PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Living conditions, HIV and gender affirmation care pathways of transgender people living with HIV in France: a nationwide, comprehensive, cross-sectional, community-based research protocol (ANRS Trans&HIV)
AUTHORS	Mora, Marion; Rincon, Giovanna; Bourrelly, Michel; Maradan, Gwenaëlle; Freire Maresca, Anaenza; Michard, Florence; Rouveix, Elisabeth; Pannetier, Julie; Leriche, Diane; Alain, Tristan; yazdanpanah, yazdan; Michels, David; Spire, Bruno

VERSION 1 – REVIEW

REVIEWER	Lacombe-Duncan, A University of Michigan, School of Social Work
REVIEW RETURNED	25-May-2021

GENERAL COMMENTS	Thank you for the opportunity to review ‘Living conditions and patient care pathways of transgender people living with HIV in France: a cross-sectional, exhaustive, community-based research study protocol (ANRS Trans & HIV)’. I believe that this study protocol would be of interest to advancing scholarship on health and healthcare access among trans people living with HIV, particularly in contexts in which these studies are scant. I commend the authors for taking a community-based approach to ensure meaningful inclusion of trans communities in their work. While I am enthusiastic about the topic, there are several areas that require need clarification and expansion. Please see my notes by section below. Abstract By taboo subject do the authors mean stigmatized identity? The first sentence would be clearer if the authors clarified and mentioned what is poorly documented – health needs? Experiences? Please spell out TRHIV at first use. What is an exhaustive study? I am unfamiliar with this term and it would be helpful to have it explained or removed as a study descriptor. Does respectively indicate that trans women are included in the quantitative component and trans men in the qualitative? Please clarify or remove the term respectively. I also wonder about nonbinary trans persons. By transitioning do you mean medical transition or broader? Please clarify here and in the introduction/background.

By HIV structures do the authors mean HIV care settings? Please expand.

Introduction
The strongest part of the literature review pertains to the local (French) context, including what the healthcare system looks like, an estimation of the trans population, invisibility and stigma, HIV among trans people in France, etc. The areas that need expansion include:

- In the first paragraph, the authors should expand on why data collected for gender affirming surgery underestimates trans people – otherwise put, many trans people, including trans people living with HIV, do not want to access or cannot access medical gender affirmation – they are still legitimate trans people whose needs should be recognized (See, for example: Scheim & Bauer, 2015; Report of the 2015 U.S. Trans Survey; Nolan et al., 2019).
- The literature review pertaining to HIV vulnerability and HIV disparities could use some updating, please consider adding results of a more recent meta-analysis (Becasen et al., 2019) and more recent writings from Poteat and colleagues (Poteat, Wirtz, & Reisner, 2019; Mayo-Wilson et al., 2020).
- In the fourth paragraph, are there references regarding that trans women may have a higher risk of transmitting HIV? The second sentence of that paragraph pertains to risk of acquiring not transmitting HIV, so I am unclear if this is what the authors meant.
- Please also say more about concerns about drug-drug interactions and how this impacts access to HIV care and uptake of ART among trans women (See, for example: Lacombe-Duncan et al., 2019). There are other vulnerabilities to HIV described among trans men, that are not extrapolated on in this literature review (See, for example: Scheim et al., 2017).
- I commend the authors for their community-based approach; I wonder what role the community partners had in the writing of the protocol?

Minor: There are a number of acronyms (e.g., TRHIV) that need to be spelled out at first use.

Methods and Analysis
There is no mention of dates, which is required of study protocols.

There are a number of specific objectives listed for the study and I am currently unclear about the study’s ability to meet each of these objectives.

Is there a reason nonbinary trans-identified people are not included? If so, please clarify.

As noted in reference to the abstract, what is an exhaustive study? I am unfamiliar with this term and it would be helpful to have it explained or removed as a study descriptor.

When referring to a study as mixed methods, it necessitates description of a mixed methods typology (see Creswell & Plano-Clark, 2011) as well a description of how data will be mixed. I believe what the authors have described is a multi-method study. This should be clarified.

	I am also unclear why the authors refer to their study as cross-sectional but then mention longitudinal analyses as one of their objectives? Please add context about sex work into the introduction if that factors as a significant component in the study design. Will trans women also be participating in qualitative interviews? If not, it is definitely not a mixed methods study nor is it a multi-methods study. It is a quantitative study with trans women, and a qualitative study with trans men. Can the authors provide examples of the questions and/or share the questionnaire in it's entirety? How (has) the questionnaire been adapted for use with trans women? What role, if any, did the community partners play in adapting the questionnaire? Similarly, what role did the community partners play in developing the interview guide with trans men. Can the authors share the interview guide or provide sample questions? Adding these details will enhance the utility of the study protocol for informing future research with trans populations. Please expand on all variables that will be collected about the healthcare settings and/or provide sample or full questions/instruments for data collection. What are the potential ethical issues of having one's doctor recruit? Is there potential for coercion and how has the study team accounted for/mitigated that potential risk? The analyses should be described in the methods and analysis section; the final section could be called Implications and Planned Dissemination, or Discussion. Given the long list of study objectives, it would be helpful for the authors to describe their analysis plan by objective. At this point, the planned analyses do not map onto the study objectives, and actually introduce new objectives (to analyze data based on geographic variation). Throughout, it is unclear what outcomes are being looked at. And again, I am unclear based on the authors' description of the study as cross-sectional how longitudinal analyses apply. I believe the authors have a well-constructed study and have paid a lot of attention to be comprehensive - we the audience could benefit from hearing more of the details. How many care settings will be involved in the study and is the study powered for multi-level analyses? A power calculation would be helpful here. References are needed for thematic content analysis. Please also expand on study limitations. A summary paragraph discussing the implications for the study would be helpful to end the protocol. Please also note that the manuscript needs editing for grammar.

