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# Prevalence and Determinants of High-risk HPV Infection among 11549 Women from an Opportunistic Screening in Hubei Province*

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**Summary**: High-risk human papillomavirus (hrHPV) infection plays an important role in the development of cervical intraepithelial neoplasia and cervical cancer. A total of 11 549 women were enrolled from the Maternal and Child Health Hospital of Hubei Province. Each participant accepted hrHPV testing and completed a self-administered questionnaire about basic information and potential risk factors. The univariable and multivariable logistic regression model was used to explore the associations between variants and hrHPV infection. Our results showed that hrHPV prevalence was 16.09% in Hubei Province, among which, hrHPV was more likely to be positive in women aged 51 years or above (OR=1.65, 95% CI: 1.28–2.14), and in women who had symptoms of bleeding after intercourse (OR=1.32, 95% CI:1.17–1.50), had first sexual intercourse at the age of 18 years or below (OR=1.33, 95% CI:1.07–1.64), had at least three male sexual partners (OR=2.50, 95% CI:2.07–3.03), and who had been diagnosed with sexually transmitted infections (OR=1.50, 95% CI:1.12–2.03). Married women (OR=0.66, 95% CI: 0.55–0.78) and women who frequently used condoms (OR=0.75, 95% CI:0.67–0.84) had a relatively lower hrHPV prevalence. This study confirms that hrHPV infection was associated with age, marital status, symptoms of intercourse bleeding, history of sexually transmitted infections, and sex-related behaviors. Above all, this study provides a baseline database prior to obtaining vaccinations for dynamic tracking of the changes in hrHPV prevalence.
**Key words**: high-risk human papillomavirus; cervical cancer; prevalence; risk factors; China

According to official reports from the World Health Organization (WHO), cervical cancer is the fourth most frequent cancer in women, with an estimated 530 000 new cases and 270 000 deaths in 2012. Of the estimates, more than 85% of these deaths occurred in less developed countries[1]. In China, the National Central Cancer Registry estimated that the number of new cervical cancer cases reached nearly 100 000, and cervical cancer resulted in an estimated 30 500 deaths in 2015[2]. Persistent infection with high-risk types of human papillomavirus (HPV) has been recognized as a major cause of cervical cancer and its precursors (cervical intraepithelial neoplasia)[3, 4]. In 2014, the U.S. Food and Drug Administration (FDA) approved cobas® HPV testing for primary cervical cancer screening in women aged ≥25 years[5].

The distribution of high-risk human papillomavirus (hrHPV) prevalence and types varies substantially among different regions and populations. Guan *et al* studied HPV types in 115 789 HPV-positive women worldwide, and found the overall HPV prevalence was 31.36%, ranging from 22%–23% in Western/Central Asia and Europe to more than 50% in North America, South/Central America, and Oceania[6]. Another meta-analysis study estimated the genotype distribution in the world and found that the five most common HPV types in HPV-positive women worldwide were HPV16, 18, 31, 58, and 52, and that there was variation in the ranking of the prevalence of these types by region[7]. However, there is no standard screening system in China; therefore, there are no large-scale data resources regarding the overall hrHPV prevalence. Wu *et al* conducted a survey that included five geographical sites. They found that the overall hrHPV prevalence was 12.4%, and that the most prevalent types were HPV16, 52, 58, 33, and 18[8]. Additionally, some local hospitals carried out related surveys in some regions. From their results, we noted that the distribution of

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hrHPV prevalence and type was different in different regions in mainland China[9–11].

HPV is the most common sexually transmitted virus, and risk factors for hrHPV infection have been identified and mainly consist of high-risk sexual behavior, such as younger age at first sexual intercourse[12, 13], and large numbers of sexual partners[14, 15]. Several studies also found that prior sexually transmitted infections (STIs)[16, 17], and menstrual flow and length of menstrual period[18] had an association with hrHPV infection. In addition, some experts suggested that the consistent use of condoms can effectively reduce HPV infection[19, 20]. As to daily lifestyle and reproductive history, smoking, passive smoking, and high numbers of births were confirmed to be risk factors for cervical cancer[21–23]. Whether these factors affect hrHPV infection is uncertain at present. In this study, we included variables to reflect different aspects and aimed to conduct a comprehensive discussion on the factors affecting hrHPV infection of women in Hubei Province.

