

# Incidence of persistent and high-risk human papillomavirus infection and associated factors among HIV-positive women in China, 2015–2016<sup>☆</sup>

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## ABSTRACT

**Background:** Persistent human papillomavirus (HPV) infection is the necessary factor for cervical cancer. Human immunodeficiency virus (HIV)-positive women are a high-risk population for cervical cancer, but little is known about persistent HPV infection among HIV-positive women in China. We aimed to investigate the persistence and incidence of infection with high-risk HPV (hrHPV) and associated factors among HIV-positive women in China.

**Method:** Using a prospective observational study design, we collected data from 670 HIV-positive women in five counties of three provinces through interviews, medical record reviews, health examination, and laboratory tests at a baseline survey in 2015 and a follow-up survey in 2016. We tested HIV-positive women for hrHPV infection using the Cobas 4800 HPV test, and analyzed factors associated with persistence and new incidence of hrHPV infection using logistic regression.

**Results:** After an average of 15 months at follow-up, the persistence and new incidence rates of hrHPV infection were 38.0% (46/121, 95% CI: 29.2%–46.8%) and 8.3% (35/420, 95% CI: 5.7%–11.1%), respectively. HIV-positive women in Yunnan and Guangxi were more likely to have persistent hrHPV infections than those in Xinjiang (aOR = 3.18, 95% CI: 1.00–10.14,  $p = 0.05$ ; aOR = 6.38, 95% CI: 2.29–17.77,  $p < 0.001$ ). Migrant women had a higher rate of new hrHPV incidence than local women (aOR = 4.48, 95% CI: 1.65–12.15,  $p = 0.003$ ). HIV-positive women from Xinjiang were 6.5 times more likely to be newly infected with hrHPV than those from Yunnan (95% CI: 2.40–17.60,  $p < 0.001$ ). HIV-positive women with HBV infection had a higher risk of being infected with hrHPV than those without HBV infection (aOR = 3.48, 95% CI: 1.13–10.71,  $p = 0.029$ ).

**Conclusions:** The persistence and new incidence rates of hrHPV infection among HIV-positive women were high and varied significantly between regions. HBV infection and being among the migrant population were associated with new hrHPV infection.

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least a 6-month interval. Persistent hrHPV infection is a necessary factor for cervical cancer<sup>2,3</sup> and is closely associated with cervical cancer and precancerous lesions in middle-aged women.<sup>4,5</sup>

While the majority of women with HPV do not develop persistent infections, women with human immunodeficiency virus (HIV) infections are particularly susceptible to HPV infection and have a reduced ability to clear the virus due to immune suppression.<sup>6</sup> Previous studies have shown that the risk of persistent HPV infection is higher in HIV-positive women than in HIV-negative women,<sup>7</sup> and HIV-positive women are 4–5 times more likely than HIV-negative women to develop cervical cancer.<sup>8</sup> It has been reported that persistent hrHPV infection in HIV-infected women is associated with antiretroviral treatment, having multiple sexual partners, and long follow-up time.<sup>9–11</sup>

As of the end of 2015, there were 577,423 reported HIV/acquired immunodeficiency syndrome (AIDS) patients in China, of whom ~165,000 were female (28.6%). Among the 115,465 newly-reported HIV/AIDS patients in 2015, ~25,100 cases were female (21.7%).<sup>12</sup> HIV-positive women are mainly concentrated in several areas, including Yunnan, Guangxi, Xinjiang, and Henan. Due to the negative physical, psychological, and social effects of HIV infection, HIV-positive women face more severe reproductive health problems than HIV-negative women. As a result, HIV-positive women are extremely vulnerable.

Prior surveys with small sample sizes in Hubei and Yunnan reported that the persistent hrHPV infection rate was higher in HIV-positive women than in HIV-negative women.<sup>13–16</sup> However, there are very few studies exploring persistent hrHPV infection and associated factors among HIV-positive women in China, and no such research on new hrHPV infection rates was found. Considering the large number of HIV-positive women in China who are vulnerable to HPV infection and cervical cancer, it is necessary to address those issues. Therefore, this study aimed to determine the rate of new and persistent hrHPV infections, and factors associated with them, among HIV-infected women in China. This will ultimately provide scientific evidence for strategies to prevent and treat HPV infection and cervical cancer among HIV-positive women in China.

