PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Dyspareunia in HIV positive and negative middle-aged women: a cross sectional study
AUTHORS	Valadares, Ana; Pinto-Neto, Aarão; Gomes, Débora; D'Avanzo, Walquíria; Moura, Alexandre; Costa-Paiva, Lúcia; Sousa, Maria Helena

VERSION 1 - REVIEW

REVIEWER	Katherine Sutton, Ph.D. Canada
REVIEW RETURNED	01-Apr-2014

GENERAL COMMENTS	Thank you for your submission. The paper addresses two important questions: 1) Is dyspareunia associated with HIV status in middle-aged women? 2) Amongst the HIV + women who experience dyspareunia, what are the associated factors? The research idea is excellent, and is an understudied area and a valuable contribution to the research literature. The sample size is also impressive. Unfortunately, the execution of the study and the write-up of the paper are lacking. Please see the specific comments below for suggestions on improving the readability of the paper. While the methods cannot be changed, perhaps certain portions can be clarified for the readers.
	Abstract and points: To be changed and clarified as the rest of the paper comes together.
	Introduction: A concrete definition of dyspareunia in the introduction would be useful. Paragraph 2 is only one sentence long. Please expand or combine with another paragraph. Page 4, line 5 has an extra space before the paragraph begins. Page 5, line 4: The citation for reference 5 is hanging alone and needs to be tied to a sentence. Page 5, line 7: What is meant by "nervousness"? Perhaps anxiety is a better choice of word? Elaborating on the psychological factors associated with dyspareunia would help to flesh out the introduction and to make this a stronger paper. Page 5, line 25: Is the mental health predictor current mental health or mental health prior to the diagnosis?
	Methods: Page 6, line 7: Rephrase the first sentence for clarity (perhaps break this into two sentences).

Inclusion/Exclusion criteria could be stated more explicitly prior to listing the final number of women in the study. What were some of the reasons women were excluded, aside from intercourse?

The authors stated their measure was "based on" the SPEQ. What was changed about this measure? Please provide more detail. Also please provide reliability coefficients for the measure.

Since individuals from various fields will be reading this, please elaborate on the definition of the 'rapid test' and what it is used for.

The "sample size" section can be removed and replaced by a single sentence in the discussion about sample size and effect size.

Most researchers use a 0-10 or 0-100 scale for pain ratings. What is the justification behind the 1-6 scale, and where did the rationale for a cut-off of 2 points come from? Please elaborate.

Was the cut-off of 2/6 for all intercourse attempts or on average? Future research may also want to inquire about percentage of intercourse attempts that are painful.

Page 7, line 36: Hot flushes should be "hot flashes".

The operalization of some of the variables is unclear. How was dryness defined for the participants? What is meant by weight gain?

The rationale for some of the variables is unclear. Why was the education dichotomy at 7 and 8 years? Why were cholesterol meds inquired about specifically?

Page 7, line 52: For clarity, it would be helpful to change passive and active oral sex to giving and receiving oral sex.

The methods section could benefit from stating the research questions and hypothesis and then speaking about data analysis specific to each question.

Results:
In reading through the results, it is also unclear why the variables in table 1 do not match up with all the variables listed in the methods section. It may be simpler to indicate in the methods that a variety of demographic, health, sexual, and psychological variables were examined, and then list them in tables for the results. (variables that came up in the results that were not operationalized were menopausal status and physical activity – please provide more information about how these were determined).

Table 1
This table is quite confusing. It is not clear what the information at the bottom of the table is about ("*sample of women with partner and info on occurrence…"). Please clarify.

The use of & and # is confusing for the legend. Please choose other symbols and superscript them.

It is important to indicate where significant differences are through use of symbols such as *.

Make sure the p-values have periods rather than commas.

Change "smoking habit" to "current smoker"

Page 9, line 30: What is meant by "(data not shown as table)"?
There are a lot of predictive variables in the analysis. Why were so many used? How was this controlled? There is no need to repeat them all again in the results section.

Page 10, line 22: What is meant by "(Table not presented)"?

Table 2
The word "acquisition" is italicized. The no-response has not been translated to English.

It would be useful to move the duration variables to the top of this table.

Table 3
It is unclear why there is an astrix beside the "p".
P-values need to have periods rather than commas.
The note/legend could be cut down. There is no need to repeat information if it is already clarified earlier in the paper.

Table 4
Please translate all text to English.
The note/legend could be cut down. There is no need to repeat information if it is already clarified earlier in the paper.

Overall, the results section could be presented in a clearer manner.