REVIEWER	Tomaz de Lima, Rafael Federal University of Rio Grande do Norte, Public Health

REVIEW RETURNED	13-Jun-2021

GENERAL COMMENTS	The evaluated protocol is theoretically and methodologically well-founded, highlighting its relevance and possible impacts on the health of trans people living with HIV in France. However, for it to be accepted for publication, it is necessary to make some adaptations or include some details. 1) The author presents in the section "study population" a definition of trans people. I understand that this definition should be included in the introduction, so that readers know from the outset who is the population referred to in the study. 2) The justifications for the participation of trans women only in the quantitative component and trans men only in the qualitative component of the research are explained. However, cannot these criteria be considered a limitation of the study? The investigation proposes to make an exhaustive description of the socio-behavioral data. But how to carry out this exhaustive description with quantitative techniques, especially with regard to trans women? How to understand the subjective aspects related to life history and health care experiences with quantitative research techniques? In this matter, I realize that there is an incongruity between the objectives and the chosen methods. Therefore, it would be relevant to include further clarification on this issue. 3) On the topic of ethical aspects, adjust the name of the city that is the headquarters of the 64th General Assembly of the World Medical Association. The correct one is Fortaleza. 4) What is the forecast for the beginning and end of the study? It is important to add this information to see if all objectives can be achieved and methodological strategies can be met. Nothing more to declare, I am available for further explanation and to review a new version of the manuscript.

REVIEWER	Chakrapani, Venkatesan Centre for Sexuality and Health Research and Policy
REVIEW RETURNED	23-Jun-2021

GENERAL COMMENTS	The proposed study addresses an important topic in transgender people's health – to document and explain care trajectories of transgender people living with HIV. Introduction section: 1. Transgender people living with HIV are likely to face double or triple discrimination due to their multiple marginalised identities (e.g., due to gender identity, HIV status and sex work status). Hence, information about intersectional or multiple stigmas can be explicitly stated in the Introduction section (and appropriate measures/scales can be added in the Methods section). 2. It is unclear whether the 'TRHIV transition trajectories' will be documented only in relation to HIV care but also for gender transition care. Documenting the trajectories of both HIV care and gender transition care will result in rich data. If documenting gender transition care trajectories is also one of the objectives of the study, then it can be explicitly stated in the objectives and the

	title. For example, ‘HIV and gender transition care pathways’ instead of ‘patient care pathways’ in the title. Methods: 1. It is not clear what kind of mixed methods design will be followed. Also, it is not clear how many TRHIV will be recruited for the survey and using what sampling technique (e.g., census, systematic random, or convenient sampling?). Brief information about the type and number of settings can be stated. Similarly, for the qualitative data collection, whether a subset of survey participants will be recruited, or all the survey participants will be interviewed? i.e., sampling techniques to be followed in the qualitative component can be included. Currently, it looks like qualitative data collection is restricted only to “TRHIV men”. If that is the case, labelling the study as a mixed methods study may be misleading as a vast majority of the survey participants are likely to be transgender women living with HIV (as per the data provided by the authors in the Introduction section). 2. Doctors recruiting their patients may be seen as a conflict of interest. Can the authors justify this recruitment process? Can they consider alternative ways of recruitment so that there are low chances of pressure or coercion for the participants who seek care in the study settings? Will the study participants be compensated for their time? 3. The analysis section states that “cross-sectional (questionnaires) and longitudinal (biographical trajectory)” data will be used. The information provided in the protocol seems to indicate one-time cross-sectional data collection (quantitative or qualitative) and not cohort or longitudinal data. The authors can clarify whether they will follow-up the same individuals over time (longitudinal cohort) or just ask for information about the past care pathways and use that information to understand care trajectories. Minor: The following terms can be used: ‘gender-affirmative surgery’ instead of ‘sex reassignment surgery’ or ‘gender reassignment surgery’, and ‘comprehensive’ instead of ‘exhaustive’ (in the title).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. A Lacombe-Duncan, University of Michigan
Comments to the Author:
Thank you for the opportunity to review ‘Living conditions and patient care pathways of transgender people living with HIV in France: a crosssectional, exhaustive, community-based research study protocol (ANRS Trans & HIV)’. I believe that this study protocol would be of interest to advancing scholarship on health and healthcare access among trans people living with HIV, particularly in contexts in which these studies are scant. I commend the authors for taking a community-based approach to ensure meaningful inclusion of trans communities in their work. While I am enthusiastic about the topic, there are several areas that require need clarification and expansion. Please see my notes by section below.

Abstract

1. By taboo subject do the authors mean stigmatized identity? The first sentence would be clearer if the authors clarified and mentioned what is poorly documented – health needs? Experiences?
   Trans identity is poorly recognized in French society, and there is little data on their living conditions and daily difficulties.

