

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Physical activity among HIV-positive patients receiving antiretroviral therapy in Hanoi and Nam Dinh, Vietnam : A cross - sectional study
AUTHORS	Dang, Anh; Nguyen, Long; Nguyen, Anh; Xuan Bach, Tran; Tran, Tung; Latkin, Carl; Zhang, Melvyn; Ho, Roger

VERSION 1 – REVIEW

REVIEWER	Allison Webel Case Western Reserve University, USA
REVIEW RETURNED	20-Nov-2017

GENERAL COMMENTS	<p>This manuscript is much improved and its clear the authors have worked hard on it. However, there are still many editorial issues (subject verb agreement, double words) that make this very hard to read. I still think it needs a very careful read by an English language editor.</p> <p>The authors continue to argue the IPAQ is objective (strengths and limitations) but it is not. It is a self-report, retrospective, gross measure of physical activity. Please do not diminish this - it simply means that objective prospective studies are needed to confirm what the team found. This is an interesting paper and I encourage the authors to spend the time to carefully revise it so that it can be easily read and its impact understood.</p> <p>How was serious illness assessed as inclusion criteria?</p> <p>Be careful with saying any one study confirmed something. At the very least, it only confirms it for those who participated in the study.</p> <p>Patients is still used in several places instead of respondents. Please be consistent.</p>
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REVIEWER	Kelly O'Brien University of Toronto, Canada
REVIEW RETURNED	22-Dec-2017