Discussion

The authors note that there are no other studies of middle-aged women and HIV/dyspareunia. Are there studies with other age groups? If so, please comment.
Page 11, line 26: If the woman is HIV +, what is meant by HIV-status in this sentence? "It has been reported that sexual function in HIV-positive women may be driven principally by psychological factors and by HIV status."
Please be more clear throughout the paper about what is meant by women having "few HIV symptoms." Do the authors suppose the results might be different in a sample with many HIV symptoms?
Page 12, line 23: Please clarify this sentence regarding the study by Salonia et al. The authors may also wish to cite and explain some of the literature on the overlap between IC and dyspareunia.
Page 12, line 45. Be very careful about correlation versus causation. Is there longitudinal research to suggest that urinary incontinence "leads to" dyspareunia? The literature that I am aware of speaks to their association, not any causation.
Page 13, line 5. Please elaborate on why issues might be more likely to arise in a steady relationship. Did the study control for frequency of intercourse? Might it be the amount of intercourse, rather than the relationship?
Page 13, line 26. If no association was found in the literature, provide your own hypothesis.
Page 13, line 40. Please clarify why recruiting the HIV-negative women at menopause clinics influenced the findings.
Please clarify which results are referring to the whole group and which are specifically in the HIV positive group. It would be useful to provide subtitles and break up the discussion into a section for each study question.
It is important to note in the paper that the sample is a clinical sample, rather than one collected from the general population. As such, the percentages of women with dyspareunia in both of your groups will be higher than the general population.
The conclusions section is great, but it comes out of nowhere. Perhaps tie in some of the justifications to the introduction and the rest of the discussion. It is important to sell the utility of your clinical study throughout the paper. It will also be important to find a reference to support that dyspareunia is tied to lesion risk.

The discussion certainly can have speculation as to the reason behind the results, but the speculation requires more research and points to back up where it is coming from. Points need to be elaborated and better explained. For example, tension and dyspareunia are mentioned at the bottom of page 12, but the

	authors did not previously draw a link between tension and dyspareunia in order to facilitate the understanding of this point. The link between muscle tension and pain does not come until a few paragraphs later.

REVIEWER	Carol Bova PhD, RN University of Massachusetts Medical School Worcester, MA USA
REVIEW RETURNED	04-May-2014

GENERAL COMMENTS	Outcomes - need information about the SPEQ Limitations- need to address sample size issues in HIV-infected women analysis Thank you for the opportunity to review this manuscript. This study evaluated the possible link between dyspareunia and HIV infection in middle-aged women. The manuscript is clearly written and organized. The topic is important. The following comments/suggestions are made to enhance the manuscript: 1. More information about the short personal experience questionnaire is needed. What does this scale measure and how was it used in this study? What was the reliability of the scale in this particular sample? What were the findings related to this scale? 2. Please clarify why blood samples were taken. Were all women re-tested for HIV infection? What were the results? 3. Need further discussion of the inadequate sample size for the analysis on the HIV positive woman. Results regarding steady partner (p = .047) and the use of lamivudine/zidovudine (p = .048) are not significant since when rounded up the p = .05. This issue needs to be discussed in the limitations section. 4. In the discussion section, you may want to delete the assumption that the HIV-infected women in this study had fewer HIV-related symptoms; since symptoms were not measured in this study. (Note: CD4 cell count is not a good predictor of the presence or absence of HIV-related symptoms). 5. The demographic variables and how they are categorized are mentioned 3 times in the manuscript – you may want to present this only once and then reference this detailed description in other parts of the manuscript.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name Katherine Sutton, Ph.D.
Institution and Country Canada
Please state any competing interests or state 'None declared': None declared.

Dyspareunia in HIV + and HIV – middle-aged women

Thank you for your submission. The paper addresses two important questions: 1) Is dyspareunia associated with HIV status in middle-aged women? 2) Amongst the HIV + women who experience dyspareunia, what are the associated factors? The research idea is excellent, and is an understudied area and a valuable contribution to the research literature. The sample size is also impressive. Unfortunately, the execution of the study and the write-up of the paper are lacking. Please see the specific comments below for suggestions on improving the readability of the paper. While the methods cannot be changed, perhaps certain portions can be clarified for the readers.

Abstract and points: To be changed and clarified as the rest of the paper comes together.

Introduction:

A concrete definition of dyspareunia in the introduction would be useful.
Answer: One has included it.

Paragraph 2 is only one sentence long. Please expand or combine with another paragraph.
Answer: One has included it.

Page 4, line 5 has an extra space before the paragraph begins.
Answer: One has excluded it.