To clarify the point, the first sentence has been changed to "**Transgender identity is poorly accepted in France , and data on living conditions and the daily difficulties transgender people encounter are scarce.**"

2. Please spell out TRHIV at first use.

This has been done.

3. What is an exhaustive study? I am unfamiliar with this term and it would be helpful to have it explained or removed as a study descriptor.

The term "comprehensive" is now used throughout the paper. Furthermore, what this term means in the present article is now clarified in great detail with the following new sentence in the third paragraph of the study design section (p6): "**Given the small size of the active patient file, we decided to conduct a comprehensive survey instead of a sampling-based one. Recruitment is still ongoing and we hope to have similar numbers of TRHIV (i.e., 890 and 5) in the present study."**

4. Does respectively indicate that trans women are included in the quantitative component and trans men in the qualitative? Please clarify or remove the term respectively. I also wonder about nonbinary trans persons.

Yes. To avoid any potential doubt, the second sentence has been reworded to ensure clarity: "**TRHIV women are exclusively included in the quantitative component, and TRHIV men in the qualitative component**."

5. By transitioning do you mean medical transition or broader? Please clarify here and in the introduction/background.

The term "**transitioning**" has been changed for "**gender reassignment**".

6. By HIV structures do the authors mean HIV care settings? Please expand.

The terms "**HIV services**" and "**HIV structures**" have been changed throughout to "**HIV care units**".

~~Introduction~~

The strongest part of the literature review pertains to the local (French) context, including what the healthcare system looks like, an estimation of the trans population, invisibility and stigma, HIV among trans people in France, etc. The areas that need expansion include:

1. •In the first paragraph, the authors should expand on why data collected for gender affirming surgery underestimates trans people – otherwise put, many trans people, including trans people living with HIV, do not want to access or cannot access medical gender affirmation – they are still legitimate trans people whose needs should be recognized (See, for example: Scheim & Bauer, 2015; Report of the 2015 U.S. Trans Survey; Nolan et al., 2019).

The following sentence has been added at the end of the first paragraph p3: "**gender-affirmative surgery vastly underestimate the true number of people concerned, as surgery is not systematic for economic reasons (expensive and not always**

reimbursed) [2], and because some people wish to live their sexuality without it [3]"

2. •The literature review pertaining to HIV vulnerability and HIV disparities could use some updating, please consider adding results of a more recent meta-analysis (Becasen et al., 2019) and more recent writings from Poteat and colleagues (Poteat, Wirtz, & Reisner, 2019; Mayo-Wilson et al., 2020).

Thank you for these references. The literature review has been updated with a sentence at the end of the second paragraph of the introduction, p3: "**A systematic review, covering January 2006 to March 2017, highlighted gender disparities between transgender men and transgender women in terms of HIV infection risk and risky sexual behaviors [11]. In the United States, HIV prevalence in transgender women is high, especially for African-American and Latina women [12].**"

3. •In the fourth paragraph, are there references regarding that trans women may have a higher risk of transmitting HIV? The second sentence of that paragraph pertains to risk of acquiring not transmitting HIV, so I am unclear if this is what the authors meant.

The last paragraph was unclear (p3). The first part has been changed as follows: "**TRHIV women may also have a greater risk of drug-drug interactions between ART and feminizing hormonal regimens. Hormonal treatments may increase the risk of comorbidities (osteopenia, cardiovascular risk factor, venous thromboembolism). However, data on possible interactions are scarce [18] and contradictory [19]. TRHIV women are more adherent to ART when they have few side effects and when female hormone effectiveness is not affected [20]"**

4. •Please also say more about concerns about drug-drug interactions and how this impacts access to HIV care and uptake of ART among trans women (See, for example: Lacombe-Duncan et al., 2019). There are other vulnerabilities to HIV described among trans men, that are not extrapolated on in this literature review (See, for example: Scheim et al., 2017).

TRHIV women may also have a greater risk of drug-drug interactions between ART and feminizing hormonal regimens. Hormonal treatments may increase the risk of comorbidities (osteopenia, cardiovascular risk factor, venous thromboembolism). However, data on possible interactions are scarce [18] and contradictory [19]. TRHIV women are more adherent to ART when they have few side effects and when female hormone effectiveness is not affected [20].
With regard to transgender men, little information is available about interactions between masculinizing hormone and ART. The few studies to date estimating HIV prevalence in this population reported a small number of positive cases [21,22], which suggests that the HIV burden is lower in transgender men than in transgender women. TransPulse (see above) is one of these studies; it looked at the effects of testosterone in transgender men who have sex with men and showed that using the hormone did not influence HIV-related sexual risk behaviors, despite the fact that testosterone increases libido [23]

The following sentence has been moved to the end of the second paragraph p3 **"In a study of 3,818 people living with HIV (PLHIV) conducted in San Francisco, 35 were TRHIV women on ART. Results showed that they had a lower rate of adherence to ART, experienced more side effects, had a higher rate of depression, and had less positive interactions with care providers than non-transgender people(Sevelius et al., 2010)."**

5. •I commend the authors for their community-based approach; I wonder what role the community partners had in the writing of the protocol?

Community partners were involved in both the conception and design of the protocol study. Not only did they propose research questions and problems to be investigated, they also suggested how the field survey could be organized. Further details have been added at the end of the introduction paragraph, just before objectives paragraph (p5). "**They highlighted important issues to be investigated (gender reassignment trajectories and specific discriminations situations), played a role in adapting the questionnaire and interview guide, and suggested how the field survey could be organized.**"

Minor: There are a number of acronyms (e.g., TRHIV) that need to be spelled out at first use.