GENERAL COMMENTS	<p>In this manuscript authors describe the levels of, and factors associated with physical activity among adults living with HIV on antiretroviral therapy (ART). They assessed the level of physical activity using the International Physical Activity Questionnaire (IPAQ) among 1133 patients living with HIV taking ART in rural and urban settings in Vietnam and examined associations between IPAQ scores and demographic and clinical characteristics (including rural and urban settings). This is an important topic as physical activity is</p>
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	<p>an increasingly important concept to consider in the context of healthy aging with HIV.</p> <p>Authors made a good attempt in addressing the reviewer comments as demonstrated by the substantive revisions addressing in this updated manuscript. Authors revised the introduction to provide working definitions of key concepts, provided detail on recruitment, inclusion criteria and outcome measures, and clarified the results and discussion. Some areas continue to warrant further attention and clarification (see below). Further, many grammatical errors persist throughout. The manuscript would benefit from a very thorough editorial review and revision. See below some specific considerations for further revision.</p> <p>1) Abstract</p> <p>a. Please include the study design in the abstract – unclear if this is a cross-sectional or observational longitudinal study. Authors refer to a cross-sectional study design but later report ‘changes in physical activity’.</p> <p>b. Define ‘symptomatic stage’.</p> <p>2) Grammatical errors persist throughout. Below are a few example:</p> <p>a. Abstract – results (likely to have higher ‘a’ IPAQ score or be active...)</p> <p>b. Strengths and limitations - The study employed validated international instruments to increase the comparability between our results and other studies ‘in’ elsewhere.....etc.</p> <p>Introduction - First sentence of paragraph unclear - Vietnam is still in ‘a’ concentrated HIV epidemic stage and the proportion of ART coverage estimated approximately 42% (of people living with HIV/AIDS) in 2015..” However, little attention ‘is’ paid to...</p> <p>d. Methods – exclusion (not exclusive) criteria included those being suffered; ‘patients were invited to participate in 20 minute interviews conducted...(not conducting), etc.....</p> <p>e. Conclusion statement does not make sense – ‘In conclusion, the study confirmed the high percentage of HIV patients receiving ART treatment physically active.’</p> <p>f. Note ‘data’ are plural.</p> <p>3) Consistency of Terminology</p> <p>a. Authors refer to ‘patients’ ‘participants’ and respondents’ interchangeably throughout which confuses the reader. Suggest authors use the term ‘participants’ throughout.</p> <p>4) References</p> <p>a. Please check references to statements throughout to ensure accuracy. For example, reference 24 does not support the statement made by authors that PLWH are unmotivated to do physical activity.</p> <p>b. Formatting of references requires careful review (e.g. 45).</p> <p>5) Introduction – Great to see the definition of physical activity added to the introduction; this would be further articulated by providing examples of activity in the definition of physical activity in the introduction.</p> <p>6) Methods</p> <p>a. Authors made ample revisions to the methods to more clearly describe the participants and recruitment. The last sentence prior to ‘measures and instruments’ that reports on the number of participants enrolled and response is results (not methods).</p> <p>b. It is still unclear the use of the term ‘response rate’ as this is</p>
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	<p>a term is used to describe response to a survey which does not align with this study design. By 'response rate' do authors mean consent or participation rate was 80-90%? Please include details of how many participants were recruited, and how many refused to participate in order to end up with 1133 agreeing to participate.</p> <p>c. Measures and Instruments – Authors stated participants were involved in '20 minute face-to-face interviews' however, it remains unclear how the data were collected as either self-administered questionnaires (e.g. participant completes the questionnaire independently) or interview administered questionnaires (e.g. the researcher reads out the question and response options and completes the questionnaire based on the participant responses to the interview administered questions). Clarity of the data collection procedure is needed.</p> <p>d. Authors provide a clearer description of measurement properties and scoring of the instruments and removed the duplication of ART adherence measurement– however, justification for why two measures of QOL were administered (EQ5D5L and EQ-VAS) would be beneficial.</p> <p>e. IPAQ scoring remains unclear – HEPA was defined as vigorous activity at least 3 days of obtaining at least 1500 METS-minutes/week OR 7 or more days (note, there cannot be more than 7 days in the week) of walking combined with moderate or vigorous activity at least 3000 MET-minutes/week. However, minimally active was defined as 3 or more days of vigorous activity of at least 20 minutes per day (note - isn't this also considered HEPA?) or 5 or more days of moderate activity..... **Definitions of HEPA and minimally active do not appear to be mutually exclusive. More clarification here would be helpful.</p> <p>f. Analysis – Unclear why age was considered a categorical variable. Continuous measure of age would allow for mean and standard deviation.</p> <p>7) Results</p> <p>a. Table 3 - Explanation of why there are differences in EQ-VAS but not the EQ5D would strengthen the discussion.</p> <p>b. Table 5 interpretation – relationship between inactivity in physical therapy among those with longer duration of ART is not significant (95% confidence interval reaches 1.0). Please clarify.</p> <p>c. Authors report that IPAQ score was associated with ART duration with those on treatment longer having lower IPAQ score - Have authors considered the potential influence of age in this relationship? One hypothesis might be that age (not ART duration) is influencing this association. Those on ART for longer duration may comprise include more individuals living longer since their diagnosis and as a result may experience longstanding adverse effects associated with older treatment regimens compared with those more newly diagnosed who are younger and may be exposed to newer ART regimens with fewer side effects. Careful consideration of potential confounders would be beneficial to offer possible explanation for the relationships between physical activity, geographical region, and ART use.</p> <p>8) Discussion</p> <p>a. Authors could discuss the reasons why moderate activity were higher among rural versus urban participants whereas walking and vigorous activity did not differ between rural and urban participants. Authors refer to more urban participants having difficulty with mobility, pain and discomfort – more discussion as to the reasons why this was found would be beneficial.</p>
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	<p>b. Authors provide a nice description for reasons for differences in moderate activity found among women, those unemployed, and rural areas due to 'issues of urbanization'. They also provide some insight into reasons for differences related to ART adherence.</p> <p>c. Note (as mentioned above) authors include duration of ART as an associated factor with physical activity, however, the 95% confidence interval reaches 1 which suggests this is not significant (Table 5). Please clarify.</p> <p>d. Consideration of the potential influence of age (in combination with ART duration) on physical activity would add to the discussion and implications for practice as an increasing number of individuals age with HIV.</p> <p>e. Nice discussion of implications for clinical practice related to vocation, exercise programs, and social supports. The statement that refers to the O'Brien et al systematic reviews is not accurate; we did not 'find that PLWH should do exercise to obtain stable health, rather participants in this review were medically stable as part of the criteria for inclusion in the included studies. A more accurate statement would be that exercise (aerobic and resistive or a combination) performed at least three times per week for at least five weeks may lead to improvements in cardiopulmonary fitness, strength, weight and body composition and quality of life among adults with HIV who are medically stable.</p> <p>9) Conclusions – Overall well done, however, authors continue to overstate their conclusion as per this statement; 'Our study also emphasized the association between high level of physical activity and the improvement of ART adherence, health-related quality of life and CD4 cell count.' – 'improvement' suggests that there was a change in ART related to physical activity, which is not the case.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1

Comment: The authors continue to argue the IPAQ is objective (strengths and limitations) but it is not. It is a self-report, retrospective, gross measure of physical activity. Please do not diminish this - it simply means that objective prospective studies are needed to confirm what the team found.