## 2. Method

### 2.1. Study setting and population

We conducted a prospective observational study in China between 2015 and 2016. The baseline survey was carried out between May and August 2015. Sample size calculations and the recruitment of HIV-positive women in the baseline survey were reported previously.<sup>17</sup> The follow-up survey followed the same procedure and was conducted 15 months later.

We utilized random cluster sampling and selected three provinces/autonomous regions: Yunnan province, Guangxi Zhuang Autonomous Region, and Xinjiang Uygur Autonomous Region. These regions had high incidence of new HIV infections in women aged 15–49 before the research conducted, representing areas where the AIDS epidemic emerged earlier and hit harder than in other areas of China.<sup>18</sup>

We defined our study population as HIV-positive women, meaning they had confirmed HIV status by laboratory test and were aged 18–49 years. We excluded HIV-positive women who: 1) were ill at the time of the study contacted; 2) could not be contacted after meeting the requirements of the study; 3) had no sexual

intercourse experience, or 4) had a history of uterectomy or high-grade squamous intraepithelial lesion (HSIL) or above.

### 2.2. Data collection and procedures

The field team consisted of trained healthcare staff in local maternal and child health (MCH) hospitals. After obtaining informed consent, the field team conducted face-to-face interviews with participants to collect data related to sociodemographic characteristics and sexual practices using a structured questionnaire. The field team reviewed the HIV-positive women's medical records to extract data on antiretroviral treatment (ART) and laboratory results.

Trained clinicians conducted gynecological physical examinations as follows: 1) observed the vulva, vagina, cervix, and vaginal discharge for abnormalities; 2) collected vaginal discharge and exfoliative cervical cell specimens; 3) conducted a pelvic examination, and provided B-ultrasound to those with abnormal uterus or uterine adnexa. Blood samples of participants were also collected.

The study team sent cervical cell specimens for cytological examination and HPV DNA analysis with the Cobas 4800 HPV test (Roche Molecular Diagnostics [Shanghai] Co. Ltd., Shanghai, China) in Beijing Di'an Laboratory. The HPV test produced individual results for two hrHPV strains, HPV16 and HPV18, and a pooled result for the other 12 hrHPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68b).