All the acronyms have been spelled out at their first use.
~~Methods and Analysis~~

1. There is no mention of dates, which is required of study protocols.

The following sentence has been added "**Data collection began in October 2020 and is should be completed in December 2021. Dissemination of results will likely start in late 2022.**" in the study design paragraph of the methods section (p7).

2. There are a number of specific objectives listed for the study and I am currently unclear about the study's ability to meet each of these objectives.

We believe that the data collected in the sociodemographic, life-event and medical questionnaires, together with the data on the HIV care units will allow us to reach our objectives.

3. Is there a reason nonbinary trans-identified people are not included? If so, please clarify.

We made the choice not to include non-binary people first of all because our gateway for study is through healthcare records. Only the categories "transgender men" and "transgender women" are available in French medical records; the category "nonbinary" does not yet exist.
Moreover, the issue of gender transition does not occur in the same way for the latter group, as their gender identity is fluid. This issue is of major importance in our study.
A question was included in the questionnaire asking how participants define themselves and the non-binary item was one of the response modalities.

4. As noted in reference to the abstract, what is an exhaustive study? I am unfamiliar with this term and it would be helpful to have it explained or removed as a study descriptor.

As the term "exhaustive" wasn't clear, I changed by the term "comprehensive", in all the paper. And I have explained this part better, by adding the following sentence in the third paragraph of the study design section (p7) "**Given the small size of the active patient file, we decided to conduct a comprehensive survey instead of a sampling-based one. Recruitment is still ongoing and we hope to have similar numbers of TRHIV (i.e., 890 and 5) in the present study."**

5. When referring to a study as mixed methods, it necessitates description of a mixed methods typology (see Creswell & Plano-Clark, 2011) as well a description of how data will be mixed. I believe what the authors have described is a multi-method study. This should be clarified.

Thank you for your comments. This clarification has been added to specify the methodology, in the last paragraph of the study design section (p7): **ANRS Trans&HIV uses two approaches to explore TRHIV life trajectories and healthcare pathways, as well as their living conditions with regard to gender reassignment and HIV. The first approach is quantitative, where data are collected to measure the difficulties encountered by TRHIV women, in order to inform public policy. The second approach is qualitative, whereby data are collected for TRHIV men to help describe their needs and living conditions.**

6. I am also unclear why the authors refer to their study as crosssectional but then mention longitudinal analyses as one of their objectives?

The word “longitudinal” has been substituted with “retrospective” throughout.

7. Please add context about sex work into the introduction if that factors as a significant component in the study design.

A paragraph on sex work has been added to the introduction section (p5): **“Although sex work was legalized in France in 2016, the law penalizes clients; this is detrimental to SW safety, health and living conditions (e.g., more risks at work, less condom use) [32]. These negative effects are more frequent in transgender SW [33]”**

8. Will trans women also be participating in qualitative interviews? If not, it is definitely not a mixed methods study nor is it a multimethods study. It is a quantitative study with trans women, and a qualitative study with trans men.

The term "mixed methods" has been removed. In fact, this is neither a mixed method nor a multi-method study. We now explain that we used two approaches in the data collection, one specifically for trans women and the other for trans men. At no time will data between the two be combined or compared.

9. Can the authors provide examples of the questions and/or share the questionnaire in it’s entirety? How (has) the questionnaire been adapted for use with trans women? What role, if any, did the community partners play in adapting the questionnaire? Similarly, what role did the community partners play in developing the interview guide with trans men. Can the authors share the interview guide or provide sample questions? Adding these details will enhance the utility of the study protocol for informing future research with trans populations.

The following sentences have been added to the section “quantitative data collection” p(8): “**Community partners from ACCEPTESS-T and AIDES were involved in adapting the questionnaires and interview guide to the study population. For example, in the gender affirming trajectory section in the questionnaire, they suggested questions such as "When did you first identify yourself as a woman?" and "By what means? with ‘Makeup, Wig/long hair, Removable prostheses, Clothing, shoes (dresses, skirts, heels, etc.), Hair removal, and Other’ as response options. It was very important for the community that this question be asked so that researchers could discover whether there is a specific moment and a specific way in the lives of transgender people where they self-identify as women, or whether it is a progressive process.”**

The following opening question of the interview guide has been added to the manuscript: “**Starting an identity transition is an important moment in one’s life. Could you tell me about your personal experience?”** Examples of exploratory questions from the guide are also now presented in the article (cf. p8 “qualitative data section”).

10. Please expand on all variables that will be collected about the healthcare settings and/or provide sample or full questions/instruments for data collection.

More precise details are now provided in the " *Data collection in* HIV care units " section (p9) as follows: **In order to document the healthcare of TRHIV in the various HIV care units participating in the study, another questionnaire collects structural data on these units, including the number of doctors, opening hours, specificity of the consultation (therapeutic education consultation or not), the range of care services offered (Are other medical care specialties available in the unit? (e.g., psychiatry, endocrinology, proctology)) (Do transgender associations have a permanent presence in the unit?), etc. These data will be used to construct variables for each unit and for the quality of care offered. They will also be used in statistical analyses to identify the potential impact of structural factors on individual factors.**

11. What are the potential ethical issues of having one's doctor recruit? Is there potential for coercion and how has the study team accounted for/mitigated that potential risk?

