

RESEARCH ARTICLE

Knowledge of Human Papillomavirus (HPV) Infection, Cervical Cancer, and HPV Vaccine and its Correlates among Medical Students in Southwest China: a Multi-center Cross-sectional Survey

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Abstract

Background: Since cervical cancer can be prevented and controlled through human papillomavirus (HPV) vaccination, it is important to train health care providers and provide them with appropriate knowledge. This study aimed to understand the level of HPV related knowledge among medical students and correlates in Southwest China in order to address any potential gap in their knowledge base. **Methods:** We conducted a cross-sectional survey among medical students in six selected universities across Southwest China based on a pretested questionnaire regarding HPV infection, cervical cancer, and HPV vaccines. **Results:** We successfully surveyed 1,878 medical students, of whom 32.1% were males and 67.9% were females. Their mean age was 20.8 (standard deviation: 1.3) years. 91.8% of them were ethnic Han Chinese, and 43.8% were students in clinical medicine. While 76.5% had heard of HPV only 48.8% knew that the prevention of cervical cancer was possible through HPV vaccination. Only 42.9% of the male and 49.2% of the female students correctly answered over 10 out of 22 questions on HPV related knowledge. Female students appeared to know more about HPV and HPV vaccination (OR: 1.39; 95% CI: 1.11-1.75). In addition, the student knowledge improved with the grade ($p < 0.001$). University courses were the most selected source of knowledge about HPV vaccination (66.4%). 83.6% of males and 91.4% of females were willing to have more HPV related education by experts ($p < 0.001$). Only 10.1% of the students acknowledged that people had asked for their advice regarding HPV vaccination. **Conclusions:** Our survey indicates that medical students from Southwest China have poor knowledge of HPV and HPV vaccination, but are willing to receive more relevant information. Targeted education should be incorporated into school courses to inform these future health care providers and ensure success of programs for cervical cancer control and prevention.

Keywords: Cervical cancer - human papillomavirus vaccine - knowledge - medical students - China

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Introduction

Cervical cancer is the fourth most common cancer among women worldwide, with an estimated 528,000 new cases and 266,000 deaths in 2012 (Ferlay et al., 2013). Over 85% of cases occur in less developed regions, where cervical cancer accounts for almost 12% of female cancers and stands out as a major cause of cancer-related deaths. In China, more than 60,000 women are diagnosed with cervical cancer contributing to about 30,000 deaths every year (Ferlay et al., 2013).

Human papillomavirus (HPV) is one of the most prevalent sexually transmitted infections in the world today. About 70-80% of sexually active women acquire

infection with at least one type of HPV during their lifetime (Baseman et al., 2005; Weaver, 2006). The highest prevalence rates of HPV infections are found in young women aged below 25 years (Schiffman et al., 2005; Stanley, 2010). Most HPV infections are temporary and asymptomatic, and cleared by body's immune response without treatment. However, the persistent infections with some types of HPV may lead to HPV related diseases, such as genital warts and cervical cancer (Moscicki, 2005; Huh, 2009). In particular, high-risk HPV types are estimated to cause over 99% of cervical cancers worldwide (Munoz et al., 2003). For this reason, it is vitally important to control HPV infection for prevention of sexually transmitted diseases and cervical cancer.

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Since 2006, two prophylactic HPV vaccines have been commercially available in over 100 countries, including Gardasil quadrivalent vaccine and Cervarix bivalent vaccine. Both target at HPV-16 and HPV-18, which are responsible for about 70% of all cervical cancer cases (Munoz et al., 2003; Adams et al., 2007). Gardasil also targets at HPV-6 and HPV-11, which are estimated to cause at least 80% of all genital warts (Dunne et al., 2006; Chang et al., 2013). In mainland China, Phase III clinical trials of two vaccines and a newly developed HPV16/18 vaccine by Xiamen Innovax Biotech (Xiamen, China) are still ongoing (Wei et al., 2009; Xie et al., 2009). Since China lacks a national cervical cancer screening program, HPV vaccine will significantly impact the reduction of the burden of cervical cancer in the future (Lancet, 2009; Li et al., 2013).