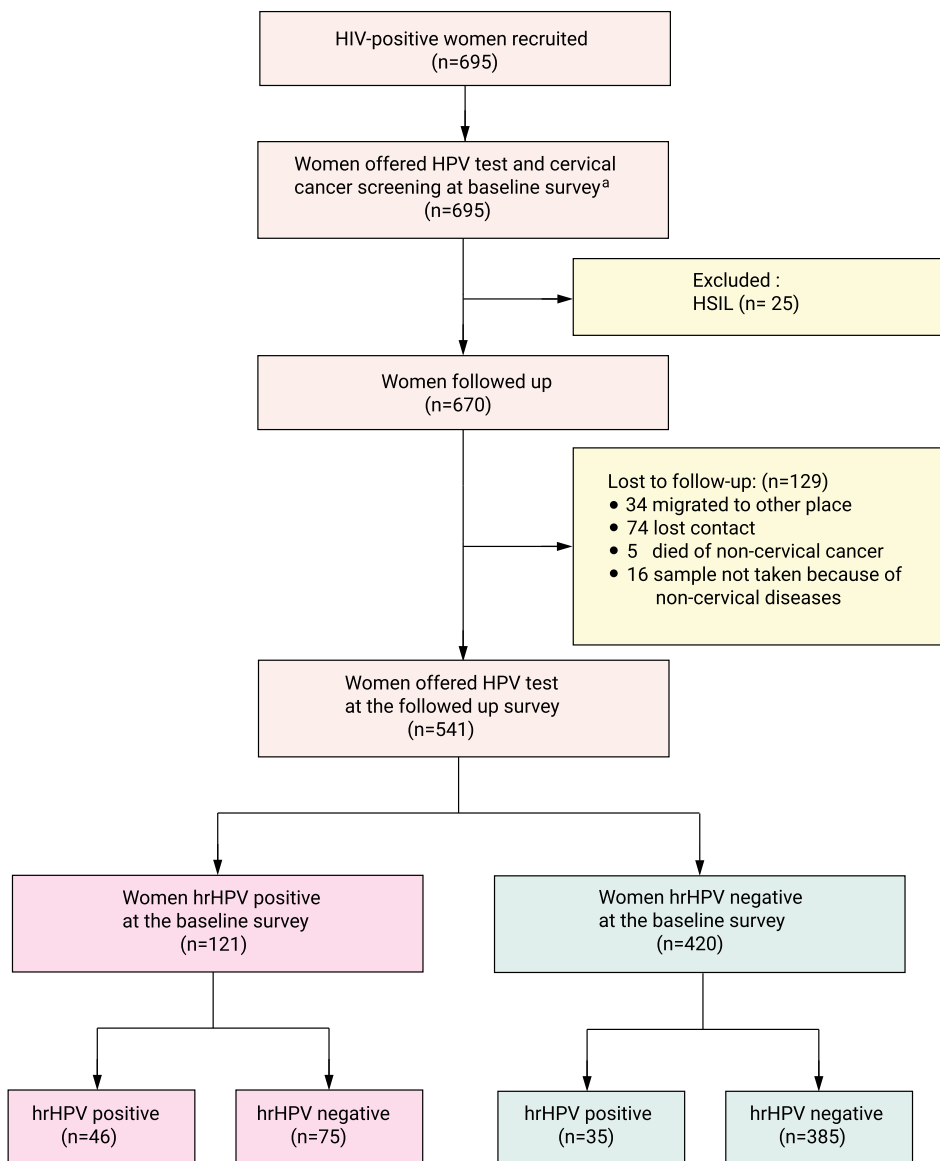
Data related to CD4 lymphocyte count tests and HIV viral load tests in the six months prior to fieldwork were obtained from clinical records. For participants who had not CD4 lymphocyte counts or HIV viral load results in the prior six months, serum samples were sent to local prefecture CDC laboratories for the appropriate test(s). Other tests were conducted at the county level MCH hospital laboratories, including microscopic examination of vaginal secretions with amine test and pH measurement as appropriate, syphilis treponema pallidum particle agglutination (TPPA) and syphilis toluidine red unheated serum test (TRUST) for syphilis diagnosis, enzyme-linked immunosorbent assay (ELISA) for presence of hepatitis B surface antigen (HBsAg).

HIV-positive women with cytological abnormality or hrHPV infection received a biopsy with colposcopy for cervical cancer screening, following the technical protocol for rural women cervical cancer screening.<sup>19</sup> We referred the HIV-positive women with HSIL and above to appropriate treatment.

### 2.3. Study variables

We defined hrHPV infection as a positive result of the Cobas 4800 HPV test for HPV16, HPV18, or any of the other 12 hrHPV types. "Persistent hrHPV infection" refers to positive results of HPV DNA tests at both the baseline and follow-up surveys. "Persistent hrHPV infection rate" refers the proportion of women with persistent hrHPV infection (established at the follow-up survey) among those with hrHPV infection at baseline. "New hrHPV infection" refers to a negative HPV test result at the baseline survey but a positive result at a follow-up survey. "New hrHPV infection rate" refers to the proportion of women with hrHPV infection at the follow-up among those who were hrHPV-negative at the baseline.

Trichomonas vaginitis, vulvovaginal candidiasis, bacterial vaginosis, and other infections were collectively referred to as vaginitis. Cervicitis was diagnosed depending on vaginal discharge



**Fig. 1.** Diagram showing processes for recruitment, hrHPV test, and follow-up survey processes among HIV-positive women from high HIV-burden areas in China, 2015–2016. <sup>a</sup> Cervical cancer screening procedure included liquid-based cytology, colposcopy, and biopsy; HIV, human immunodeficiency virus; HSIL, high-grade squamous intraepithelial lesion; hrHPV, high-risk human papillomavirus.

examination and particular signs found in gynecological physical examinations. Syphilis infection was diagnosed when the results for both TPPA and TRUST were positive. Degrees of cervical lesions were defined as Normal, low-grade squamous intraepithelial lesion (LSIL), or HSIL.