Currently, the major methods for preventing cervical cancer are cervical cancer screening and HPV vaccine. Large-scale epidemiological studies are necessary to obtain reliable data for both methods. However, no related reports have been published thus far in Hubei Province, which is the most developed region in central China, with 27.84 million females. Therefore, we aimed to estimate the prevalence of hrHPV infection, hrHPV types, and risk factors associated with hrHPV infection from an opportunistic screening in Hubei Province for cervical cancer. This survey could fill the vacancy in this area and provide valuable data for the development and promotion of appropriate strategies for cervical cancer screening and HPV vaccine administration.

## 1 MATERIALS AND METHODS

### 1.1 Study Design and Population Characteristics

The purpose of this cross-sectional study was to obtain data on the prevalence of hrHPV infection in women in Hubei Province and to explore risk factors related with hrHPV infection. This study was conducted by the Maternal and Child Health Hospital of Hubei Province, which is the leading unit of the maternal and child health industry in Hubei Province. A total of 12830 women from Hubei Province were enrolled in the study from February 2015 to September 2016. The inclusion criteria were as follows: (1) a history of sexual activity; (2) agreed to undergo a HPV test and voluntarily participate in this study. Women who were pregnant or had a history of cervical cancer or cervical intraepithelial neoplasia were excluded.

### 1.2 HPV Detection

In this study, all the samples were obtained by 4 experienced gynecologists. A cervical brush was inserted by a doctor into the cervix 1.0 to 1.5 cm, until the outermost bristles touched the external cervix. The cervical brush was rotated 3 times in the same direction, and was then removed from the patient and inserted into a preservation tube, broken off and placed in the sample preservation tube. All the samples were sent to the Pathology Department for testing and analysis. The automated Roche cobas HPV Test (Roche Molecular Systems, USA) was used to test for HPV infection and 14 high-risk HPV types were detected by using the cobas 4800 system. The cobas 4800 can separately detect HPV16 and HPV18 genotypes, as well as detect a pool of 12 hrHPV genotypes (HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). The cobas test was performed according to the manufacturer's protocol.

### 1.3 Self-administered Questionnaire

The data on potential risk factors were obtained in the self-administered questionnaire that was completed prior to undergoing their HPV screening test. The questionnaire consisted of four parts: (1) demographic characteristics, (2) health status and reproductive history, (3) daily lifestyle, and (4) sexual history and sexual habits.

### 1.4 Data Analysis

Statistical analysis was conducted by SAS 9.1 software (North Carolina State University, USA). The univariable and multivariable logistic regression model was used to evaluate the associations between risk factors and hrHPV infection. The risk factors included demographic characteristics, health status and reproductive history, daily lifestyle, sexual history, and sexual habits. The odds ratio (OR) value and their 95% CIs were calculated to estimate the correlations, and a value of $P<0.05$ was considered statistically significant.

### 1.5 Ethical Issues

This study was approved by the Ethics Review Committee of the Maternal and Child Health Hospital of Hubei Province in accordance with the principles expressed in the Declaration of Helsinki. Participants voluntarily took part in the study on the condition that they were fully informed of the aim and details of the research in advance, and written informed consent was obtained from each one.

## 2 RESULTS

### 2.1 Participant Characteristics

A total of 11549 valid responses (out of 12830 individuals) were collected, with a valid return rate of 90.01%. Among them, most women were aged between 25 and 50 years old, married (80.46%), had at least a high school degree (95.36%), and had a monthly income of ¥1000 or more (82.50%). Nearly half of the women indicated that they had a general or

poor physical condition (46.64%), and 2161 (18.71%) women had a history of bleeding upon intercourse. Only 267 (2.31%) women had a family history of cervical cancer/HPV infection, and 3568 women did not have regular menstruation. There were 7828 (67.78%) women with a reproductive history, and 6909 (59.82%) women underwent abortion. Only 370 women were smokers, 691 women habitually consumed alcohol, and 75 women had taken cannabis. Most women reported that their first sexual intercourse occurred at the age of 18 or above (93.63%), and just 5.46% of women reported having at least three male sexual partners. Totally, 243 women indicated that they had been diagnosed with STIs. Over 40% of the women (42.62%) frequently used condoms, and 381 (3.30%) women frequently used oral contraceptives (table 1).