Answer: Thank you for your comment. We have changed "objective" into "The IPAQ was an subjectively self-reported measure"

Paragraph/page/line: Page 3

Comment: This manuscript is much improved and its clear the authors have worked hard on it. However, there are still many editorial issues (subject verb agreement, double words) that make this very hard to read. I still think it needs a very careful read by an English language editor.

Answer: We attempted to edit grammar of the manuscript. I hope that it is clearer now.

Comment: How was serious illness assessed as inclusion criteria?

Answer: We do not use serious illness as inclusion criteria. We collected information related to serious illness such as number of CD4 cells, HIV stage

Paragraph/page/line: Discussion – para 1

Comment: Be careful with saying any one study confirmed something. At the very least, it only confirms it for those who participated in the study

Answer: We have changed into "our study suggests".

Comment: Patients is still used in several places instead of respondents. Please be consistent
Answer: Thank you for your comment. We have changed “respondents” and “patients” into “participants” throughout paper.

Reviewer #2

Comment: Abstract

a. Please include the study design in the abstract – unclear if this is a cross-sectional or observational longitudinal study. Authors refer to a cross-sectional study design but later report 'changes in physical activity'.

b. Define 'symptomatic stage'

Answer: a. Our study design was cross-sectional. We have added more detail in study design and changed "changes in physical activity" into "PLWH with longer duration of ART were less likely to be physically active", in order to show the association more clearly.

b. We have added the definition of "symptomatic stage" in method section

Paragraph/page/line: Page 2 – Result

Page 6 – para 4

Comment: Grammatical errors persist throughout. Below are a few example:

a. Abstract – results (likely to have higher 'a' IPAQ score or be active...)

Answer: Thank you for your comments.

We have changed this sentence into "a higher IPAQ-score"

Paragraph/page/line: Page 2 –Result

Comment: b. Strengths and limitations - The study employed validated international instruments to increase the comparability between our results and other studies 'in' elsewhere.....etc

Answer: We have changed into "between our results and other studies elsewhere"

Paragraph/page/line: Page 3

Comment: c. Introduction - First sentence of paragraph unclear - Vietnam is still in 'a' concentrated HIV epidemic stage and the proportion of ART coverage estimated approximately 42% (of people living with HIV/AIDS) in 2015..” However, little attention 'is' paid to...

Answer: We have changed into "little attention has been paid to"

Paragraph/page/line: Page 5 – para 2-line 5

Comment: d. Methods – exclusion (not exclusive) criteria included those being suffered; 'patients were invited to participate in 20 minute interviews conducted...(not conducting), etc.....

Answer: We have changed into "exclusion criteria"

Paragraph/page/line: Page 6 – para 1 – line 1

Comment: e. Conclusion statement does not make sense – 'In conclusion, the study confirmed the high percentage of HIV patients receiving ART treatment physically active.'

f. Note 'data' are plural.

Answer: Thank you for your comment. We have re-written the conclusion in a more appropriate way.

Paragraph/page/line: Page 15

Comment: 3) Consistency of Terminology

a. Authors refer to 'patients' 'participants' and respondents' interchangeably throughout which confuses the reader. Suggest authors use the term 'participants' throughout.

Answer: Thank you for your comment. We have changed "respondents" and "patients" into "participants"

Comment: 4) References

a. Please check references to statements throughout to ensure accuracy. For example, reference 24 does not support the statement made by authors that PLWH are unmotivated to do physical activity.

b. Formatting of references requires careful review (e.g. 45).

Answer: We have revised all references, especially reference 24 to ensure accuracy.

We also re-formatted the citation of references

Ref.24

Comment: 5) Introduction – Great to see the definition of physical activity added to the introduction; this would be further articulated by providing examples of activity in the definition of physical activity in the introduction.

Answer: We have added examples of activity, including subgroups and level of intensity.

Paragraph/page/line: Page 4 – para 2

Comment: 6) Methods

a. Authors made ample revisions to the methods to more clearly describe the participants and recruitment. The last sentence prior to ‘measures and instruments’ that reports on the number of participants enrolled and response is results (not methods).