Page 5, line 4: The citation for reference 5 is hanging alone and needs to be tied to a sentence.
Answer: One has excluded it.

Page 5, line 7: What is meant by "nervousness"? Perhaps anxiety is a better choice of word?
Answer: One has changed it.

Elaborating on the psychological factors associated with dyspareunia would help to flesh out the introduction and to make this a stronger paper.
Answer: One has done it.

Page 5, line 25: Is the mental health predictor current mental health or mental health prior to the diagnosis?
Answer: It was current mental health. One has corrected it.

Methods:
Page 6, line 7: Rephrase the first sentence for clarity (perhaps break this into two sentences).
Answer: One has done it.

Inclusion/Exclusion criteria could be stated more explicitly prior to listing the final number of women in the study. What were some of the reasons women were excluded, aside from intercourse?
Answer: One has done it. and included reasons women were excluded,

The authors stated their measure was "based on" the SPEQ. What was changed about this measure? Please provide more detail. Also please provide reliability coefficients for the measure.
Answer: One has done it.

Since individuals from various fields will be reading this, please elaborate on the definition of the 'rapid test' and what it is used for.
The "sample size" section can be removed and replaced by a single sentence in the discussion about sample size and effect size.
Answer: One has done it.

Most researchers use a 0-10 or 0-100 scale for pain ratings. What is the justification behind the 1-6 scale, and where did the rationale for a cut-off of 2 points come from? Please elaborate. Was the cut-off of 2/6 for all intercourse attempts or on average? Future research may also want to inquire about percentage of intercourse attempts that are painful.
Answer: SPEQ questionnaire considers dyspareunia, defined as pain
during sexual intercourse, was graded from 1 to 6, where 1 referred to the absence of pain and 6 to maximum pain. A score of less than 2 was considered to represent the absence of dyspareunia and a score of 2 or more to represent the presence of dyspareunia.
Page 7, line 36: Hot flushes should be "hot flashes".
Answer: One has changed it.

The operalization of some of the variables is unclear. How was dryness defined for the participants?
Answer: One has included it.
Vaginal lubrication during sexual activity was graded from 1 to 6, where 1 referred to the absence of lubrication and 6 to maximum lubrication. This was dichotomized into 4 or less or more than 4.
What is meant by weight gain?
Answer: The gain of weight that could be noted by the woman.

The rationale for some of the variables is unclear. Why was the education dichotomy at 7 and 8 years?
Answer: Because 8 years is the mean formal education in Brazil.

Why were cholesterol meds inquired about specifically?
Answer: One has excluded itt.

Page 7, line 52: For clarity, it would be helpful to change passive and active oral sex to giving and receiving oral sex.
Answer: One has changed it.

The methods section could benefit from stating the research questions and hypothesis and then speaking about data analysis specific to each question.
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In reading through the results, it is also unclear why the variables in table 1 do not match up with all the variables listed in the methods section. It may be simpler to indicate in the methods that a variety of demographic, health, sexual, and psychological variables were examined, and then list them in tables for the results. (variables that came up in the results that were not operationalized were menopausal status and physical activity – please provide more information about how these were determined).
Answer: One has changed it.

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Make sure the p-values have periods rather than commas.
Change "smoking habit" to "current smoker"
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There are a lot of predictive variables in the analysis. Why were so many used? How was this controlled? There is no need to repeat them all again in the results section.
Answer: One has changed it.

Page 10, line 22: What is meant by "(Table not presented)"?
Answer: One has put the data in the results section but has not presented the table.

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Answer: One has changed it.

Table 4
Please translate all text to English.
The note/legend could be cut down. There is no need to repeat information if it is already clarified earlier in the paper.
Overall, the results section could be presented in a clearer manner.
Answer: One has changed it.

Discussion

The authors note that there are no other studies of middle-aged women and HIV/dyspareunia. Are there studies with other age groups? If so, please comment.
Answer: One has changed it. .In fact, one has not found any specific paper on dyspareunia in HIV woman
Page 11, line 26: If the woman is HIV +, what is meant by HIV-status in this sentence?
Answer: One has changed it.
"It has been reported that sexual function in HIV-positive women may be driven principally by psychological factors and by HIV status."
Please be more clear throughout the paper about what is meant by women having "few HIV symptoms."

Answer: One has changed it.

It has been reported that sexual function in HIV-positive women may be driven principally by psychological factors and other problems related to HIV infection

….This finding is in agreement with the results of another author, who also reported that few women believed HIV in itself to be the cause of any decline in their sexual functioning, since those women had good immunovirological status 10 One supposes that results would be different in a sample of women without a good HIV control..