**2.2 hrHPV Prevalence**

Among the 11 549 individuals, there were 1858 (16.09%) positive hrHPV test results, and 9691 (83.91%) negative hrHPV test results (table 2). The prevalence of hrHPV infection was different among different age groups, ranging from 19.53% (470/2406) for women under 25 years of age to 19.28% (43/223) for those who were 56 years of age and older, reaching two peaks in the general trend, with 19.53% for women under 25 years of age, and 20.37% for women aged 51 to 55 years (fig. 1). As for the genotypes of HPV infection, there were 673 overall individuals infected with HPV16/18, with an incidence of 5.83%, among which the incidence of HPV16 was 3.92% (table 3).

**2.3 Logistic Regression Analysis of hrHPV Infection**

Table 4 shows the logistic regression outcomes of hrHPV infection of the participants surveyed. Both univariate logistic regression and multilevel logistic regression analyses revealed that subjects' hrHPV was significantly correlated to their age, marital status, symptoms of intercourse bleeding, alcohol consumption, age at first sexual intercourse, number of sexual partners, history of STIs, and condom use (table 4). Women aged 51 years or above had higher hrHPV infection rates than women aged 50 years or below (OR=1.65, 95% CI: 1.28–2.14). Married women

**Table 1 Characteristics of 11549 women**

| Items | *n* | Percent % | Items | *n* | Percent % |
|---|---|---|---|---|---|
| Age (years) | | | Abortion | | |
| <25 | 2406 | 20.83 | Yes | 6909 | 59.82 |
| 25–50 | 8483 | 73.45 | No | 4640 | 40.18 |
| ≥51 | 660 | 5.71 | Smoking | | |
| Marital status | | | Yes | 370 | 3.20 |
| Unmarried | 2058 | 17.82 | No | 11179 | 96.80 |
| Married | 9292 | 80.46 | Alcohol consumption | | |
| Divorced/widowed/separated | 199 | 1.72 | Yes | 691 | 5.98 |
| Education | | | No | 10858 | 94.02 |
| Elementary school | 536 | 4.64 | Taking cannabis | | |
| Secondary school | 6015 | 52.08 | Yes | 75 | 0.65 |
| College | 4486 | 38.84 | No | 11474 | 99.35 |
| Postgraduate | 512 | 4.43 | Exercise regularly | | |
| Income (Yuan/month) | | | Yes | 5566 | 48.19 |
| <1000 | 2021 | 17.50 | No | 5983 | 51.81 |
| 1000–2999 | 5043 | 43.67 | Age at first sexual intercourse (years) | | |
| 3000–4999 | 3268 | 28.30 | <18 | 736 | 6.37 |
| ≥5000 | 1217 | 10.54 | 18–21 | 6273 | 54.32 |
| Physical condition | | | ≥22 | 4540 | 39.31 |
| Good | 6163 | 53.36 | Number of sexual partners | | |
| General | 5108 | 44.23 | 1 | 9514 | 82.38 |
| Poor | 278 | 2.41 | 2 | 1405 | 12.17 |
| Family history of cervical cancer/HPV infection | | | ≥3 | 630 | 5.46 |
| Yes | 267 | 2.31 | Sexually transmitted diseases | | |
| No | 11282 | 97.69 | Yes | 243 | 2.10 |
| Menstrual regularity | | | No | 11306 | 97.90 |
| Yes | 7981 | 69.11 | Frequently using condoms | | |
| No | 3568 | 30.89 | Yes | 4922 | 42.62 |
| Intercourse bleeding | | | No | 6627 | 57.38 |
| Yes | 2161 | 18.71 | Frequently using oral contraceptives | | |
| No | 9388 | 81.29 | Yes | 381 | 3.30 |
| Births | | | No | 11168 | 96.70 |
| Yes | 7828 | 67.78 | | | |
| No | 3721 | 32.22 | | | |