Answer: We have added more information in the result section.

Paragraph/page/line: Page 8 – para 3 – line 2

Comment: b. It is still unclear the use of the term ‘response rate’ as this is a term is used to describe response to a survey which does not align with this study design. By ‘response rate’ do authors mean consent or participation rate was 80-90%? Please include details of how many participants were recruited, and how many refused to participate in order to end up with 1133 agreeing to participate.

Answer: We have added more detail related to number of participants who were recruited and refused to participate in the study.

Paragraph/page/line: Page 6- para 1- line 11

Comment: c. Measures and Instruments – Authors stated participants were involved in ‘20 minute face-to-face interviews’ however, it remains unclear how the data were collected as either self-administered questionnaires (e.g. participant completes the questionnaire independently) or interview administered questionnaires (e.g. the researcher reads out the question and response options and completes the questionnaire based on the participant responses to the interview administered questions). Clarity of the data collection procedure is needed.

Answer: Thank you for your comment. In this study, data were collected through interview-administered questionnaires.

Paragraph/page/line: Page 6 – para 2

Comment: d. Authors provide a clearer description of measurement properties and scoring of the instruments and removed the duplication of ART adherence measurement– however, justification for why two measures of QOL were administered (EQ5D5L and EQ-VAS) would be beneficial.

Answer: Thank you for your comment, we have added explanation in discussion section. As such, EQ5D5L is an indirect-preference instrument for assessing HRQOL in long term. While EQ-VAS is a preference instrument that directly measures the perception of patients about their health status in short term

Paragraph/page/line: Page 13 – para 4

Comment: e. IPAQ scoring remains unclear – HEPA was defined as vigorous activity at least 3 days of obtaining at least 1500 METS-minutes/week OR 7 or more days (note, there cannot be more than 7 days in the week) of walking combined with moderate or vigorous activity at least 3000 MET-minutes/week. However, minimally active was defined as 3 or more days of vigorous activity of at least 20 minutes per day (note - isn't this also considered HEPA?) or 5 or more days of moderate

activity..... **Definitions of HEPA and minimally active do not appear to be mutually exclusive. More clarification here would be helpful.

Answer: We have revised IPAQ scoring and compared to IPAQ guideline.

- HEPA is defined as 7 or more days of combination between days of walking and days of moderate-intensity or vigorous activities

=> therefore the total number of days will less than or equal to 14 days (7 days for walking + 7 days for moderate or vigorous activity).

- minimally active was defined as 3 or more days of vigorous activity of at least 20 minutes per day which equal to 800 MET-minutes/week and less than 1500 MET-minutes/week.

=> therefore if total physical activity was 1500 MET-minutes/week or higher, participants would be classified in HEPA

Paragraph/page/line: Page 7 – Physical activity section

Comment: f. Analysis – Unclear why age was considered a categorical variable. Continuous measure of age would allow for mean and standard deviation.

Answer: We have changed age into continuous variable

Paragraph/page/line: Page 9 – table 1

Comment: 7) Results

a. Table 3 - Explanation of why there are differences in EQ-VAS but not the EQ5D would strengthen the discussion

Answer: We have added more detail in discussion section

Paragraph/page/line: Page 13 – para 4

Comment: b. Table 5 interpretation – relationship between inactivity in physical therapy among those with longer duration of ART is not significant (95% confidence interval reaches 1.0). Please clarify.

Answer: Thank you for your comment. 95%CI was rounded up in the first manuscript. We have checked the result again: 95%CI was 0.82 – 0.98

Paragraph/page/line: Page 12 – table 5

Comment: c. Authors report that IPAQ score was associated with ART duration with those on treatment longer having lower IPAQ score - Have authors considered the potential influence of age in this relationship? One hypothesis might be that age (not ART duration) is influencing this association. Those on ART for longer duration may comprise include more individuals living longer since their diagnosis and as a result may experience longstanding adverse effects associated with older treatment regimens compared with those more newly diagnosed who are younger and may be exposed to newer ART regimens with fewer side effects. Careful consideration of potential confounders would be beneficial to offer possible explanation for the relationships between physical activity, geographical region, and ART use.

Answer: Thank you very much for your suggest.