2.4. Statistical analysis

Before data entry, we reviewed the questionnaire data and undertook checks for quality assurance. We double entered and validated the data using EpiData software (version 3.1, The EpiData Association, Odense Denmark), and used SPSS software (version 23.0, IBM Corp, Armonk, NY, USA) to analyze the data.

Categorical variables (sociodemographic characteristics, sexual practices, and laboratory characteristics) were presented as frequencies and proportions. Continuous variables with normal distribution were presented as mean ± standard deviation (SD). Persistent and new hrHPV infections are described by frequencies

and proportions, as appropriate. Pearson's chi-squared test and Fisher's exact test as appropriate was used to determine the association of categorical and continuous variables with hrHPV infection categories. Factors with a *p*-value of <0.1 were entered into a binary logistic regression to build the final model. A *p*-value of <0.05 was defined as statistically significant, and Odds Ratios (OR) and 95% confidence intervals (95% CI) were calculated as indicators of the magnitude of association and statistical significance of hrHPV infection.

The Institutional Review Board of the National Centre for Women and Children's Health, China CDC reviewed and approved the study (No. FY2015–014). All participants provided informed consent to participate in the study.

3. Results

The recruitment, hrHPV test, and follow-up processes are shown in Fig. 1. During the baseline survey, 695 HIV-positive women were

**Table 1**

Characteristics of followed and lost follow-up HIV-positive women enrolled in the study from HIV high-burden areas in China, 2015–2016.

Characteristics	Women enrolled		Followed		Lost follow-up		$\chi^2$	p-value
	n	%	n	%	n	%		
Total	670		541		129			
Age (years old)								
18–29	116	17.3	89	16.4	27	20.9	3.77	0.152
30–39	383	57.2	319	59.0	64	49.6		
40–49	171	25.5	133	24.6	38	29.5		
Ethnic group								
Han and others	237	35.4	219	40.5	18	13.9	30.02	<0.001
Jingpo and Dai	206	30.7	164	30.3	42	32.6		
Uighur	227	33.9	158	29.2	69	53.5		
Education level								
Primary school and below	316	47.2	255	47.1	61	47.3	0.001	0.975
Junior high and above	354	52.8	286	52.9	68	52.7		
Current employment								
Farmer	302	45.1	240	44.4	62	48.1	2.81	0.245
Housewife	228	34.0	181	33.4	47	36.4		
Other	140	20.9	120	22.2	20	15.5		
Marital status								
Married/cohabiting	494	73.7	408	75.4	86	66.7	4.12	0.042
Single/divorced/widowed	176	26.3	133	24.6	43	33.3		
Annual income (RMB per capita)								
<5000	491	73.3	391	72.3	100	77.5	1.46	0.226
≥5000	179	26.7	150	27.7	29	22.5		
Local citizen								
Yes	580	86.6	472	87.2	108	83.7	1.11	0.291
No	90	13.4	69	12.8	21	16.3		
Residence registration								
Urban	177	26.4	135	25.0	42	32.6	3.10	0.078
Rural	493	73.6	406	75.0	87	67.4		
ART at the baseline (n = 659)								
Yes	626	95.0	510	95.9	116	91.3	4.42	0.036
No	33	5.0	22	4.1	11	8.7		
hrHPV infection								
Yes	157	23.4	121	22.4	36	27.9	1.78	0.182
No	513	76.6	420	77.6	93	72.1		

hrHPV, high-risk human papillomavirus; ART, antiretroviral treatment.

recruited, and 25 women were diagnosed with HSIL, excluding them from the study. Therefore, 670 women were enrolled in the study following the baseline survey. A total of 541 women (80.7%) participated in the follow-up survey after  $14.5 \pm 0.7$  months from the baseline.