**Table 2 The overall prevalence of hrHPV in different age groups**

| hrHPV Infection | Age groups (years) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ≤25 | 26–30 | 31–35 | 36–40 | 41–45 | 46–50 | 51–55 | ≥56 | Total |
| hrHPV positive | 470 | 428 | 265 | 199 | 216 | 148 | 89 | 43 | 1858 |
| hrHPV negative | 1936 | 2555 | 1605 | 1210 | 1136 | 721 | 348 | 180 | 9691 |
| Total | 2406 | 2983 | 1870 | 1409 | 1352 | 869 | 437 | 223 | 11549 |

**Table 3 The overall distribution of HPV types in different age groups**

| HPV type | Age groups (years) | | | | | | | | *n* | Incidence (95% CI) | Percent |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | ≤25 | 26–30 | 31–35 | 36–40 | 41–45 | 46–50 | 51–55 | ≥56 | | | |
| 16 | 121 | 89 | 64 | 60 | 49 | 37 | 25 | 8 | 453 | 3.92 (3.57, 4.28) | 24.38% |
| 16/18 | 177 | 142 | 91 | 88 | 72 | 54 | 36 | 13 | 673 | 5.83 (5.40, 6.25) | 36.22% |
| 12 | 293 | 286 | 174 | 111 | 144 | 94 | 53 | 30 | 1185 | 10.26 ( 9.71, 10.81) | 63.78% |

HPV12=HPV DNA test was positive for the pooled 12 high-risk types; HPV 16/18=HPV DNA test was positive for HPV 16 or HPV 18 or both; HPV 16=HPV DNA test was positive for HPV 16

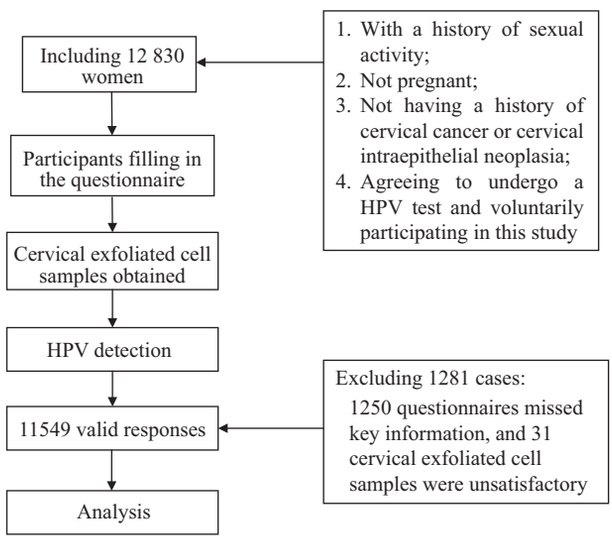


**Fig. 1** Flow chart summary of the study

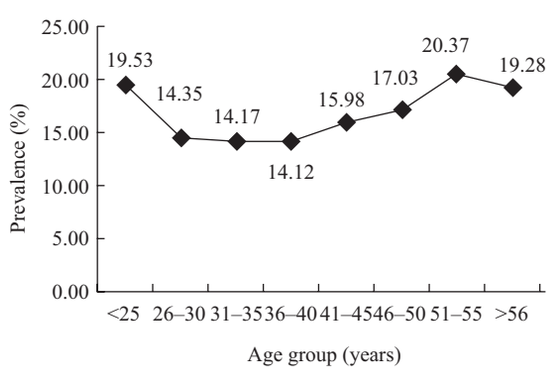


**Fig. 2** The overall prevalence of hrHPV in the different age groups

had relatively lower hrHPV infection rates than women who were unmarried or divorced/widowed/separated (OR=0.66, 95% CI: 0.55–0.78). Women with symptoms of intercourse bleeding were more likely to be hrHPV positive than those without (OR=1.32, 95% CI: 1.17–1.50). Detection of hrHPV infection was also more common among women with first sexual intercourse at the age of 18 years or below (OR=1.33, 95% CI: 1.07–1.64), those with at least three male sexual partners (OR=2.50, 95% CI: 2.07–3.03), and those being diagnosed with STIs (OR=1.50, 95% CI:1.12–2.03). Women who frequently used condoms were less likely to be hrHPV positive than those who did not (OR=0.75, 95% CI: 0.67–0.84). Univariate logistic regression analysis showed that there were significant correlations between the hrHPV infection of the participants and their physical condition, family history of cervical cancer/HPV infection, reproductive history, smoking status, use of cannabis, etc; however, in the multilevel logistic regression analysis, there was no association between them.