We have considered the potential influence of age in this relationship. When analyzing the data, variables of demographics were included in multivariate regression model. However, the influence of age on physical activity was not statistically significant since it was dropped out of multivariate regression model.

Paragraph/page/line: Page 13 – para 3 – line 7

Comment: 8) Discussion

a. Authors could discuss the reasons why moderate activity were higher among rural versus urban participants whereas walking and vigorous activity did not differ between rural and urban participants. Authors refer to more urban participants having difficulty with mobility, pain and discomfort – more discussion as to the reasons why this was found would be beneficial.

Answer: We have discussed more about the reasons why moderate activity were higher among rural versus urban participants whereas walking did not differ between rural and urban participants. Our finding shows that more urban participants having difficulty with mobility. However, we decided to not mention this result in discussion because “mobility” variable was not statistically significant in multivariate regression model.

Paragraph/page/line: Page 12 – para 2- line 9

Comment: b. Authors provide a nice description for reasons for differences in moderate activity found among women, those unemployed, and rural areas due to ‘issues of urbanization’. They also provide some insight into reasons for differences related to ART adherence.

Answer: We have added more reasons to explain for differences related to ART adherence.

Paragraph/page/line: Page 13 – para 3 – line 15

Comment: c. Note (as mentioned above) authors include duration of ART as an associated factor with physical activity, however, the 95% confidence interval reaches 1 which suggests this is not significant (Table 5). Please clarify.

Answer: Thank you for your comment. 95%CI was rounded up in the first manuscript. We have checked the result again: 95%CI was 0.82 – 0.98

Paragraph/page/line: Page 12 – table 5

Comment: d. Consideration of the potential influence of age (in combination with ART duration) on physical activity would add to the discussion and implications for practice as an increasing number of individuals age with HIV.

Answer: We have added more detail in discussion section

Paragraph/page/line: Page 13 – para 3 – line 7

Comment: e. Nice discussion of implications for clinical practice related to vocation, exercise programs, and social supports. The statement that refers to the O’Brien et al systematic reviews is not accurate; we did not ‘find that PLWH should do exercise to obtain stable health, rather participants in this review were medically stable as part of the criteria for inclusion in the included studies. A more accurate statement would be that exercise (aerobic and resistive or a combination) performed at least three times per week for at least five weeks may lead to improvements in cardiopulmonary fitness, strength, weight and body composition and quality of life among adults with HIV who are medically stable.

Answer: Thank you for your substantial comment about the statement that refers to the O’Brien et al systematic reviews. We have revised and changed by the more accurate statement that you commented.

Paragraph/page/line: Page 13 – para 4

Comment: 9) Conclusions – Overall well done, however, authors continue to overstate their conclusion as per this statement; ‘Our study also emphasized the association between high level of physical activity and the improvement of ART adherence, health-related quality of life and CD4 cell count.’ – ‘improvement’ suggests that there was a change in ART related to physical activity, which is not the case

Answer: Thank you for your comment. We have re-written the conclusion in a more appropriate way.

Paragraph/page/line: Page 15

VERSION 2 – REVIEW

REVIEWER	Allison Webel Case Western Reserve University, USA
REVIEW RETURNED	25-Jan-2018

GENERAL COMMENTS	Thank you for attending to the additional suggestions carefully and quickly. The manuscript is much improved and I wish you the best of luck.
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VERSION 2 – AUTHOR RESPONSE

* Editor:

1. Comments: The title should include both the study design and the setting. This is the preferred format for the journal. We suggest: "Physical activity among HIV-positive patients receiving antiretroviral therapy in Hanoi and Nam Dinh, Vietnam: A cross-sectional study."

- Answers: Thank you for your comment. We have changed the title into "Physical activity among HIV-positive patients receiving antiretroviral therapy in Hanoi and Nam Dinh, Vietnam: A cross-sectional study".

- Paragraph/page/line:

2. Comments: We still feel that the quality of English is not at the requisite standard for publication in places. There are still a number of typos/ grammatical errors and in places the quality of English is affecting the clarity of your work. Some examples are included below. Can you please thoroughly copy-edit the paper one more time? We strongly recommend consulting a native English speaker or professional copy-editing service.

- Answers: We attempted to edit grammar of the manuscript. I hope that the manuscript is now meet your requirement now.