Among the 670 women enrolled in the study, 33.9% (227) were Uighur, 30.7% (206) were Jingpo and Dai, and 45.1% (302) were farmers (Table 1). Among the 659 women who reported their ART status, 95.0% (626) were on ART at the baseline. The distribution of ethnic group, marital status, and ART status was significantly different between women who completed the follow-up survey (“follow-up women”) and women who did not (“lost-follow-up women”;  $p < 0.05$ ). The proportions of women who were Uighur, not on ART, and widowed/single/divorced among lost-follow-up women were higher than those among follow-up women. We found no statistically significant differences in the distribution of other sociodemographic characteristics and hrHPV infection at baseline between these two groups of women.

### 3.1. hrHPV infection

Among the 670 women in the baseline survey, 157 (23.4%) were infected with hrHPV. Among the 541 women at the follow-up survey, the hrHPV infection rate was 15.0%, lower than that at the baseline ( $\chi^2 = 12.046$ ,  $p < 0.001$ ). Among 121 follow-up women who were positive for hrHPV at the baseline survey, 46 women tested positive for hrHPV at the follow-up survey, for a hrHPV persistent infection rate of 38.0% (95% CI: 29.2%–46.8%). Among

420 women who were hrHPV-negative at the baseline survey, 35 were hrHPV-positive at the follow-up survey, making the new hrHPV infection rate 8.3% (95% CI: 5.7%–11.1%).

### 3.2. Factors associated with persistent hrHPV infection

In the univariate analyses, persistent hrHPV infection rates varied significantly by province, ethnic group, rural/urban status, and ART status during the follow-up period (Table 2). We entered the factors at  $p < 0.1$  in univariate analyses into the logistic regression model and found that provinces were statistically associated with persistent hrHPV infection; compared with women from Xinjiang, women from Yunnan and Guangxi were more likely to have persistent hrHPV infections (aOR = 3.18, 95% CI: 1.00–10.14,  $p = 0.05$ ; aOR = 6.38, 95% CI: 2.29–17.77,  $p < 0.001$ ).

### 3.3. New hrHPV infections and associated factors

Like persistent hrHPV infection rates, new hrHPV infection rates were significantly different in women from different provinces and ethnic groups, with additional significant differences based on occupation (Table 3). We entered the factors at  $p < 0.1$  in univariate analyses into the logistic regression model and found that compared with women from Yunnan, women from Xinjiang were more likely to become newly infected with hrHPV (aOR = 6.50, 95% CI: 2.40–17.60,  $p < 0.001$ ). Women who were migrant were more likely to be newly infected with hrHPV during the follow-up period (aOR = 4.48, 95% CI: 1.65–12.15,  $p = 0.003$ ). HBsAg-positive women