As preventing cancer through prophylactic vaccine is a relatively new concept in China, the acceptance of HPV prophylactic vaccine will be expected to depend on factors such as knowledge about HPV infection, cervical cancer, and HPV vaccine and perspectives and attitudes toward the vaccination (Li et al., 2009; Zhao et al., 2012; Zhang et al., 2013). As future health professionals, medical students will play a crucial role in future vaccination programs. They will be inquired by the general population as one of the most important information resources and their knowledge and attitudes will affect their recommendations. In this regard, it is thus essential to know whether medical students have adequate knowledge so that they can provide reliable information and help the public make right decisions in the near future.

Currently, although HPV related knowledge has been evaluated among medical students in other countries (Pandey et al., 2012; Rashwan et al., 2012; Mccusker et al., 2013; Al-Darwish et al., 2014), little is known in mainland China. To address this gap, the present study was conducted to explore the level of knowledge about HPV infection, cervical cancer, and HPV vaccine among students of six medical colleges in Southwest China. Results from this study may be beneficial for developing effective health education programs among medical students regarding this important public health issue. In addition, since the investigation was conducted before the implementation of HPV vaccination program, findings can be used to further examine and compare with those from studies carried out after the program in the future.

Materials and Methods

Study Design and Data Collection

The survey was conducted in six medical universities or colleges including Sichuan University and Chengdu Medical College in Chengdu, Luzhou Medical University in Luzhou, North Sichuan Medical College in Nanchong, Chongqing Medical University in Chongqing, and Kunming Medical University in Kunming between May and September 2013. Since the six schools are located in different cities in Southwest China, participants were considered as proper representatives of medical students in this region. We planned to sample 200-400 medical students from different year cohorts and from both clinical

medicine and nonclinical majors at each university based on our contacts. At each school, we surveyed medical undergraduates from different majors before or after class. They answered the questionnaire independently at the beginning or the end of a class in their schools. A summary of research objectives was given in the cover page of each questionnaire, and indicated that the survey was answered on a voluntary basis and the confidentiality of the information was guaranteed. Consent was solicited from the students and they could decline the survey at their discretion. Queries of the questionnaire were responded appropriately by trained investigators during the survey, and doubts and concerns about HPV related knowledge were clarified after the survey. The study was approved by the Ethics Committee of Sichuan University Fourth Hospital/West China School of Public Health.

Study Instrument

An anonymously structured 58-item questionnaire was used for the survey. The questionnaire was designed based on several earlier studies in different populations in China (Li et al., 2009; Zhao et al., 2012; Zhang et al., 2013) and two studies among medical students (Pandey et al., 2012; Rashwan et al., 2012), and was piloted among medical students in the Chinese Academy of Medical Sciences Cancer Institute. Overall, the questionnaire consisted of three sections including basic information about participants, knowledge and perceptions of HPV infection, cervical cancer, HPV vaccine, and cervical

Table 1. Demographic Characteristics of Medical Students

Characteristics	Frequency	%
Gender		
Male	595	32.1
Female	1260	67.9
Age (years)		
17-19	260	14.2
20-22	1379	75.4
23-25	191	10.4
Ethnic groups		
Han	1697	91.8
Other	151	8.2
Grade		
1	243	12.9
2	679	36.2
3	695	37.0
4	204	10.9
5	57	3.0
Major		
Clinical	823	43.8
Nonclinical	1055	56.2
Clinical internship		
Yes	280	14.9
No	1598	85.1
Attitude towards premarital sexual behavior		
Positive	276	15.2
Negative	435	24.0
Neutral	927	51.0
Uncertain	178	9.8
Previous sexual behavior		
Yes	150	8.3
No	1661	91.7

Table 2. Knowledge of HPV Infection, Cervical Cancer and HPV Vaccine among Medical Students