- Paragraph/page/line:

3. Comments: In the 'Methods' section you say "A total of 1200 patients were invited to participate into the study, but only 1133 patients agreed to enroll. The reasons for refusal included insufficient health, discomfort or having busy work schedule." This should be removed from the methods section and included near the beginning of the results section.

- Answers: We have added this information at the beginning of the result section.

- Paragraph/page/line: Results - para 1

4. Comments: We found it difficult understanding your response to reviewer 2's comment 6e ("IPAQ scoring remains unclear - HEPA was defined as vigorous activity at..") Can you improve the quality of English of the following: "OR 7 or more days of combination between.."? Is this definition of HEPA taken from the IPAQ guideline? If not then where does this definition come from?

- Answers: This definition was taken from the IPAQ guideline and we have edited this sentence as following "OR 7 or more days of combination physical activities of walking, moderate-intensity or vigorous activities"

- Paragraph/page/line: Method - physical activity section

5. Comments: Your response to reviewer 2's comment 7a ("Table 3 - Explanation of why there are differences in EQ-VAS but not the EQ5D would strengthen the discussion") was as follows: "We have added more detail in discussion section. Paragraph/page/line: Page 13 - para 4" We can't locate the section in the manuscript where you discuss the differences in results between the EQ-VAS and the EQ5D. Can you please include the relevant extract from your paper in the next rebuttal letter?

- Answers: Thank you for your comment, we have included the relevant extract from my paper.

"In this study, we combined both EQ-5D-5L and EQ-VAS instruments due to the variation of health utility scores based on different instruments. EQ-VAS is a self-reported instrument that directly assesses the perceived health status of patients in the short-term. Meanwhile, the EQ-5D index is composed by five domains that indirectly measures the quality of life in the long-term. In the short-

term, the patient's hope for improving their health condition might influence their perceived health status. On the other hand, in the long-term, because of the acclimation with their health status, the patient tends to report quality of life more accurately"

- Paragraph/page/line: Discussion - para 6 - page 14

* Reviewer 2:

1. Comments: Abstract

a. Please include the study design in the abstract - unclear if this is a cross-sectional or observational longitudinal study. Authors refer to a cross-sectional study design but later report 'changes in physical activity'.

- Answers: Our study design was cross-sectional. We have added more detail in study design and changed "changes in physical activity" into "PLWH with longer duration of ART were less likely to be physically active", in order to show the association more clearly.

- Paragraph/page/line: Abstract - Result - Page 2

b. Define 'symptomatic stage'

- Answers: We have added the definition of "symptomatic stage" in method section

- Paragraph/page/line: Method - ART related characteristic - Page 6

2. Comments: Grammatical errors persist throughout. Below are a few example:

a. Abstract - results (likely to have higher 'a' IPAQ score or be active...)

- Answers: Thank you for your comments. We have changed this sentence into "a higher IPAQ-score"

- Paragraph/page/line: Abstract - Result - Page 2

b. Strengths and limitations - The study employed validated international instruments to increase the comparability between our results and other studies 'in' elsewhere.....etc

- Answers: We have changed into "between our results and other studies elsewhere

- Paragraph/page/line: Page 3

c. Introduction - First sentence of paragraph unclear - Vietnam is still in 'a' concentrated HIV epidemic stage and the proportion of ART coverage estimated approximately 42% (of people living with HIV/AIDS) in 2015.." However, little attention 'is' paid to...

- Answers: We have changed into "little attention has been paid to"

- Paragraph/page/line: Introduction - para 5 - line 6 - page 5

d. Methods - exclusion (not exclusive) criteria included those being suffered; 'patients were invited to participate in 20 minute interviews conducted...(not conducting), etc.....

- Answers: We have changed into "exclusion criteria"

- Paragraph/page/line: Method - study setting section - Page 6 - para 2 - line 5

e. Conclusion statement does not make sense - 'In conclusion, the study confirmed the high percentage of HIV patients receiving ART treatment physically active.'

- Answers: Thank you for your comment. We have re-written the conclusion in a more appropriate way.

- Paragraph/page/line: Conclusion - Page 15

f. Note 'data' are plural.

- Answers: We have edited

- Paragraph/page/line:

3. Comments: Consistency of Terminology

a. Authors refer to 'patients' 'participants' and respondents' interchangeably throughout which confuses the reader. Suggest authors use the term 'participants' throughout.