**Table 2**  
Persistent hrHPV infection among HIV-positive women from HIV high-burden areas in China, 2015–2016.

Characteristics	No. of Women		Persistent hrHPV infection		$\chi^2$	P-value
	n	%	n	%		
Provinces						
Xinjiang	47	38.8	8	17.0	<b>14.41</b>	<b>0.001</b>
Yunnan	28	23.2	14	50.0		
Guangxi	46	38.0	24	52.2		
Age (years old)					0.47	0.792
18–	22	18.2	9	40.9		
30–	77	63.6	30	39.0		
40–49	22	18.2	7	31.8		
Ethnic group					<b>13.27</b>	<b>0.001</b>
Han and others	61	50.4	28	45.9		
Jingpo and Dai	19	15.7	11	57.9		
Uighur	41	33.9	7	17.1		
Education level					0.35	0.514
Primary school and below	51	42.1	21	41.2		
Junior high and above	70	57.9	25	35.7		
Current employment					3.48	0.175
Farmer	37	30.6	17	45.9		
Housewife	44	36.4	12	27.3		
Other	40	33.0	17	42.5		
Marital status					0.01	0.944
Married/cohabiting	89	73.6	34	38.2		
Single/divorced/widowed	32	26.4	12	37.5		
Migrant population					0.04	0.850
No	107	88.4	41	38.3		
Yes	14	11.6	5	35.7		
Residence registration					<b>5.51</b>	<b>0.019</b>
Urban	42	34.7	10	23.8		
Rural	79	65.3	36	45.6		
Husband/sexual partner					0.16	0.689
Yes	102	84.3	38	37.3		
No	19	15.7	8	42.1		
Condoms use					1.53	0.217
Yes	65	53.7	28	43.1		
No	56	46.3	18	32.1		
ART at the baseline (n = 118)						
Yes	109	92.4	42	38.5		0.735 <sup>a</sup>
No	9	7.6	4	44.4		
ART during the follow-up (n = 118)						
Continuous	107	90.7	42	39.3		<b>&lt;0.001<sup>a</sup></b>
Initiated	6	5.1	2	33.3		
No/discontinues	5	4.2	2	40.0		
CD4 lymphocyte count at the baseline (/mm <sup>3</sup> )					0.08	0.779
<349	36	29.8	13	36.1		
350–	85	70.2	33	38.8		
CD4 lymphocyte count at the follow-up (/mm <sup>3</sup> )(n = 115)					0.81	0.367
<350	30	26.1	13	43.3		
≥350	85	73.9	29	34.1		
CD4 lymphocyte count change compared with baseline (n = 115)					2.44	0.119
Increased/no change	63	54.8	19	30.2		
Decreased	52	45.2	23	44.2		
HIV viral load at the baseline (copies/mL)					0.44	0.508
<1000	99	81.8	39	39.4		
≥1000	22	18.2	7	31.8		
HIV viral load at follow-up (copies/mL) (n = 101)					2.89	0.089
<1000	85	84.2	35	41.2		
≥1000	16	15.8	3	18.8		
Vaginitis					1.64	0.201
Yes	22	18.2	11	50.0		
No	99	81.8	35	35.4		
cervicitis					2.43	0.119
Yes	30	24.8	15	50.0		
No	91	75.2	31	34.1		
LBC at baseline					3.31	0.069
Normal/Ascus	97	80.2	23	23.7		
SIL	24	19.8	13	54.2		
Syphilis						
Yes	8	6.6	3	37.5		1.000 <sup>a</sup>
No	113	93.4	43	38.1		
HBsAg Positive						
Yes	11	9.1	5	45.5		0.746 <sup>a</sup>
No	110	90.9	41	37.3		
hrHPV infection						

**Table 2** (continued)

Characteristics	No. of Women		Persistent hrHPV infection		$\chi^2$	P-value
	n	%	n	%		
Multiple	33	27.3	12	36.4	0.05	0.819
Single	88	72.7	34	38.6		
hrHPV type					1.04	0.308
HPV16/18	27	22.3	8	29.6		
other 12 hrHPV	94	77.7	38	40.4		

hrHPV, high-risk human papillomavirus; ART, antiretroviral treatment; LBC, liquid-based cytology; SIL, squamous intraepithelial lesion; HBsAg, HBV surface antigen.

<sup>a</sup> Fisher exact test.

**Table 3**

New hrHPV infection among HIV-positive women from HIV high-burden areas in China, 2015–2016.