If we understand the reviewer's comment correctly, the recruiting doctors do not choose between one TRHIV and another for recruitment. All patients are invited to participate and therefore there is no conflict of interest in having doctors recruit. The following sentence has been added to the study procedure section p (7): **"All physicians of participating HIV care units following TRHIV will be recruited to participate in the study. The study protocol specifies that they offer the survey to all TRHIV in their active patient file".** With regard to the risk of coercion, patients are told that they can refuse to participate without any consequences on the quality of care they receive.

12. The analyses should be described in the methods and analysis section; the final section could be called Implications and Planned Dissemination, or Discussion.

The last section is now called "Ethics and dissemination" and the analysis section is integrated at the end of the Method section.

Furthermore, the layout of the two last paragraphs of the Methods section has been changed as follows: *Study design/ Study procedure/Quantitative data collection/ Qualitative data collection/ Data collection in* HIV care units */Patient and Public Involvement/ Analyses and expected results*. The paragraph "Ethics and dissemination is now composed of the following sections: *Ethical aspects/Information, consent and data confidentiality/ Dissemination*

13. Given the long list of study objectives, it would be helpful for the authors to describe their analysis plan by objective. At this point, the planned analyses do not map onto the study objectives, and actually introduce new objectives (to analyze data based on geographic variation). Throughout, it is unclear what outcomes are being looked at. And again, I am unclear based on the authors' description of the study as cross-sectional how longitudinal analyses apply. I believe the authors have a well-constructed study and have paid a lot of attention to be comprehensive - we the audience could benefit from hearing more of the details.

The "expected results" section p 9/10 has been reworked as follows:

The statistical analyses techniques will be adapted to each of the study's objectives and the type of data collected (cross-sectional (questionnaires) and retrospective (biographical trajectory))

a. **Life trajectories of transgender women which may represent factors of HIV infection vulnerability:**

The demographic and socioeconomic characteristics of TRHIV women participating in the quantitative component will first be described. The data collected in the life-event questionnaire will make it possible to study the link between life trajectory and HIV infection risk [41] in general in transgender women for various contexts (residential, administrative, sexual and emotional, gender transition stage, etc.) that expose them to the risk of HIV infection, and other contexts that facilitate or hamper general and HIV-specific healthcare in those who become infected. These data will also help us to better understand the current living conditions and health needs of TRHIV women, and will be analyzed with techniques adapted to retrospective data (e.g., groupbased trajectory model technique) in order to identify specific profiles (e.g., in connection with biographical ruptures) [42–44].

b. **TRHIV women's access to and retention in HIV care:**

To analyze TRHIV women's access to and retention in HIV care, individual factors will be identified, including social factors (employment, living conditions, etc.) and psychosocial factors (self-esteem, mental health etc.). We will also document their experience of

discrimination and perceived stigma, and estimate the burden of each of these factors on access and retention.
Structural data collected on HIV care units will allow us to complement the above analyses by evaluating structural effects on the different indicators highlighted above (e.g., the specific context of a hospital; the HIV care unit's technical and human resources available). Multilevel modeling will be used to disentangle individual barriers to care access and retention from their structural counterparts.

c. **Sexual health**
The data collected will document sexualities according to TRHIV women's gender reassignment trajectories, risk-taking (sexual or substance use), and relationship to prevention. We will measure the impact of each of these factors on their sexual health needs in order to propose comprehensive HIV strategies and interventions for gender reassignment.

d. **COVID-19 health crisis impact on TRHIV women**
We will describe the impact of the ongoing COVID-19 health crisis on the everyday lives of TRHIV women, specifically in terms of HIV medical care, sexuality, social precarity (e.g., financial resources, housing), and mental health.

e. **Specific needs of TRHIV men**
A thematic content analysis [45] of the individual qualitative interviews with TRHIV men will be performed using the software package NVIVO [46] to categorize the themes which emerge. Similar themes will be coded, compared and combined. They will then be compared with the textual variables obtained from the whole TRHIV men sample to highlight problems specific to that population in terms of HIV care access retention.

14. How many care settings will be involved in the study and is the study powered for multi-level analyses? A power calculation would be helpful here.

As this is a comprehensive survey, we hope to collaborate with all HIV care units following at least one TRHIV patient. If all the targeted TRHIV agree to participate, we should achieve the maximum study power possible at the national level. In terms of analysis, the multilevel analysis will allow us to see HIV care unit effects, and depending on the results, it will be possible to identify structural factors which are most strongly associated with the individual factors studied.

15. References are needed for thematic content analysis.

The following two references have been added:

- Paillé P, Mucchielli A. Chapitre 11 - L'analyse thématique. U 2012;:231–314.
- Deschenaux F, Association pour la recherche qualitative. Introduction à l'analyse qualitative informatisée à l'aide du logiciel QSR Nvivo 2.0. Rimouski: ARQ 2005.

15. Please also expand on study limitations.

A section on study limitations has been added at the end of the Method section (p 10):

The fact that we are recruiting only TRHIV patients followed in hospital HIV care units means that those followed in primary care (i.e., nonhospital contexts) will be missed. However, as all TRHIV patients must officially go to a hospital care unit at least once a year, it is possible that

some will be recruited. TRHIV who refuse to participate will also be missed. Moreover, some TRHIV will probably be missed because HIV care units may not identify all potentially eligible patients.