- Answers: Thank you for your comment. We have changed "respondents" and "patients" into "participants"

- Paragraph/page/line:

4. Comments: References

a. Please check references to statements throughout to ensure accuracy. For example, reference 24 does not support the statement made by authors that PLWH are unmotivated to do physical activity.

b. Formatting of references requires careful review (e.g. 45).

- Answers: We have revised all references, especially reference 24 to ensure accuracy.

We also re-formatted the citation of references

- Paragraph/page/line: Ref.24

5. Comments: Introduction - Great to see the definition of physical activity added to the introduction; this would be further articulated by providing examples of activity in the definition of physical activity in the introduction.

- Answers: We have added examples of activity, including subgroups and level of intensity.

- Paragraph/page/line: Introduction - para 2 - page 4

6. Comments: Authors made ample revisions to the methods to more clearly describe the participants and recruitment. The last sentence prior to 'measures and instruments' that reports on the number of participants enrolled and response is results (not methods).

- Answers: We have added more information in the result section.

- Paragraph/page/line: Result - para 2

b. It is still unclear the use of the term 'response rate' as this is a term is used to describe response to a survey which does not align with this study design. By 'response rate' do authors mean consent or participation rate was 80-90%? Please include details of how many participants were recruited, and how many refused to participate in order to end up with 1133 agreeing to participate.

- Answers: We have added more detail related to number of participants who were recruited and refused to participate in the study.

- Paragraph/page/line: Page 3

c. Measures and Instruments - Authors stated participants were involved in '20 minute face-to-face interviews' however, it remains unclear how the data were collected as either self-administered questionnaires (e.g. participant completes the questionnaire independently) or interview administered questionnaires (e.g. the researcher reads out the question and response options and completes the questionnaire based on the participant responses to the interview administered questions). Clarity of the data collection procedure is needed.

- Answers: Thank you for your comment. In this study, data were collected through interview-administered questionnaires.

- Paragraph/page/line: Method - measure and instrument section - para1

d. Authors provide a clearer description of measurement properties and scoring of the instruments and removed the duplication of ART adherence measurement- however, justification for why two measures of QOL were administered (EQ5D5L and EQ-VAS) would be beneficial.

- Answers: Thank you for your comment, we have added explanation in discussion section. As such, EQ5D5L is an indirect-preference instrument for assessing HRQOL in long term. While EQ-VAS is a

preference instrument that directly measures the perception of patients about their health status in short term.

The sentence in the manuscript as following:

"In this study, we combined both EQ-5D-5L and EQ-VAS instruments due to the variation of health utility scores based on different instruments. EQ-VAS is a self-reported instrument that directly assesses the perceived health status of patients in the short-term. Meanwhile, the EQ-5D index is composited by five domains that indirectly measures the quality of life in the long-term. In the short-term, the patient's hope for improving their health condition might influence their perceived health status. On the other hand, in the long-term, because of the acclimation with their health status, the patient tends to report quality of life more accurately"

- Paragraph/page/line: Discussion - para 6 - page 14

e. IPAQ scoring remains unclear - HEPA was defined as vigorous activity at least 3 days of obtaining at least 1500 METS-minutes/week OR 7 or more days (note, there cannot be more than 7 days in the week) of walking combined with moderate or vigorous activity at least 3000 MET-minutes/week. However, minimally active was defined as 3 or more days of vigorous activity of at least 20 minutes per day (note - isn't this also considered HEPA?) or 5 or more days of moderate activity.....

**Definitions of HEPA and minimally active do not appear to be mutually exclusive. More clarification here would be helpful.

- Answers: We have revised IPAQ scoring and compared to IPAQ guideline.

- HEPA is defined as 7 or more days of combination between days of walking and days of moderate-intensity or vigorous activities

=> therefore the total number of days will less than or equal to 14 days (7 days for walking + 7 days for moderate or vigorous activity.

- minimally active was defined as 3 or more days of vigorous activity of at least 20 minutes per day which equal to 800 MET-minutes/week and less than 1500 MET-minutes/week.

=> therefore if total physical activity was 1500 MET-minutes/week or higher, participants would be classified in HEPA

- Paragraph/page/line: Page 7 - Physical activity section

f. Analysis - Unclear why age was considered a categorical variable. Continuous measure of age would allow for mean and standard deviation.