Characteristics	No. of women		new hrHPV infection		$\chi^2$	P-value
	n	%	n	%		
Province					<b>10.28</b>	<b>0.006</b>
Yunnan	181	43.1	8	4.4		
Guangxi	108	25.7	8	7.4		
Xinjiang	131	31.2	19	14.5		
Age (years old)					1.30	0.523
18-	67	16.0	7	10.4		
30-	242	57.6	17	7.0		
40-49	111	26.4	11	9.9		
Ethnic group					<b>9.34</b>	<b>0.009</b>
Han and others	158	37.6	12	7.6		
Jingpo and Dai	145	34.5	6	4.1		
Uighur	117	27.9	17	14.5		
Education level					2.00	0.158
Primary school and below	204	48.6	13	6.4		
Junior high and above	216	51.4	22	10.2		
Current employment					<b>6.95</b>	<b>0.031</b>
Farmer	203	48.3	11	5.4		
Housewife	137	32.6	12	8.8		
Other	80	19.1	12	15.0		
Marital status					2.19	0.139
Married/cohabiting	319	76.0	23	7.2		
Single/divorced/widowed	101	24.0	12	11.9		
Migrant population					3.20	0.074
No	365	86.9	27	7.4		
Yes	55	13.1	8	14.5		
Residence registration					1.91	0.167
Urban	93	22.1	11	11.8		
Rural	327	77.9	24	7.3		
ART (n = 414)					1.000 <sup>a</sup>	
Yes	401	96.9	33	8.2		
No	13	3.1	1	7.7		
ART during the follow-up (n = 414)					0.600 <sup>a</sup>	
Continous	396	95.7	33	8.3		
Initiated	8	1.9	1	12.5		
No/discontinous	10	2.4	0	0.0		
CD4 lymphocyte count at baseline (/mm <sup>3</sup> )					1.44	0.231
<350	80	19.0	4	5.0		
≥350	340	81.0	31	9.1		
CD4 lymphocyte count at follow-up (/mm <sup>3</sup> )(n = 398)					1.000 <sup>a</sup>	
<350	58	14.6	5	8.6		
≥350	340	85.4	28	8.2		
CD4 lymphocyte count change compared with baseline (n = 397)					0.24	0.623
Increased/no change	244	61.5	19	7.8		
Decreased	153	38.5	14	9.2		
HIV viral load at baseline (copies/mL) (n = 417)					0.757 <sup>a</sup>	
<1000	382	91.6	33	8.6		
≥1000	35	8.4	2	5.7		
HIV viral load at follow-up (copies/mL) (n = 374)					1.000 <sup>a</sup>	
-999	346	92.5	31	9.0		
1000-	28	7.5	2	7.1		
HIV viral load change compared with baseline (n = 374)					0.206 <sup>a</sup>	
Increased/no change	27	7.2	4	14.8		
Decreased	347	92.8	29	8.4		
husband/sexual partner						

(continued on next page)



Table 3 (continued)

Characteristics	No. of women		new hrHPV infection		$\chi^2$	P-value
	n	%	n	%		
Yes	359	85.5	31	8.6	2.54	0.111
No	61	14.5	4	6.6		
Condoms use (n = 358)					0.63	0.427
Yes	264	73.7	21	8.0		
No	94	26.3	10	10.6		
Vaginitis					0.02	0.890
Yes	100	23.8	8	8.0		
No	320	76.2	27	8.4		
cervicitis					0.58	0.446
Yes	87	20.7	9	10.3		
No	333	79.3	26	7.8		
Syphilis (n = 419)						0.101 <sup>a</sup>
Yes	22	5.3	4	18.2		
No	397	94.7	31	7.8		
HBsAg Positive (n = 418)						0.064 <sup>a</sup>
Yes	27	6.5	5	18.5		
No	391	93.5	30	7.7		

hrHPV, high-risk human papillomavirus; ART, antiretroviral treatment; HBsAg, HBV surface antigen.

<sup>a</sup> Fisher exact test.

had a higher risk of hrHPV infection compared with HBsAg-negative women (aOR = 3.48, 95% CI: 1.13–10.71,  $p = 0.029$ ).

#### 4. Discussion

Persistent and new hrHPV infection rates were studied in HIV-positive women from high HIV-burden areas in China. The persistent hrHPV infection rate was 38.0% (95% CI: 29.2%–46.8%) and the new hrHPV infection rate was 8.3% (95% CI: 5.7%–11.1%) at a 15-month follow-up. In a previous study conducted in Wuhan, China, the persistent HPV infection rates among HIV-positive and HIV-negative women were 47.5% (48/101) and 21.1% (8/38), respectively, after a 12-month follow-up.<sup>16</sup> We did not find statistically significant differences between the persistence rates in our study and the previous study ( $\chi^2 = 2.039$ ,  $p = 0.153$ ). The new hrHPV infection rate reported here is similar to results reported by Ahdieh et al. that hrHPV among HIV-infected women in the United States occurred at a rate of 8.05/100 person-years.<sup>11</sup> Konopnicki et al. also reported the hrHPV incidence was 13/100 person-years after 66 months among 651 African HIV-infected women in Belgium, which was higher than the rate (5/100 person-years) in HIV-negative women.<sup>20</sup> Consistent with these prior studies, our results indicate that HIV-positive women had an increased susceptibility to infection with hrHPV, and that HIV-positive women with hrHPV infection were at higher risk of developing persistent infection compared to HIV-negative women.