16. A summary paragraph discussing the implications for the study would be helpful to end the protocol.

This has been added at the end to the "dissemination section" (p11)
"The results of this research will allow us to better understand TRHIV women's health needs in order to suggest possible national recommendations for comprehensive HIV and transition medical care for this population."

17. Please also note that the manuscript needs editing for grammar.

The manuscript has been thoroughly revised by an English mother-tongue professional copyeditor with over fifteen years' experience in the field.

Reviewer: 2

Dr. Rafael Tomaz de Lima, Federal University of Rio Grande do Norte
Comments to the Author:
The evaluated protocol is theoretically and methodologically well-founded, highlighting its relevance and possible impacts on the health of trans people living with HIV in France. However, for it to be accepted for publication, it is necessary to make some adaptations or include some details.

1) The author presents in the section "study population" a definition of trans people. I understand that this definition should be included in the introduction, so that readers know from the outset who is the population referred to in the study.

This definition has been added in the first paragraph of the introduction (p3): **"That is why, in the present study, transgender refers to all persons whose self-identified gender is different from the sex they were assigned at birth;"**

2) The justifications for the participation of trans women only in the quantitative component and trans men only in the qualitative component of the research are explained. However, cannot these criteria be considered a limitation of the study? The investigation proposes to make an exhaustive description of the socio-behavioral data. But how to carry out this exhaustive description with quantitative techniques, especially with regard to trans women? How to understand the subjective aspects related to life history and health care experiences with quantitative research techniques? In this matter, I realize that there is an incongruity between the objectives and the chosen methods. Therefore, it would be relevant to include further clarification on this issue.

In order to inform public policy, it is essential to evaluate the difficulties encountered by TRHIV women in the various dimensions of their lives and not just describe them. This is why we chose a quantitative method for this specific population. This point has now been included at the end to the study design subsection in the Methods section (p7) as follows: **"ANRS Trans&HIV uses two approaches to explore TRHIV life trajectories and healthcare pathways, as well as their living conditions with regard to gender reassignment and HIV. The first approach is quantitative, where data are collected to measure the difficulties encountered by TRHIV women, in order to inform public**

policy. The second approach is qualitative, whereby data are collected for TRHIV men to help describe their needs and living conditions"

3) On the topic of ethical aspects, adjust the name of the city that is the headquarters of the 64th General Assembly of the World Medical Association. The correct one is Fortaleza.

This has been corrected.

4) What is the forecast for the beginning and end of the study? It is important to add this information to see if all objectives can be achieved and methodological strategies can be met.

At the end of the paragraph "study design" in the Methods section, the following sentence has been added: "**Data collection began in October 2020 and is should be completed in December 2021. Dissemination of results will likely start in late 2022".**

Reviewer: 3

Dr. Venkatesan Chakrapani, Centre for Sexuality and Health Research and
Policy
Comments to the Author:
The proposed study addresses an important topic in transgender people's health – to document and explain care trajectories of transgender people living with HIV.

Introduction section:

1. Transgender people living with HIV are likely to face double or triple discrimination due to their multiple marginalised identities (e.g., due to gender identity, HIV status and sex work status). Hence, information about intersectional or multiple stigmas can be explicitly stated in the Introduction section (and appropriate measures/scales can be added in the Methods section).

The introduction has been reorganized to consider intersectional stigma and the following sentence has been added to introduce the discrimination paragraph (p4):
"Transgender people are more affected by intersectional stigma [28], specifically gender identity discrimination, combined with stigma related to HIV, sex work, and migration."

Details of the discrimination scale have been added in the "quantitative data collection" paragraph in the method section p7: **"Discrimination is measured using a scale adapted from The Trajectories and Origins survey (TeO)[39] which explored discrimination in various contexts including employment, family, services, healthcare, ethnic origin, trans identity, HIV status, and dress code."**

2. It is unclear whether the 'TRHIV transition trajectories' will be documented only in relation to HIV care but also for gender transition care. Documenting the trajectories of both HIV care and gender transition care will result in rich data. If documenting gender transition care trajectories is also one of the objectives of the study, then it can be explicitly stated in the objectives and the title. For example, 'HIV and gender transition care pathways' instead of 'patient care pathways' in the title.

We will indeed document both gender transition care trajectories and their relationship to HIV care. Related data will be collected in the "HIV testing and management" and "transition trajectory" sections of the questionnaire.

I specify this in the main objective too (p6 “objectives”): **“The main objective of ANRS Trans&HIV is to identify personal and social situations of vulnerability in TRHIV, the obstacles they encounter in terms of access to and retention in medical care, and their gender reassignment and HIV care needs.”**

Furthermore, the title of the manuscript has been changed: **Living conditions, HIV and gender reassignment care pathways of transgender people living with HIV in France: a nationwide, comprehensive, cross-sectional community-based research study protocol (ANRS Trans&HIV).**

Methods:

1. It is not clear what kind of mixed methods design will be followed. Also, it is not clear how many TRHIV will be recruited for the survey and using what sampling technique (e.g., census, systematic random, or convenient sampling?). Brief information about the type and number of settings can be stated. Similarly, for the qualitative data collection, whether a subset of survey participants will be recruited, or all the survey participants will be interviewed? i.e., sampling techniques to be followed in the qualitative component can be included. Currently, it looks like qualitative data collection is restricted only to “TRHIV men”. If that is the case, labelling the study as a mixed methods study may be misleading as a vast majority of the survey participants are likely to be transgender women living with HIV (as per the data provided by the authors in the Introduction section).