	Total		Males		Females		P-value
	Frequency	%	Frequency	%	Frequency	%	
HPV infection related							
Have you ever heard of HPV?	1436	76.5	441	74.1	982	77.9	0.069
Is HPV sexually transmitted?	878	46.8	271	45.5	599	47.7	0.396
Is HPV infection common among women?	672	35.9	182	30.6	485	38.6	0.001
Can HPV infect a man?	1101	58.7	322	54.2	763	60.7	0.009
Can most HPV infections be asymptomatic?	792	42.3	211	35.6	569	45.3	<0.001
Can HPV be cleared by the immune system?	682	36.6	210	35.5	462	37.0	0.512
Is treatment necessary for HPV infection?	153	8.2	52	8.8	98	7.8	0.486
Cervical cancer related							
Can HPV cause cervical cancer?	1211	64.6	350	58.8	848	67.4	<0.001
Is persistent HPV infection the necessary cause of cervical cancer?	271	14.5	87	14.7	178	14.1	0.749
Can HPV cause genital warts?	925	49.4	269	45.3	644	51.4	0.015
Can some HPV genotypes cause both cervical cancer and genital warts?	455	24.3	141	23.9	306	24.4	0.828
Can cervical cancer be cured?	898	47.9	264	44.4	624	49.6	0.04
HPV vaccine related							
Can cervical cancer be prevented by HPV vaccine?	916	48.8	269	45.3	636	50.5	0.036
How much protection can HPV vaccine provide for cervical cancer?	437	23.4	122	20.7	308	24.5	0.07
Is there any HPV vaccine available for cervical cancer/genital warts in the world?	544	29.0	147	24.7	390	31.0	0.006
Is there any HPV vaccine available in China?	414	22.2	123	20.9	287	22.9	0.335
Can HPV vaccine be given to a sexually active woman?	1099	58.8	309	52.0	780	62.3	<0.001
Can HPV vaccine be given to a woman already having HPV infection?	822	44.0	252	42.6	563	44.9	0.37
Do girls/women need to be screened for HPV before getting vaccinated?	142	7.6	56	9.5	82	6.6	0.027
How many doses of HPV vaccine are required for protection?	396	21.2	125	21.2	267	21.2	0.988
Is it safe to have multiple sexual partners after full course of HPV vaccine?	915	48.9	269	45.5	638	50.7	0.038
Do women who have already been vaccinated require cervical cancer screening?	1364	72.9	376	63.6	976	77.6	<0.001

cancer screening, and sexual behavior and attitude. The current study analyzed demographic characteristics of students and 22 knowledge questions, including seven on HPV infection, five on cervical cancer, and ten on HPV vaccine, while other questions were assessed in separate articles. In regard to most knowledge questions, respondents could choose only one of the three options, "Yes", "No", or "I do not know". Only for the question about information sources, they could choose more than one option.

Data Analysis

All completed questionnaires were sent to the West China School of Public Health. Data were entered in a database developed by EpiData (EpiData Association, Odense, Denmark). After having been checked for accuracy, they were analyzed using IBM SPSS 19.0 (Armonk, New York, USA). When responses to some questions were missing or invalid, they were excluded from statistical analysis of these questions. For the questions on HPV related knowledge, each correct answer was counted as one point, and each incorrect or "I do not know" answer received zero points. If the answer was missing, zero points were also awarded for the question. Individual scores were summed up as a total knowledge score ranging between 0-22, and a higher score indicates a higher level of knowledge. 0-9 and 10-22

were regarded as two dichotomized low and high levels. Continuous variables were presented as mean \pm standard deviation (SD), and categorical ones were expressed as frequencies and percentages. The level of HPV related knowledge among female students was compared with that among males, given that cervical cancer is primarily a female health problem. The differences in the answer distribution were analyzed using Pearson Chi-square test. Logistic regression analysis was used to explore independent determinants of HPV related knowledge, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Statistical significance was assessed by two-tailed tests with α level of 0.05.