We found that the rates of persistent and new hrHPV infections among HIV-infected women in different research sites were different. This variation was likely associated with the variation in sociodemographic characteristics of HIV-infected women in different sites. It has been previously reported that the hrHPV infection rate was higher among Uighur women than among other ethnic groups.<sup>21</sup> Of the 36 baseline hrHPV-infected women lost to follow-up, 27 were from Xinjiang. The lost follow-up indicated poor adherence and less healthcare-seeking behavior of the participants. The low ART treatment rate of lost-follow-up women also increased the risk of persistent infections. A lower follow-up rate in Xinjiang than in the other two provinces may explain the low persistent hrHPV infection rate among HIV-infected women in Xinjiang reported here. We also found that the new hrHPV infection rate in HIV-infected women from Xinjiang was higher than in participants from other regions. Our findings indicate a need to address hrHPV infection in HIV-positive Uighur women in Xinjiang.

It was previously reported that a CD4 lymphocyte count  $\geq 500/\text{mm}^3$  for more than 18 months and an HIV viral load  $< 50$  copies/mL for more than 40 months were protective factors against persistent hrHPV infection.<sup>9</sup> However, our study did not find correlations between CD4 lymphocyte count level and either persistent or new hrHPV infection, which was consistent with the conclusions of previous studies.<sup>20</sup> Previous research reported that the rate of persistent HPV infection among HIV-positive women dropped from 67.7% at six months to 45.2% at 36 months, indicating that HPV infection persistence decreased over time.<sup>11</sup> Our study was followed up for only 15 months and therefore a prolonged observation to explore the relationship between persistent hrHPV infection and CD4 lymphocyte count levels may be necessary.

We found that women with hepatitis B infection had an increased risk of hrHPV infection compared with hepatitis B virus (HBV)-negative women. Siu et al. reported that women with high-grade cervical lesions were more likely to have HBV infection.<sup>22</sup> Liu et al. analyzed the data of 4,290 women in northern China who were co-infected with HPV, hepatitis B, HIV, or other infections, and found that HPV infection was closely linked to HBV infection.<sup>23</sup> Immunogenic responses can eliminate most infections with HPV or HBV, but HIV/AIDS weakens the body's ability to clear infections, and thus the probability of long-term infection increases. However, the interaction between HBV and HPV infections is not yet understood, and further research is still needed.

We found that the new hrHPV infection rate in HIV-infected women from the migrant population was higher than that in HIV-infected women from the local population. Increased attention should be paid to migrant HIV-positive women in the future. HPV infection relates to having multiple sexual partners, which might increase the risk of HPV exposure.<sup>24</sup> However, no association between HPV infection and sexual behavior was observed in this study. This is likely because sexual topics are sensitive; as sexual behavior was directly related to their HIV infection, some HIV-positive women did not respond to questions about high-risk sexual behaviors such as multiple sexual partners. Nevertheless, our findings indicate that health education targeted to HIV-positive women, especially the migrant population, is necessary to improve their awareness of the role of safe sexual behavior in preventing cervical cancer.

The study is subject to several limitations. First, most lost-follow-up women had not received ART, had low CD4<sup>+</sup> T lymphocyte counts and had high HIV viral load levels. Hence the rates of

persistent and new HPV infection reported here may be lower than the reality. Second, limited by the hrHPV test method, this study did not provide type-specific persistent hrHPV infection rates. Third, limited by the short follow-up period, our results could not provide evidence-based suggestions related to HPV screening frequency for HIV-positive women. Hence, long-term follow-up of HIV-infected women should be conducted to obtain more evidence on HIV infection-related factors and screening strategies.

## 5. Conclusion

This research suggests that HIV-positive women are at higher risk of infection or developing a persistent hrHPV infection than. The rates of persistent hrHPV infection and new infections varied significantly by region. The migrant population and HBV-infected women had a higher risk of new hrHPV infection than others.

## Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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