

## PEER REVIEW HISTORY

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## ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Prevalence and distribution of HPV types in genital warts in Xi'an, China: a prospective study
<b>AUTHORS</b>	Zhu, Cansheng; Wang, Yaofei; Mao, Weihua; Zhang, Hongshan; Ma, Jiaju

## VERSION 1 - REVIEW

<b>REVIEWER</b>	Katina Robison Program in Women's Oncology Women & Infants' Hospital of Rhode Island The Warren Alpert Medical School of Brown University United States
<b>REVIEW RETURNED</b>	06-Aug-2018

<b>GENERAL COMMENTS</b>	<p>Overall: This is a prospective study over nearly 3 years evaluating the prevalence and HPV type distribution among men and women presenting to a large clinic for genital warts screening. This is a moderately important topic and HPV vaccine development continues it is useful to understand the global distribution of HPV and to know the prevalence of low-risk and high-risk HPV types in various regions. The major limitation of this manuscript is the methods section is very limited and the results section is not well-organized. I believe this study does add to the literature and would warrant publication after revisions.</p> <p>Abstract: The methods are quite limited in the abstract and it is not clear they can make such a strong statement "Our data suggests that current vaccines covering HPV types 6, 11, 16, and 18 are not best vaccines in Xi'an, China" with the information presented in this manuscript. Currently, these are the best vaccines available and they still cover the majority of HPV infections in China as well.</p> <p>Materials and Methods:</p> <ul style="list-style-type: none"><li>• The methods section is overall very limited. It appears they did a prospective cohort study, but lines 31-33 state those being screened for genital warts were recruited in the study and then line 39 states the 879 participants that screened positive for genital warts were selected to participate. The manuscript would benefit from a clearer section outlining the study design, the eligibility and ineligibility criteria and how recruitment was conducted. In addition, how many people declined participation or was this HPV testing standard of care at this site?</li></ul>
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	<ul style="list-style-type: none"> <li>• HPV Genotyping section states 23 type of HPV were detected from the stored specimens. Again, it is unclear if this study was performed retrospectively or prospectively. In addition, this line 47 should be in the results section.</li> </ul> <p>Results – This section is not well organized overall. It would be helpful to have the demographics, then the prevalence of the HPV low-risk and high-risk types followed by the other factors they wanted to evaluate.</p> <ul style="list-style-type: none"> <li>• Table 1 – This table is confusing and it is unclear why the authors are looking at HPV by age as this was not discussed in the methods. The first table should address the prevalence of the HPV types identified as this was the main objective. In general Table 1 should be the demographics of the population being studied as well.</li> </ul> <p>Discussion – There are a number of grammatical errors. Would have this reviewed one more time.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Overall: This is a prospective study over nearly 3 years evaluating the prevalence and HPV type distribution among men and women presenting to a large clinic for genital warts screening. This is a moderately important topic and HPV vaccine development continues it is useful to understand the global distribution of HPV and to know the prevalence of low-risk and high-risk HPV types in various regions. The major limitation of this manuscript is the methods section is very limited and the results section is not well-organized. I believe this study does add to the literature and would warrant publication after revisions.

Response: revised the methods section and the results section is organized.

Abstract: The methods are quite limited in the abstract and it is not clear they can make such a strong statement “Our data suggests that current vaccines covering HPV types 6, 11, 16, and 18 are not best vaccines in Xi’an, China” with the information presented in this manuscript. Currently, these are the best vaccines available and they still cover the majority of HPV infections in China as well.

Response: revised the methods section as:

Design a cross-sectional study.

Setting The study was conducted in Xi’an in northwest China during September 2014 to April 2017.

Participants A total of 912 cases of genital warts were eligible for this study. Among them, 879 cases were recruited in this study.

“Our data suggests that current vaccines covering HPV types 6, 11, 16, and 18 are not best vaccines in Xi’an, China” revised to “HPV 6, 11, 52 and 16 are the most common HPVs in genital warts in Xi’an, China. The burden of genital warts can potentially be lowered with increasing usage of vaccination.”

## Materials and Methods:

- The methods section is overall very limited. It appears they did a prospective cohort study, but lines 31-33 state those being screened for genital warts were recruited in the study and then line 39 states the 879 participants that screened positive for genital warts were selected to participate. The manuscript would benefit from a clearer section outlining the study design, the eligibility and ineligibility criteria and how recruitment was conducted. In addition, how many people declined participation or was this HPV testing standard of care at this site?

Response: revised the methods section as:

### Study design

The present study was a cross-sectional study during September 2014 to April 2017. Patients who attended the Clinic, Shaanxi Provincial Institute for Skin Diseases and STD, for the treatment of newly diagnosed genital warts were invited to participate. Specimens from lesions of warts were collected and 23 types of HPV were detected.

### Inclusion and exclusion criteria

Patients of genital warts were diagnosed according to the diagnostic criteria of genital warts of China.<sup>6</sup> Briefly, they had epidemiological history, such as unsafe sex(es), or sexual partner(s) with a history of genital warts, or multiple sexual partners. Additionally, they had skin lesions. Skin lesions appeared as needles or mung bean-sized papules. Skin lesions could gradually increase, to papillary, cockscomb, cauliflower-like masses. Patients who had the above-mentioned epidemiological history and skin lesions were diagnosed as genital warts cases. Acetic acid white test were used in differential diagnosis and positive results confirmed the diagnosis of genital warts when skin lesions were atypical. Newly diagnosed patients of genital warts were eligible for the study. Patients who were not permanent residents of Xi'an City, or who had warts in non genital area, were excluded from the study..

### Participants

A total of 912 cases of genital warts were eligible for this study during September 2014 to April 2017. Among them, 33 cases declined to participate. The remaining 879 cases including 512 men and 367 women were recruited in this study. They were between 16 and 28 years old and none of them received any HPV vaccination before enrollment.

### Specimen collection

Specimens from lesions of warts were collected by using a cell brush to collect shedding cells that might be infected with viruses and stored at -80°C before testing.

- HPV Genotyping section states 23 type of HPV were detected from the stored specimens. Again, it is unclear if this study was performed retrospectively or prospectively. In addition, this line 47 should be in the results section.

Response: HPV genotyping

HPV testing was the standard of care at our clinic. An automatic nucleic acid hybridization system manufactured by Yaneng Bioscience (Shenzhen) Co.,Ltd was employed. 23 types of human papillomavirus genotyping detection kit manufactured by Yaneng Bioscience (Shenzhen) Co.,Ltd. was used to detect HPV in the specimens. All procedures were carried out following the manufacturer's instructions. HPV genotyping techniques used both DNA amplification and hybridization to simultaneously identify 23 HPV genotypes, including 5 low-risk HPV types (HPV 6, 11, 42, 43, and

81), and 18 high-risk HPV types (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82 and 83). Quality control was implemented during HPV DNA detection.

Results – This section is not well organized overall. It would be helpful to have the demographics, then the prevalence of the HPV low-risk and high-risk types followed by the other factors they wanted to evaluate.

Response: reorganized Results section.

•Response: Table 1 – This table is confusing and it is unclear why the authors are looking at HPV by age as this was not discussed in the methods. The first table should address the prevalence of the HPV types identified as this was the main objective. In general Table 1 should be the demographics of the population being studied as well.

Response: revised old Table 1 to new Table 1 and Table 2

Discussion – There are a number of grammatical errors. Would have this reviewed one more time.

Response: revised a number of grammatical errors.