Results

Demographic Characteristics

We handed out a total of 2150 questionnaires, and about 2000 were completed by students (response rate: 93.0%). After excluding those with contradictory or inconsistent information, we finally had 1878 questionnaires for analysis. Demographic characteristics of the participants are presented in Table 1. Of the surveyed students, 595 (32.1%) were males, and 1260 (67.9%) were females. 1697 (91.8%) were ethnic Han Chinese. The mean age was 20.8 (standard deviation: 1.3) years. In particular, 1379 (75.4%) were 20-22 years old. 679 (36.2%) and

695 (37.0%) were second-year or third-year students, 823 (43.8%) were students in clinical medicine, and 1598 (85.1%) did not have clinical internship. Regarding the attitude to premarital sexual behavior, 927 (51.0%) students were neutral, and 435 (24.0%) were negative. In reality, 150 (8.3%) had been sexually active.

Knowledge of HPV Infection

Knowledge of HPV infection among medical students is presented in Table 2. 1436 (76.5%) students had heard of HPV: 441 (74.1%) males versus 982 (77.9%) females. 878 (46.8%) were aware of the sexually transmitted nature of HPV infection. 182 (30.6%) and 485 (38.6%) male and female students agreed that HPV infection was common among woman ($p=0.001$). Regarding whether HPV could infect a man, 1101 (58.7%) selected the right answer (54.2% in males versus 60.7% in females, $p=0.009$). In addition, 211 (35.6%) and 569 (45.3%) males and females, respectively, knew that most HPV infections were asymptomatic. 682 (36.6%) agreed that HPV could be cleared by the immune system, and only 52 (8.8%) males and 98 (7.8%) females believed that treatment was not necessary for HPV infection.

Knowledge of Cervical Cancer

Knowledge of cervical cancer among medical students is presented in Table 2. 350 (58.8%) males and 848 (67.4%) females knew that HPV could cause cervical cancer ($p<0.001$), but most (85.5%) were not sure whether persistent HPV infection was a necessary cause of cervical cancer. 925 (49.4%) agreed with that HPV could cause genital warts, but only 141 (23.9%) males and 306 (24.4%) females were aware that some HPV genotypes could cause both cervical cancer and genital warts. 898 (47.9%) students, including 264 (44.4%) males and 624 (49.6%) females knew that cervical precursor lesions and early stage cancer could be cured ($p=0.04$).

Knowledge of HPV Vaccine

Knowledge of HPV vaccine among medical students is presented in Table 2. Overall 916 (48.8%) students were aware about the preventable effect of HPV vaccine on cervical cancer, and the awareness was more evident in the female students ($p=0.036$). Only 437 (23.4%) reported that it could protect against approximately 70% of cervical cancers. Most did not know whether the vaccine was available in the world (71.0%) or specifically in China (77.8%). 309 (52.0%) males and 780 (62.3%) females thought that HPV vaccine could be given to a sexually active woman ($p<0.001$), and 252 (42.6%) males and 563 (44.9%) females believed a woman with HPV infection could not receive the vaccine. 142 (7.6%) students thought that girls/women did not need to be screened for HPV before receiving vaccination. In regard to the vaccine schedule, 396 (21.2%) knew that a standard HPV vaccine scheme required three doses. 915 (48.9%) respondents thought that it was not safe to have multiple sexual partners after a full course of the vaccine. 376 (63.6%) males and 976 (77.6%) females agreed that a woman should receive cervical cancer screening even though she had already been vaccinated ($p<0.001$).

Scores of HPV Related Knowledge

Table 3 summarizes HPV related knowledge scores among medical students. 435 (23.2%) participants achieved 5-7 points in the HPV infection knowledge (at a 7-point scale), and 293 (15.6%) had 4-5 points in the cervical cancer knowledge (at a 5-point scale). Only 46 (7.7%) males and 130 (10.3%) females had 7-10 points in the HPV vaccine knowledge (at a 10-point scale). Overall, the mean knowledge score was 8.8 (SD=4.4). In addition, a total of 886 (47.2%) students, including 255 (42.9%) males and 620 (49.2%) females, obtained 10-22 points. We noticed statistically significant difference between males and females in the sub-scores and overall score in HPV related knowledge ($p<0.05$).

