

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cross-sectional study of HPV-16 infection in a population-based sub-sample of Hispanic adults.
AUTHORS	Ortiz, Ana; Unger, Elizabeth; Muñoz, Cristina; Panicker, Gitika; Tortolero-Luna, Guillermo; Soto-Salgado, Marievelisse; Otero, Yomayra; Suarez, Erick; Perez, Cynthia

VERSION 1 - REVIEW

REVIEWER	Sharmila Sengupta National Institute of Biomedical Genomics Netaji Subhas Sanatorium, 2nd Floor
REVIEW RETURNED	27-Oct-2013

GENERAL COMMENTS	<p>Positives of the paper:</p> <ol style="list-style-type: none">1) The study is first of its kind to be carried out on Puerto-Rican population to make a good assessment of HPV16 exposure in terms of seropositivity, both among men and women, in the region and finding its epidemiological correlates.2) Appropriate statistical tests have been done with the required stringency considering the output of the HPV16 seroprevalence results and the population demographics. <p>Negatives of the paper:</p> <ol style="list-style-type: none">1) The authors have stated in the results that they have used residual serum from a sub-sample of the last 450 consecutive adults aged 21 to 64 years who participated in the study and agreed to participate in HPV testing. However, there is no mention of the precise period, such as the last two or one year or so, during which these last 450 samples were collected although the overall period for the larger sample collection is given- between 2005 and 2008.2) Secondly, since these subjects are distributed into various age groups, there sexual exposure period should also be variable, which is likely to impact exposure to HPV and hence seropositivity to HPV16. Therefore, the authors need to test the association between sexual exposure period and HPV16 seropositivity, as well. Also, the number of sexual partners should also be normalized to the sexual exposure period.3) The point highlighted "Strengths and limitations of this study" discusses about the major findings of the study and not the strengths and limitations. This section can be avoided or reframed under the heading "Major findings". <p>Comments: Overall, the work is carried out and described very well and appears acceptable for publication with the required modifications stated above.</p>
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REVIEWER	Hui-Yi Lin Moffitt Cancer Center & Research Institute
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GENERAL COMMENTS

This is an interesting paper to estimate prevalence of HPV-16 IgG responses and factors associated with HPV-16 seropositivity in a cross-section of 450 adults in Puerto Rico. I don't have major concern for the statistical parts in general. My comments are listed below.

1. In the first paragraph of page 9, please clarify the values of 2.68-16.01 and 3.04-7.13. Are they for a range or interquartile range? Please provide descriptive statistics for the HPV-16 antibody titers for the whole group.
2. It is recommended to show the exact p-values with three decimal places in the whole contents and tables, instead of simply showing $p > 0.05$ and $p > 0.10$.
3. It is not clear how history of smoking was measured. Please add definition of ever smokers.
4. In Table 1, the chi-square test is not suitable for some variables with a small sub-group, such as "ever had sex" and "place of birth".
5. Add statistical method for the univariate analyses for Table 1 in the Statistical Analysis section.
6. Suggest changing "multivariate model" to "multivariable model" in the Statistical Analysis section.
7. The last sentence of the 2nd paragraph in page 7 is not correct. The Mann-Whitney-Wilcoxon test was used to test the overall antibody titers (not median titers) difference by gender. In addition, this sentence should be moved to the Statistical Analysis section.

VERSION 1 – AUTHOR RESPONSE

Reviewer's comments: Sharmila Sengupta

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

Response to reviewer's comments: A competing interest statement was included in the title page. The authors have no financial interest to disclose.

2. Positives of the paper:

1) The study is first of its kind to be carried out on Puerto-Rican population to make a good assessment of HPV16 exposure in terms of seropositivity, both among men and women, in the region and finding its epidemiological correlates.

2) Appropriate statistical tests have been done with the required stringency considering the output of the HPV16 seroprevalence results and the population demographics.

