observations at the two hospitals? Did this split have any bearing on the analysis given the differences in clientele and (possibly their socio economic status, and for example where the HIV care patients only at Hospital Central?) between to the two hospitals.

Regarding observations, we gave more details (first § page 7):

We used a non-standardized observation guide which was drawn up after analyzing the data from a first series of observations. The main items examined included time spent during the consultation, anamnesis, medical examination, prescription, quality of doctor-patient exchanges, and patient participation in the interaction. Observations of consultations in gastroenterology services were only carried out at the Hospital Central while observations of HIV consultations were conducted in both hospitals.

Given the fact that observations of consultations in gastroenterology services were only carried out at the Hospital Central while observations of HIV consultations were conducted in both hospitals, we think there is no need to discuss any difference in the clientele of these two hospitals.

- **In Discussion,** the authors state that the study identified "lack of simple, reliable, and low-cost diagnostic tests" as one of the major barriers for patients with HBV and HCV. However, the Findings section mentions only price for testing as a barrier while complexity of testing algorithms is not reflected. If there is **any specific data or quotes related to complexity of testing algorithm**, please include them in Findings section. It would be also helpful to describe **what the standard of care entails for HBV and HCV screening and diagnosis**.

As suggested, we have added a quotation of a HCP on the complexity of testing algorithm in Cameroon and necessity of having rapid diagnostic tests has been added in the Results section (see last paragraph, p. 13).

- The authors mentioned the average national monthly salary for which a reference/ source is needed. If the figure is reliable it is recommended to express the OOP in the Discussion section as Catastrophic health expenditure (CHE) i.e. when out-of-pocket (OOP) payments for health services consume such a large portion of a household's available income and the household may be pushed into poverty as a result.

We have added a reference for the average monthly resources and we have chosen to take the per-capita gross domestic product as basis of calculation. This part of the manuscript now reads as follow (page 16-17):

These tests cost between 220 to 440 euros i.e., approximately 2 to 4 times the monthly Cameroonian per-capita gross domestic product [18], and are therefore considered catastrophic healthcare expenditures, likely to severely affect household welfare and push patients and their household into poverty [20], [21].

- On p. 17, the authors are saying "More specifically, our results highlight the urgent need for a comprehensive national programme in Cameroon for the screening, care and treatment of HBV and HCV. Screening uptake and access to a subsidized pre-therapeutic package could be enhanced through technological innovations and point-of-care devices at a reduced cost [18]". Please consider the point that there is no evidence that **direct costs of POC test** would be much lower than cost of centralized HCV test. However, indirect costs, e.g. the OOP related to transport, will be lower.

We have re-worked this sentence that now reads as follow (page 17):

Screening uptake and access to a subsidized pre-therapeutic package could be enhanced through technological innovations and point-of-care devices which may improve both geographical and financial accessibility, especially thanks to reduced indirect costs related to transport [23], [24]. To reach this goal, national health authorities should rely on WHO guidelines on hepatitis B and C testing which propose simplified algorithms which are easy to implement [25], as well on recent WHO recommendations for the screening, care and treatment of chronic hepatitis B and C infections [26], [27].

- As it is the **Conclusion section** is incomplete if there is no mentioning on the **urgency of simplified and standardized testing algorithms** as way to reduce the overall costs. Standardized algorithm for testing would be beneficial as it could eliminate the use of unnecessary and expensive tests (such as re-testing with EIA after RDT screening which is unnecessary if high-quality RDT are used and QA programmes are implemented at screening sites, use of FIBRO test instead of APRI for liver staging, as well as the unneeded HCV RNA VL at 4 weeks and 8 week during treatment). The authors should mention the importance of aligning the national algorithms with the WHO testing guidelines (2017).

We have modified the conclusion as follows to include the need to align national algorithms with the WHO testing guidelines (page 19):

"*Free or reasonably-priced access to hepatitis B and C treatments in Cameroon can only be effective and efficient at reducing the hepatitis disease burden, if the screening algorithm and the whole package of pre-therapeutic assessment are i) simplified and standardized in accordance with the WHO guidelines (2017, 2018), ii) subsidized by national comprehensive policies orientated towards universal health care. Our results are in line with the Sustainable Development Goals*."