Do the authors suppose the results might be different in a sample with many HIV symptoms?

Answer: One supposes that results would be different in a sample of women without a good HIV control.

Page 12, line 23: Please clarify this sentence regarding the study by Salonia et al. The authors may also wish to cite and explain some of the literature on the overlap between IC and dyspareunia.

Answer: One has included it.

Page 12, line 45. Be very careful about correlation versus causation. Is there longitudinal research to suggest that urinary incontinence "leads to" dyspareunia? The literature that I am aware of speaks to their association, not any causation.

Answer:Urinary incontinence is associated with feelings of embarrassment and inadequacy as well as low self-esteem. It may also be associated to dyspareunia

Page 13, line 5. Please elaborate on why issues might be more likely to arise in a steady relationship. Did the study control for frequency of intercourse? Might it be the amount of intercourse, rather than the relationship?

Answer: One has included it.

Page 13, line 26. If no association was found in the literature, provide your own hypothesis.

Answer: One has included it.

Page 13, line 40. Please clarify why recruiting the HIV-negative women at menopause clinics influenced the findings.

Answer: As HIV – negative women were selected at specialist outpatient clinics providing care to menopausal women. So, it is probable that they had more symptoms including dyspareunia.

Please clarify which results are referring to the whole group and which are specifically in the HIV positive group. It would be useful to provide subtitles and break up the discussion into a section for each study question.

Answer: One has done it.

It is important to note in the paper that the sample is a clinical sample, rather than one collected from the general population. As such, the percentages of women with dyspareunia in both of your groups will be higher than the general population.

Answer: One has included: It is also important to note that it was a clinical sample. So the results found in the present study may not be extrapolated to the general population.

The conclusions section is great, but it comes out of nowhere. Perhaps tie in some of the justifications to the introduction and the rest of the discussion. It is important to sell the utility of your clinical study throughout the paper. It will also be important to find a reference to support that dyspareunia is tied to lesion risk.

Answer: One has included

The discussion certainly can have speculation as to the reason behind the results, but the speculation requires more research and points to back up where it is coming from. Points need to be elaborated and better explained. For example, tension and dyspareunia are mentioned at the bottom of page 12,

but the authors did not previously draw a link between tension and dyspareunia in order to facilitate the understanding of this point. The link between muscle tension and pain does not come until a few paragraphs later.
Answer: One has reviewed it.

Reviewer: 2
Reviewer Name Carol Bova PhD, RN
Institution and Country University of Massachusetts Medical School
Worcester, MA USA
Please state any competing interests or state 'None declared': None declared
Answer: One has includedit.

Outcomes - need information about the SPEQ
Answer: One has included
Limitations- need to address sample size issues in HIV-infected women analysis
Answer: One has done it.

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1. More information about the short personal experience questionnaire is needed. What does this scale measure and how was it used in this study? What was the reliability of the scale in this particular sample? What were the findings related to this scale?
Answer: The dependent variable dyspareunia, defined as pain during sexual intercourse, was graded from 1 to 6, where 1 referred to the absence of pain and 6 to maximum pain. A score of less than 2 was considered to represent the absence of dyspareunia and a score of 2 or more to represent the presence of dyspareunia. 12,13,14
As one has not found other studies on dyspareunia in HIV positive women we have used this scale.

2. Please clarify why blood samples were taken. Were all women re-tested for HIV infection? What were the results?
Answer: The blood samples tests of HIV negative and positive women were collected at admission in the present study (FSH, LH and TSH for all, ELISA or Western Blot HIV tests for HIV negative women and Viral load and CD4 cells for HIV positive women. All the women supposed to be HIV negative had exams confirming it.

3. Need further discussion of the inadequate sample size for the analysis on the HIV positive woman. Results regarding steady partner (p = .047) and the use of lamivudine/zidovudine (p = .048) are not significant since when rounded up the p = .05. This issue needs to be discussed in the limitations section.
Answer: One has done it.

4. In the discussion section, you may want to delete the assumption that the HIV-infected women in this study had fewer HIV-related symptoms; since symptoms were not measured in this study. (Note: CD4 cell count is not a good predictor of the presence or absence of HIV-related symptoms).
Answer: One has modified it. … This finding is in agreement with the results of another author, who also reported that few women believed HIV in itself to be the cause of any decline in their sexual functioning, since those women had good immunovirological status

5. The demographic variables and how they are categorized are mentioned 3 times in the manuscript – you may want to present this only once and then reference this detailed description in other parts of the manuscript.

Answer: One has done it.