- Negatives of the paper:

1) The authors have stated in the results that they have used residual serum from a sub-sample of the last 450 consecutive adults aged 21 to 64 years who participated in the study and agreed to participate in HPV testing. However, there is no mention of the precise period, such as the last two or one year or so, during which these last 450 samples were collected although the overall period for the larger sample collection is given- between 2005 and 2008.

Response to reviewer's comments: This information was clarified in the methodology section as follows: For the current analysis we used residual serum from a sub-sample of the last 450 consecutive adults aged 21 to 64 years, recruited between February 2007 and January 2008, who participated in the study and agreed to participate in HPV testing.

2) Secondly, since these subjects are distributed into various age groups, their sexual exposure period should also be variable, which is likely to impact exposure to HPV and hence seropositivity to HPV16. Therefore, the authors need to test the association between sexual exposure period and HPV16 seropositivity, as well. Also, the number of sexual partners should also be normalized to the sexual exposure period.

Response to reviewer's comments: We agree with the reviewer's suggestion. We calculated the sexual exposure period by subtracting the participant's age at the first sexual intercourse from the participant's age at the time of the interview. Then, the number of sexual partners was normalized to the sexual exposure period. The median number of sexual partners normalized to the sexual exposure period was included in Table 1. Since this variable was not significantly associated with HPV status, we did not include it in the multiple logistic regression analysis.

3) The point highlighted "Strengths and limitations of this study" discusses about the major findings of the study and not the strengths and limitations. This section can be avoided or reframed under the heading "Major findings".

Response to reviewer's comments: We reframed the information to discuss the strengths and limitations of our study. See details in page 3.

4. Overall, the work is carried out and described very well and appears acceptable for publication with the required modifications stated above.

Reviewer's comments: Hui-Yi Lin

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

Response to reviewer's comments: A competing interest statement was included in the title page. The authors have no financial interest to disclose.

2. This is an interesting paper to estimate prevalence of HPV-16 IgG responses and factors associated with HPV-16 seropositivity in a cross-section of 450 adults in Puerto Rico. I don't have major concern for the statistical parts in general. My comments are listed below.

3. In the first paragraph of page 9, please clarify the values of 2.68-16.01 and 3.04-7.13. Are they for a range or interquartile range? Please provide descriptive statistics for the HPV-16 antibody titers for the whole group.

Response to reviewer's comments: The values in the first paragraph of page 9 (2.64-16.01 and 3.04-7.13) correspond to the 25th and 75th percentiles. This has been clarified in the results section. In addition, we included the median and 25th and 75th percentiles for the HPV-16 antibody titers for the whole group.

2. It is recommended to show the exact p-values with three decimal places in the whole contents and tables, instead of simply showing $p > 0.05$ and $p > 0.10$.

Response to reviewer's comments: Exact p values were provided - see Table #1.

3. It is not clear how history of smoking was measured. Please add definition of ever smokers.

Response to reviewer's comments: Smoking status was assessed by a question asking participants if they have ever smoked in their lifetime.

4. In Table 1, the chi-square test is not suitable for some variables with a small sub-group, such as "ever had sex" and "place of birth".

Response to reviewer's comments: We used the p-value from Fisher's Exact test in variables with expected cell counts below 5. This has been clarified in the table.

5. Add statistical method for the univariate analyses for Table 1 in the Statistical Analysis section.

Response to reviewer's comments: The first sentence indicates that "To characterize the demographic, clinical, and lifestyle characteristics of study participants, summary measures for continuous variables (mean±SD or median (25th and 75th percentiles)) and frequency distributions for categorical variables were computed."

6. Suggest changing "multivariate model" to "multivariable model" in the Statistical Analysis section.

Response to reviewer's comments: Change done.

7. The last sentence of the 2nd paragraph in page 7 is not correct. The Mann-Whitney-Wilcoxon test was used to test the overall antibody titers (not median titers) difference by gender. In addition, this sentence should be moved to the Statistical Analysis section.

Response to reviewer's comments: Changes were performed.