Minor comments:

Reviewer 1

The use of English is very good with only a few points that could be improved. References 3, 15, 20 and 21 are incomplete (use of "et al" is inappropriate).

Reviewer 2:

- Typo on p.4 HBC instead of HBV
- On top of p. 5 in the sentence "Currently, the country has no national viral hepatitis program or national guidelines on screening, care and treatment for these infections", please add "diagnosis" after "screening".

We thank the reviewers for alerting on these typos and necessity to revise some references

VERSION 2 – REVIEW

REVIEWER	John Clements University of Melbourne Melbourne Australia
REVIEW RETURNED	27-Dec-2018

GENERAL COMMENTS	This is now an excellent article. I have only trivial comments on syntax and spelling. Reference 15 is inadequate. Many of the references of WHO would benefit from adding the url. References 17, 18 and 29 do not follow the rule of "et al". Delete "using" on page 7 line 13. Page 7 line 19 please find a word in more common usage than "anamnesis". Page 9 line 36 "others". Page 10 line 14 delete "like" and replace with "such as".

	Page 19 line 8 delete "have" and replace with "has". Page 19 line 17 consider using "may not".

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: John Clements

Institution and Country: University of Melbourne
Melbourne
Australia

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

- This is now an excellent article. I have only trivial comments on syntax and spelling.

We thank you for your appreciation and comments.

- Reference 15 is inadequate. Many of the references of WHO would benefit from adding the url.

We have revised entirely the references section and added the url to the references of WHO reports and those of other international organizations, they now read as follow:
[8] WHO. Guidelines on hepatitis B and C testing. 2017 https://www.who.int/hepatitis/publications/guidelines-hepatitis-c-b-testing/en/
[13] World Bank. World Bank Open Data 2018 https://data.worldbank.org/
[14] UNDP. Human Development Reports. Cameroon profile 2018 http://hdr.undp.org/en/countries/profiles/CMR
[15] WHO. World Health Statistics 2015 https://www.who.int/gho/publications/world_health_statistics/2015/en/
[20] WHO. The world health report 2000 - Health systems: improving performance 1999 https://www.who.int/whr/2000/en/
[25] WHO. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. 2017 http://www.who.int/hepatitis/publications/hepatitis-b-guidelines/en/
[26] WHO. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. 2018 https://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2018/en/

- References 17, 18 and 29 do not follow the rule of "et al".

We have revised these references and all the references of articles written by more than three authors follow the rule of author 1, author 2, author 3 et al.

- Delete "using" on page 7 line 13.

We have deleted the word using: "In addition, observations to assess doctor-patient relationships were conducted ~~using~~ during medical rounds in the gastroenterology ward or outpatient medical consultation spaces of these two facilities."

- Page 7 line 19 please find a word in more common usage than "anamnesis".

We have replaced “anamnesis” by “clinical history taking”: “The main items examined included time spent during the consultation, **clinical history taking**, medical examination, prescription, quality of doctor-patient exchanges, and patient participation in the interaction.”

- Page 9 line 36 "others".

Indeed, the sentence now reads: “The **others** were employed as follows: (…)”

- Page 10 line 14 delete "like" and replace with "such as".

We have changed the formulation of the sentence: “According to our observations, approximately 33% (16/49) of the consultations were related to patients who discovered they had hepatitis after the onset of symptoms **such as**long episodes of fatigue or ascites.”

- Page 19 line 8 delete "have" and replace with "has".

This has been corrected. “With respect to HCV treatment, the large decrease in prices obtained recently for DAA with the arrival of generic drugs **has** led to those treatments becoming very cost-effective in Cameroon”.

- Page 19 line 17 consider using "may not".

The sentence now reads: “It was only conducted in Yaoundé and thus **may not** reflect what happens elsewhere in Cameroon, especially in rural areas”.