- Answers: We have changed age into continuous variable

- Paragraph/page/line: Page 8 - table 1

7. Comments: Results

a. Table 3 - Explanation of why there are differences in EQ-VAS but not the EQ5D would strengthen the discussion

- Answers: We have added more detail in discussion section

- Paragraph/page/line: Discussion - para 6 - page 14

b. Table 5 interpretation - relationship between inactivity in physical therapy among those with longer duration of ART is not significant (95% confidence interval reaches 1.0). Please clarify.

- Answers: Thank you for your comment. 95%CI was rounded up in the first manuscript. We have checked the result again: 95%CI was 0.82 - 0.98

- Paragraph/page/line: Page 12 - table 5

c. Authors report that IPAQ score was associated with ART duration with those on treatment longer having lower IPAQ score - Have authors considered the potential influence of age in this relationship? One hypothesis might be that age (not ART duration) is influencing this association. Those on ART for longer duration may comprise include more individuals living longer since their diagnosis and as a

result may experience longstanding adverse effects associated with older treatment regimens compared with those more newly diagnosed who are younger and may be exposed to newer ART regimens with fewer side effects. Careful consideration of potential confounders would be beneficial to offer possible explanation for the relationships between physical activity, geographical region, and ART use.

- Answers: Thank you very much for your suggest.

We have considered the potential influence of age in this relationship. When analyzing the data, variables of demographics were included in multivariate regression model. However, the influence of age on physical activity was not statistically significant since it was dropped out of multivariate regression model

- Paragraph/page/line: Discussion - para 5 - page 13 - line 12

8. Comments: Discussion

a. Authors could discuss the reasons why moderate activity were higher among rural versus urban participants whereas walking and vigorous activity did not differ between rural and urban participants. Authors refer to more urban participants having difficulty with mobility, pain and discomfort - more discussion as to the reasons why this was found would be beneficial.

- Answers: We have discussed more about the reasons why moderate activity were higher among rural versus urban participants whereas walking did not differ between rural and urban participants.

Our finding shows that more urban participants having difficulty with mobility. However, we decided to not mention this result in discussion because "mobility" variable was not statistically significant in multivariate regression model.

- Paragraph/page/line: Discussion - para 2 - page 12 - line 8

b. Authors provide a nice description for reasons for differences in moderate activity found among women, those unemployed, and rural areas due to 'issues of urbanization'. They also provide some insight into reasons for differences related to ART adherence.

- Answers: We have added more reasons to explain for differences related to ART adherence.

- Paragraph/page/line: Discussion - para 3 - page 13 - line 12

c. Note (as mentioned above) authors include duration of ART as an associated factor with physical activity, however, the 95% confidence interval reaches 1 which suggests this is not significant (Table 5). Please clarify.

- Answers: Thank you for your comment. 95%CI was rounded up in the first manuscript. We have checked the result again: 95%CI was 0.82 - 0.98

- Paragraph/page/line: Page 12 - table 5

d. Consideration of the potential influence of age (in combination with ART duration) on physical activity would add to the discussion and implications for practice as an increasing number of individuals age with HIV

- Answers: We have added more detail in discussion section

- Paragraph/page/line: Discussion - para 5 - page 13 - line 12

e. Nice discussion of implications for clinical practice related to vocation, exercise programs, and social supports. The statement that refers to the O'Brien et al systematic reviews is not accurate; we did not 'find that PLWH should do exercise to obtain stable health, rather participants in this review were medically stable as part of the criteria for inclusion in the included studies. A more accurate statement would be that exercise (aerobic and resistive or a combination) performed at least three times per week for at least five weeks may lead to improvements in cardiopulmonary fitness, strength, weight and body composition and quality of life among adults with HIV who are medically stable.

- Answers: Thank you for your substantial comment about the statement that refers to the O'Brien et al systematic reviews. We have revised and changed by the more accurate statement that you commented.

- Paragraph/page/line: Discussion - para 6 - page 14 - line 13

9. Comments: Conclusions - Overall well done, however, authors continue to overstate their conclusion as per this statement; 'Our study also emphasized the association between high level of physical activity and the improvement of ART adherence, health-related quality of life and CD4 cell count.' - 'improvement' suggests that there was a change in ART related to physical activity, which is not the case

- Answers: Thank you for your comment. We have re-written the conclusion in a more appropriate way.

- Paragraph/page/line: Conclusion - Page 15