The term "mixed methods" has been removed. This clarification has been added to specify the methodology p7: **ANRS Trans&HIV uses two approaches to explore TRHIV life trajectories and healthcare pathways, as well as their living conditions with regard to gender reassignment and HIV. The first approach is quantitative, where data are collected to measure the difficulties encountered by TRHIV women, in order to inform public policy. The second approach is qualitative, whereby data are collected for TRHIV men to help describe their needs and living conditions.**

With respect to recruitment, the following sentence has been added to the third paragraph of the study design section (p7): **“Given the small size of the active patient file, we decided to conduct a comprehensive survey instead of a sampling-based one. Recruitment is still ongoing and we hope to have similar numbers of TRHIV (i.e., 890 and 5) in the present study”.**

2. Doctors recruiting their patients may be seen as a conflict of interest. Can the authors justify this recruitment process? Can they consider alternative ways of recruitment so that there are low chances of pressure or coercion for the participants who seek care in the study settings? Will the study participants be compensated for their time?

If we understand the reviewer’s comment correctly, the recruiting doctors do not choose between one TRHIV and another for recruitment. All patients are invited to participate and therefore there is no conflict of interest in having doctors recruit. The following sentence has been added to the study procedure section p (7): **All physicians of the HIV care unit following TRHIV are recruited to participate in the study. The study protocol specifies that they offer the survey to all TRHIV in their active patient file”.**

With regard to the risk of coercion, patients are told that they can refuse to participate without any consequences on the quality of care they receive.

“To thank them for their time, they are compensated with a twenty-euro gift voucher”. This information has been added at the end of the paragraph “Patient and Public Involvement”, in the methods section p9.

3. The analysis section states that “cross-sectional (questionnaires) and longitudinal (biographical trajectory)” data will be used. The information provided in the protocol seems to indicate one-time crosssectional data collection (quantitative or qualitative) and not cohort or longitudinal data. The authors can clarify whether they will follow-up the same individuals over time (longitudinal cohort) or just ask for information about the past care pathways and use that information to understand care trajectories.

The term “longitudinal” has been replaced with “retrospective” in the following sentence p 10, (expected results): **The statistical analysis techniques will be adapted to each of the study’s objectives and the type of data collected (cross-sectional (questionnaires) and retrospective (biographical trajectory)))** The study entails one-time cross-sectional data collection, where information about past care pathways will be collected (in the life-event questionnaire). Minor:
The following terms can be used: ‘gender-affirmative surgery’ instead of ‘sex reassignment surgery’ or ‘gender reassignment surgery’, and ‘comprehensive’ instead of ‘exhaustive’ (in the title).

We now use gender-affirmative surgery.

VERSION 2 – REVIEW

REVIEWER	Lacombe-Duncan, A University of Michigan, School of Social Work
REVIEW RETURNED	29-Oct-2021

GENERAL COMMENTS	Overall Thank you for the opportunity to re-review the manuscript newly entitled “Living conditions, HIV, and gender reassignment care pathways of transgender people living with HIV in France: a nationwide, comprehensive, cross-sectional community- based research study protocol (ANRS Trans&HIV)”. I appreciate the authors’ attentiveness to all the reviewer comments. In particular, the edits the authors have made to the methods bring sufficient clarity, particularly to their data analysis plan by objective. I have just a few more comments for consideration. Overall I appreciate the authors’ update of the term “transitioning” to “gender reassignment”, and the use of gender-affirming surgery throughout. However, in many contexts, the term ‘reassignment’ is outdated, and the preferred term is “medical gender affirmation”. See, for example, the following resources: https://www.albertahealthservices.ca/assets/info/pf/div/if-pf-div-terms-and-phrases-to-avoid.pdf https://transcare.ucsf.edu/guidelines/overview I recognize I am coming from a particular (U.S./Canada) worldview so if the authors’ have vetted this language of “gender reassignment” by the local transgender community and believe the language to be more applicable to the medical and transgender community in France if left as is that is also fine – I would just consider adding a caveat/description that that is the preferred language of the local context, recognizing that it is not an accepted term in other contexts. Alternately, I would suggest changing to medial gender affirmation throughout to reflect the broader English trans health literature/trans-inclusive language in a global context. Introduction In the added sentence “Gender-affirmative surgery vastly underestimate the true number of people concerned, as surgery is not systematic for economic reasons (expensive and not always reimbursed) [2], and because some people wish to live their sexuality without it [3]” the word “sexuality” needs to be changed to

	"gender". The word sexuality in this sentence conflates sexuality and gender, which are two different concepts/experiences. Please consider replacing "risky sexual behaviors" with "sexual risk practices". While the former can be perceived as having some judgment, the latter is more value neutral. The authors present a lot of background information – which is helpful. However now before stating "In order to fill the knowledge gap on TRHIV" it would be helpful for the authors to re-iterate what that knowledge gap is – as their literature review now makes it appear as though there is a lot of literature and less gaps. Methods As mentioned, I appreciated how the authors described the specific analysis plan by objective. One thing I noticed though is that the objectives listed in the introduction (a-g) do not align with the objectives listed in analysis and expected results section (a-e). These should be aligned and use the same language to make it easier for the reader. Another thing I am unclear on – I'm not a statistician, but I don't think multilevel modelling would be possible with 1 participant at 1 site – is it possible to consult with a statistician and/or to clarify how multilevel modelling would be possible? Alternately I would remove that, in the event it is not possible.