## 3 DISCUSSION

The prevalence of hrHPV varies in different countries and areas[24]. In China, an organized nationwide screening program still does not exist, and most studies have been based on selected populations in local hospitals or local cancer registries. As a result, there is no precise information on the prevalence of hrHPV at the national level. We compared regional studies and found that the hrHPV prevalence was also different in different areas. In Fujian, East China, the hrHPV prevalence was 20.53%[25]. In Guangzhou, South China, China's largest College of American Pathology (CAP)-certified laboratory tested 51 345 samples and found that the overall HPV prevalence was 26%, with 21.12% positive for hrHPV[26]. In Yunnan Province, Southwest China, the overall hrHPV prevalence was 12.2%[10]. In Beijing, North China, the HPV prevalence was 6.7% overall[27]. Until now, there were no reports describing the prevalence and subtype distribution of hrHPV infection in Hubei Province. In this study, the overall hrHPV prevalence was 16.09%, which is consistent with a study that reported an average

**Table 4 Logistic regression analysis (OR and 95% CI) for hrHPV infection**

| Items | hrHPV(+) [*n* (%)] | Crude OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|---|
| Age (years) | | | |
| <25 | 470 (19.53) | Ref. | Ref. |
| 25–50 | 1256 (14.81) | 0.72 (0.64, 0.81)** | 1.07 (0.91, 1.25) |
| ≥51 | –132 (20.00) | 1.03 (0.83, 1.28) | 1.65 (1.28, 2.14)** |
| Marital status | | | |
| Unmarried | 473 (22.98) | Ref. | Ref. |
| Married | 1328 (14.29) | 0.56 (0.50, 0.63)** | 0.66 (0.55, 0.78)** |
| Divorced/widowed/separated | 57 (28.64) | 1.35 (0.97, 1.86) | 1.02 (0.71, 1.47) |
| Education | | | |
| Elementary school | 90 (16.79) | Ref. | |
| Secondary school | 988 (16.43) | 0.97 (0.77, 1.23) | |
| College | 710 (15.83) | 0.93 (0.73, 1.19) | |
| Postgraduate | 70 (13.67) | 0.79 (0.56, 1.10) | |
| Income (Yuan) | | | |
| <1000 | 326 (16.13) | Ref. | |
| 1000–2999 | 823 (16.32) | 1.01 (0.88, 1.17) | |
| 3000–4999 | 497 (15.21) | 0.93 (0.80, 1.09) | |
| ≥5000 | 212 (17.42) | 1.10 (0.91, 1.33) | |
| Physical condition | | | |