Table 3. Summary of Knowledge Scores among Medical Students

	Total (N=1878)		Males (N=595)		Females (N=1260)		P-value
	Frequency	%	Frequency	%	Frequency	%	
Score of HPV infection knowledge							
0-2	711	37.9	252	42.4	448	35.6	0.016
3-4	732	38.9	211	35.4	515	40.9	
5-7	435	23.2	132	22.2	297	23.5	
Score of cervical cancer knowledge							
0-1	727	38.7	257	43.2	461	36.6	0.022
2-3	858	45.7	255	42.9	593	47.1	
4-5	293	15.6	83	13.9	206	16.3	
Score of HPV vaccine knowledge							
0-3	786	41.9	285	47.9	488	38.7	<0.001
4-6	916	48.7	264	44.4	642	51.0	
7-10	176	9.4	46	7.7	130	10.3	
Total knowledge score							
0-9	992	52.8	340	57.1	640	50.8	0.011
10-22	886	47.2	255	42.9	620	49.2	

Table 4. Logistic Regression Analysis of Knowledge Scores among Medical Students

	Number of subjects in analysis (N=1754)		Knowledge score ≥ 10		P-value
	N	(%)	OR	(95% CI)	
Gender					
Male	562	241 (42.9)	1		0.004
Female	1192	581 (48.7)	1.39	(1.11-1.75)	
Age (years)					
17-19	252	70 (27.8)	1		0.077
20-22	1318	654 (49.6)	1.33	(0.95-1.87)	
23-25	184	98 (53.3)	0.98	(0.59-1.63)	
Ethnic groups					
Han	1610	767 (47.6)	1		0.184
Other	144	55 (38.2)	0.78	(0.54-1.13)	
Grade					
1	211	55 (26.1)	1		<0.001
2	632	202 (32.0)	1.23	(0.85-1.77)	
3	665	422 (63.5)	4.04	(2.71-6.02)	
4	191	109 (57.1)	5.40	(2.86-10.20)	
5	55	34 (61.8)	7.47	(3.21-17.40)	
Major					
Nonclinical	998	401 (40.2)	1		0.147
Clinical	756	421 (55.7)	1.19	(0.94-1.50)	
Clinical internship					
No	1491	812 (54.5)	1		0.089
Yes	263	120 (45.6)	0.64	(0.39-1.07)	
Attitude towards premarital sexual behavior					
Positive	263	111 (42.4)	1		0.018
Negative	425	464 (51.5)	0.77	(0.54-1.09)	
Neutral	901	184 (43.3)	1.11	(0.82-1.51)	
Uncertain	165	63 (38.2)	0.79	(0.52-1.21)	

Table 5. Information Sources and Education of HPV Related Knowledge among Medical Students

	Total		Males		Females		P-value
	Frequency	%	Frequency	%	Frequency	%	
What are your sources of knowledge about HPV vaccination?							
School courses	1237	66.4	368	62.5	856	68.4	0.012
Hospital	494	26.5	177	30.1	311	24.8	0.018
Family/friends	147	7.9	48	8.1	98	7.8	0.812
Internet/television	582	31.2	187	31.7	383	30.6	0.616
Publications	330	17.7	108	18.3	217	17.3	0.598
Others	191	10.2	71	12.1	120	9.6	0.105
Has anybody (family/friends) sought your opinion regarding HPV vaccination?							<0.001
Yes	187	10.1	89	15.2	96	7.7	
No	1671	89.9	496	84.8	1154	92.3	
Would you like to have more HPV related education by experts?							<0.001
Yes	1655	88.9	489	83.6	1147	91.4	
No	207	11.1	96	16.4	108	8.6	