REVIEWER	Chakrapani, Venkatesan Centre for Sexuality and Health Research and Policy
REVIEW RETURNED	14-Oct-2021

GENERAL COMMENTS	The authors seem to have addressed the key concerns. A few minor suggestions: 1. This revised sentence is not correct: "All physicians of the HIV care unit following TRHIV are recruited to participate in the study". This can be misinterpreted as physicians are being recruited for the study. Please rephrase. For example, "Physicians of the HIV care unit will invite all TRHIV to participate in the study..." 2. In the title, rather than using '...HIV and gender reassignment care pathways', the authors can consider using '...HIV and gender transition care pathways'.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

1. I appreciate the authors' update of the term "transitioning" to "gender reassignment", and the use of gender-affirming surgery throughout. However, in many contexts, the term 'reassignment' is outdated, and the preferred term is "medical gender affirmation". See, for example, the following resources:
https://www.albertahealthservices.ca/assets/info/pf/div/if-pf-div-terms-and-phrases-to-avoid.pdf
https://transcare.ucsf.edu/guidelines/overview

I recognize I am coming from a particular (U.S./Canada) worldview so if the authors' have vetted this language of "gender reassignment" by the local transgender community and believe the language to be more applicable to the medical and transgender community in France if left as is that is also fine –

I would just consider adding a caveat/description that that is the preferred language of the local context, recognizing that it is not an accepted term in other contexts. Alternately, I would suggest changing to medial gender affirmation throughout to reflect the broader English trans health literature/trans-inclusive language in a global context.

Our thanks for this valuable piece of information. The term "gender affirmation" is now used throughout the manuscript.

Introduction

2. In the added sentence “Gender-affirmative surgery vastly underestimate the true number of people concerned, as surgery is not systematic for economic reasons (expensive and not always reimbursed) [2], and because some people wish to live their sexuality without it [3]” the word “sexuality” needs to be changed to “gender”. The word sexuality in this sentence conflates sexuality and gender, which are two different concepts/experiences.

This has been changed (2nd paragraph of introduction p.3)

3. Please consider replacing “risky sexual behaviors” with “sexual risk practices”. While the former can be perceived as having some judgment, the latter is more value neutral.

This has been done (3rd paragraph of introduction p.3)

4. The authors present a lot of background information – which is helpful. However now before stating “In order to fill the knowledge gap on TRHIV” it would be helpful for the authors to re-iterate what that knowledge gap is – as their literature review now makes it appear as though there is a lot of literature and less gaps.

To clarify this point, the sentence has been changed to “In order to improve knowledge about the situation of TRHIV in France […]” (1st sentence p5)

Methods
5. As mentioned, I appreciated how the authors described the specific analysis plan by objective. One thing I noticed though is that the objectives listed in the introduction (a-g) do not align with the objectives listed in analysis and expected results section (a-e). These should be aligned and use the same language to make it easier for the reader.

I rewrote the objectives section to be align with the expected outcomes section.(p.5)
a. Describe the life trajectories of TRHIV, especially life events which may represent HIV vulnerability factors.
b. Document access to and retention in HIV care by estimating the burden of social and psychosocial factors, as well as experiences of discrimination and perceived stigma.
c. Document sexual health (i.e., sexuality according to TRHIV transition trajectory, risk-taking (sexual or related to substance use)), and its relationship to prevention; and establish these factors’ impact on access to and retention in HIV care.
d. Document the impact of the ongoing COVID-19 health crisis on everyday TRHIV experience.
e. Identify the specific needs and health of TRHIV men.

6. Another thing I am unclear on – I’m not a statistician, but I don’t think multilevel modelling would be possible with 1 participant at 1 site – is it possible to consult with a statistician and/or to clarify how multilevel modelling would be possible? Alternately I would remove that, in the event it is not possible.

We will first perform a factor analysis of all 53 HIV care units to identify different profiles. HIV care units with similar characteristics will be grouped together (e.g., large urban centers vs. small centers in large cities vs. small centers in small cities). After this, we will perform multilevel analyses. (Coulaud.2021. Health Policy and Planning)
This detail has been added. (p.8 section b of “Analyses and expected results”)

Reviewer: 3

1. This revised sentence is not correct: "All physicians of the HIV care unit following TRHIV are recruited to participate in the study". This can be misinterpreted as physicians are being recruited for the study. Please rephrase. For example, "Physicians of the HIV care unit will invite all TRHIV to participate in the study..."

The sentence has been changed to “All physicians of participating HIV care units will invite all their TRHIV to participate in the study”. (p6. paragraph “study procedure”)

2. In the title, rather than using '...HIV and gender reassignment care pathways', the authors can consider using '...HIV and gender transition care pathways'.

The term “gender reassignment” has been changed in the title and throughout the text to “gender affirmation” as a response to the comment made by Reviewer 1.