| Good | 891 (14.46) | Ref. | Ref. |
| General | 912 (17.85) | 1.29 (1.16, 1.42)** | 1.19 (1.07, 1.33) |
| Poor | 55 (19.78) | 1.46 (1.08, 1.98) | 1.31 (0.96, 1.79) |
| Family history of cervical cancer/HPV | | | |
| Yes | 56 (20.97) | 1.40 (1.04, 1.88)* | 1.27 (0.93, 1.73) |
| No | 1802 (15.97) | Ref. | Ref. |
| Menstrual regularity | | | |
| Yes | 1235 (15.47) | Ref. | Ref. |
| No | 623 (17.46) | 1.16 (1.04, 1.28)** | 1.05 (0.94, 1.17) |
| Intercourse bleeding | | | |
| Yes | 447 (20.68) | 1.48 (1.31, 1.66)** | 1.32 (1.17, 1.50)** |
| No | 1411 (15.03) | Ref. | Ref. |
| Childbearing | | | |
| Yes | 1164 (14.87) | 0.76 (0.69, 0.85)** | 0.96 (0.82, 1.11) |
| No | 694 (18.65) | Ref. | Ref. |
| Abortion | | | |
| Yes | 1163 (16.83) | 1.15 (1.04, 1.27)** | 1.10 (0.99, 1.23) |
| No | 695 (14.98) | Ref. | |
| Smoking | | | |
| Yes | 105 (28.38) | 2.13 (1.69, 2.69)** | 1.06 (0.82, 1.37) |
| No | 1753 (15.68) | Ref. | Ref. |
| Alcohol consumption | | | |
| Yes | 219 (31.69) | 2.61 (2.21, 3.09)** | 1.82 (1.51, 2.19)** |
| No | 1639 (15.09) | Ref. | Ref. |
| Taking cannabis | | | |
| Yes | 20 (26.67) | 1.91 (1.14, 3.19)* | 1.46 (0.85, 2.51) |
| No | 1838 (16.02) | Ref. | Ref. |
| Exercising regularly | | | |
| Yes | 917 (15.33) | 0.89 (0.81, 0.98) | 0.96 (0.87, 1.07) |
| No | 941 (16.91) | Ref. | Ref. |
| Age of first sexual intercourse (years) | | | |
| <18 | 180 (24.46) | 2.26 (1.87, 2.74)** | 1.33 (1.07, 1.64)** |
| 18–21 | 1110 (17.69) | 1.50 (1.35, 1.68)** | 1.25 (1.11, 1.40)** |
| ≥22 | 568 (12.51) | Ref. | |
| Number of sexual partners | | | |
| 1 | 1295 (13.61) | Ref. | Ref. |
| 2 | 341 (24.27) | 2.03 (1.78, 2.33)** | 1.69 (1.47, 1.96)** |
| ≥3 | 222 (35.24) | 3.45 (2.90, 4.11)** | 2.50 (2.07, 3.03)** |
| Sexually transmitted infections | | | |
| Yes | 70 (28.81) | 2.15 (1.62, 2.86)** | 1.50 (1.12, 2.03)** |
| No | 1788 (15.81) | Ref. | Ref. |
| Using condoms frequently | | | |
| Yes | 686 (13.94) | 0.75 (0.68, 0.84)** | 0.75 (0.67, 0.84)** |
| No | 1172 (17.69) | Ref. | Ref. |
| Using oral contraceptives frequently | | | |
| Yes | 84 (22.05) | 1.50 (1.17, 1.92)** | 1.00 (0.77, 1.30) |
| No | 1774 (15.88) | Ref. | Ref. |

**$P$<0.01, *$P$<0.05

hrHPV prevalence of 17.7% based on a meta-analysis of 17 population-based screening studies in mainland China[28]. Compared with the same period study in central China, we found that the hrHPV prevalence was 19.53% in Jiangxi Province, which was slightly higher than that of this study[11].

In the current study, we used the cobas 4800 system to test for HPV, and focused on the HPV16/18 prevalence in the population. On one hand, approximately 73% of invasive cervical cancer (ICC) were associated with either HPV16 (57%) or HPV18 (16%) based on the latest worldwide data[29]; on the other hand, in China, the Food and Drug Administration has licensed two prophylactic HPV vaccines (Gardasil and Cervarix) that mainly protect against HPV16 and HPV18 respectively. Therefore, we need to determine the prevalence of HPV16 and HPV18 in Hubei Province. In our study, the prevalence of HPV16 was 3.92%, and that of HPV16/18 was 5.83%. These results were similar to those of other studies performed in mainland China. During the same period, Liu *et al* found that in Zhejiang Province, the prevalence of HPV16 was 4.8%, and that of HPV18 was 1.9%[30]. In Jiangxi Province, the prevalence of single HPV16 and HPV18 was 3.24% overall[11].

The Gardasil HPV vaccine has been listed and supplied in China, and the FDA recommendation for vaccination is for girls between 9 and 25 years of age. In the current study, the prevalence of overall HPV16/18 was 7.36% at the ≤25 years old group, although HPV58 and HPV52 were more prevalent among women in the South and Southwest than other regions in China. China's largest CAP-certified laboratory has found that the three most common hrHPV types were HPV52, 16, and 58 in Guangzhou Province, and HPV18 was only the 6th most common type[26]. In Shenzhen, a study also found that the five most prevalent HPV types were HPV52 (22.9%), HPV16 (12.7%), HPV53 (10.0%), HPV51 (8.6%), and HPV58 (8.1%)[31]. In central China, HPV16 was still the most prevalent type in the population[11, 32]. These findings reflect the suitability and necessity of the Gardasil HPV vaccine promotion in our province.

We analyzed the hrHPV prevalence in different age groups, and found a bimodal age distribution of hrHPV prevalence, with a peak (19.53%) at the age group of ≤25 years and a second peak (20.37%) at the age group of 51–55 years. de Sanjosé *et al* found that this age-specific pattern could be observed in major world regions, with the exception of Asia, where rates continued to decrease[7]. However, a recent study revealed that the second prevalent peak also exists in China. In Zhejiang Province, Liu *et al* found that the HPV prevalence exhibited a peak (55.7%) at the age group of ≤20 years and then reached a second peak (35.5%) at the age group of >60 years[30]. In Hunan Province, Xiao *et al* found the hrHPV prevalence reached a second peak in women over 56 years of age[32]. The first peak was observed in all studies because this is a sexually active period for younger women, who were more likely to have more sexual partners, and more likely to have sexual partners with more than one female partner. In addition, young women had worse sexual health habits; e.g., the youngest age group was less likely to clean the perineum before and after sexual intercourse than older women[33]. All these could increase the risk of hrHPV infection.

The second infection peak occurred during the menopausal period, and had been found in some countries and regions. We analyzed this age-specific pattern and put forward the following potential underlying causes. A first hypothesis is that at menopause, hormonal changes result in an impaired immune system that somehow allows reactivation of existing, perhaps latent HPV infections that were replicating at a very low, undetectable rate[7]. A second speculation is that the sexual behavior of women or their partners in middle age changes, especially concerning extramarital sex. A survey showed that in China, extramarital sex for survey respondents reached its peak at 41–45 years old, when half of the middle-aged population admitted to having different extramarital affairs[34]. Finally, a large proportion of older women who come to the hospital clinic have had clinical symptoms or have had cervical lesions[32].

We conducted univariable and multivariable logistic regression models to explore the factors related to hrHPV infection, and found that age ≥51 years, bleeding at intercourse, habitual consumption of alcohol, age at first sexual intercourse <20 years, having ≥2 sexual partners, and having a history of sexually transmitted diseases were risk factors for hrHPV infection, and that marriage and frequent use of condoms could decrease the risk of hrHPV infection.

We also analyzed intercourse bleeding symptoms, and found that women with symptoms of intercourse bleeding were more likely to be hrHPV positive than those without (OR=1.32, 95% CI:1.17–1.50). Intercourse bleeding is one of the typical symptoms of cervical intercourse and cervical cancer. However, intercourse bleeding symptoms of some patients can be attributed to cervical erosion or ovulation bleeding or other reasons, which may weaken the correlation between intercourse bleeding symptoms and HPV infection to some extent.

Studies have confirmed that HPV infection is mainly transmitted through sexual contact[12], and in this study, we also found that sexual behavior-related factors are the main risk factors. With the decrease in the age of first sexual intercourse, hrHPV infection rates increased. The hrHPV infection of women who had their first sexual intercourse at the age of 18 years

or below reached 22.46%, while for women who had their first sexual intercourse >22 years old, the hrHPV prevalence was only 12.51%. Early sexual intercourse is always accompanied by having multiple sexual partners, which increases the risk of HPV infection. In addition, because the structure of the transformation zone is immature in adolescent woman, the epithelium is more susceptible to the entry and persistence of viruses such as HPV[13].

A multi-center survey of age of sexual debut and sexual behavior in Chinese women found that the median sexual debut age for the 15 to 19-year-old age group was only 17 years old, earlier than the sexual debut age reported by older cohorts. In urban areas, 10.80% of the 15 to 19-year-old age group were already sexually active at the time of the interview[33]. In the current study, 60.69% of women reported they were aged 22 years or below at the time of their first sexual intercourse, of which, women less than 18 years of age reached 6.37%. This reflects a trend towards earlier sexual debut in younger age groups of Chinese women, and also prompts the necessity for vaccination with the HPV vaccine. As soon as girls begin having sex, their risk of infection with HPV dramatically increases. A study found that the median time from first intercourse to first infection of HPV was only three months[35], and therefore, the best vaccination age is before the first sex exposure.

We analyzed the number of sexual partners, and found that with an increasing number of sexual partners, hrHPV-positive rates significantly increased. The hrHPV-positive rate of women who had only one sex partner was 13.61%, while for those who had three or more sex partners, the rate reached 35.24%. The multivariate regression analysis showed that the OR was 2.50 (2.07, 3.03) for ≥3 partners *vs.* 1 partner. HPV infection is mainly transmitted through sexual contact, and thus, the infection risk would increase as the number of sexual partners increased. Chaturvedi *et al* found that women with an increasing number of lifetime sex partners had a higher incidence of HPV infection (OR for >5 partners *vs.* 1 partner=2.05)[36], and Roset *et al* found that the OR was 9.29 for ≥4 sex partners *vs.* 0 sex partners[13]. There have been great social and cultural changes in China due to the economic development of the past few decades. Simultaneously, Chinese attitudes and behaviors regarding sex have also dramatically changed, including topics such as premarital sex, extramarital sex, and homosexual behavior, especially in the younger population[37]. In the current study, nearly 17.63% of females had more than 2 sex partners, and this situation indicates the necessity of cervical cancer prevention work in China. In 2013, a survey concluded that among approximately 1 million Chinese respondents, nearly 23.9% Chinese females had multiple sex partners[38].

We analyzed the history of sexually transmitted disease, and found that the hrHPV prevalence in women who reported having sexually transmitted disease was 28.81%, and the OR was 1.50 (1.12, 2.03) compared with women who had no history of sexually transmitted disease. Del *et al* found that prior STIs (1.65:1.17–2.32) were associated with a greater risk of HPV infection[39], and Roset *et al* found that the OR was 3.56 (having STI history *vs.* none)[13]. China's rapid industrialization and urbanization during the last three decades have also coincided with an increased prevalence of sexually transmitted disease.

At the same time, we found that getting married and frequent use of condoms could decrease the risk of hrHPV infection. The OR value of married women was 0.66 (0.55, 0.78) compared with the unmarried group. As for the reason, we thought it was because married women were monogamous compared with unmarried or divorced/widowed/separated women. Studies have confirmed that using condoms can effectively reduce the risk of HPV infection[20], although the latest research shows that condoms are not 100% effective, and that the HPV virus can penetrate condoms or the HPV virus can be transmitted through non-penetrative sexual contact; however, partial protection can also substantially reduce the spread of STIs in populations[40]. In fact, the main method of contraception for women in China is the condom. Up to 53.6% of young people reported not using condoms during the last sexual intercourse[33], and in the current study, we found that only 42.62% of women frequently use condoms. In Europe, more than 50% of young adults reported using condoms at first sexual activity. In all countries, the proportion varied from 58.1% to 83.3%[20]. This shows that our health institutions should continue to strengthen relevant work, such as disseminating important data to the public, and increasing the number and quality of free distributed condoms.

This is the first epidemiological study of women in Hubei Province performed on a large scale to estimate the hrHPV prevalence and explore risk factors related with hrHPV infection. Our results showed that the hrHPV prevalence was 16.09% in Hubei Province; hrHPV prevalence was associated with age, marital status, symptoms of intercourse bleeding, the age at first sexual intercourse, number of sexual partners, history of sexually transmitted diseases, and condom use. We recommend popularizing HPV screening in Hubei Province, especially in high-risk populations. In addition, 2- and 4-valent HPV vaccines were approved by the China Food and Drug Administration to enter the market in 2017, and therefore, the baseline database for HPV prevalence is very important for further dynamic tracking of the change in HPV infection among vaccinated women.

**Conflict of Interest Statement**

The authors declare that there is no conflict of interest with any financial organization or corporation or individual that can inappropriately influence this work.

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