Factors Associated with HPV Related Knowledge Level

Univariable analysis using Chi-square test showed that gender ($p=0.022$), age ($p<0.001$), ethnic groups ($p=0.030$), grade ($p<0.001$), major ($p<0.001$), clinical internship ($p=0.008$), and attitude towards premarital sexual behavior ($p=0.001$) were statistically significantly associated with HPV related knowledge level ($p<0.05$). However, the association with previous sexual behavior was not considered statistically significant ($p=0.416$). The seven significant variables were further incorporated in the multivariable logistic regression analysis (Table 4). We found that female students tended to be more knowledgeable compared to males (OR: 1.39; 95% CI: 1.11-1.75). Students at a higher grade in general also had a higher knowledge level ($p<0.001$). There was a statistically significant association between attitude towards premarital sexual behavior and HPV related knowledge ($p=0.018$). However, there was no independent significant association between age and knowledge level ($p=0.077$). In addition, the students majoring in clinical medicine or had clinical internship experience did not show more knowledge about this important public issue ($p>0.05$).

Information Sources of HPV Related Knowledge

Information sources and education of HPV related knowledge are presented in Table 5. School courses (66.4%) were the major source of knowledge about HPV vaccination, followed by the Internet/television (31.2%), hospital (26.5%), publications (17.7%; including books, newspapers, and magazines), and family/friends (7.9%). In addition, 89 (15.2%) males and 96 (7.7%) females had been inquired by family or friends about HPV vaccination ($p<0.001$). 489 (83.6%) males and 1147 (91.4%) females were willing to have more HPV related education by experts ($p<0.001$).

Discussion

Although prophylactic HPV vaccines have been introduced in over 100 countries or regions so far, they are still commercially unavailable in China. Anticipating their availability in upcoming years, several studies have been conducted in general Chinese women, health care providers, and parents of young adolescents to explore knowledge, acceptability, and barriers to future HPV

vaccination programs (Li et al., 2009; Zhao et al., 2012; Zhang et al., 2013). These studies consistently showed that the knowledge of HPV infection, cervical cancer, and HPV vaccine was lacking, and many regarded doctors' recommendations as an important facilitator for vaccination. In addition, it was demonstrated that clinicians with more HPV related knowledge were more likely to recommend HPV vaccine (Hopkins et al., 2009). In this regard, it is essential to understand whether medical students as future health professionals are well-informed about HPV infection, cervical cancer, and HPV vaccine. In our study, only 47.2% of the students could correctly answer over 10 out of 22 questions on HPV related knowledge. In addition, the level of knowledge was associated with gender and year of study.

Despite the fact that most students had heard of HPV in our study, there was lack of detailed knowledge of HPV infection and cervical cancer. Many of them did not possess basic recognition of facts such as that HPV is sexually transmitted, that the infection is common, asymptomatic and can cause cervical cancer and genital warts, which is consistent with other similar studies (Medeiros et al., 2010; Wong et al., 2010; Bendik et al., 2011; Makwe et al., 2012). Poor understanding reflects lack of relevant education, and may compromise awareness of personal risk of HPV infection and the severity of its consequences. When HPV related information is delivered to students, we should focus on increasing not only the recognition of the terms but also detailed knowledge about its prevalence, characteristics and consequences. Since students' education about HPV in China has trailed behind other sexually transmitted infections (STIs) such as HIV, HPV related knowledge can be incorporated into other STI education at schools, and previous STI campaigns may provide good role models for improving their understanding on this issue.

The study also identified some gaps and misconceptions about HPV vaccine among medical students. Since safety and efficacy were the major concerns for people who did not want to get vaccinated (Wong et al., 2010; Zhao et al., 2012; Zhang et al., 2013), medical students should have comprehensive understanding of benefits and risks of HPV vaccine so that they can provide adequate and evidenced-based information to reassure the public in future clinical practice. They should also be well-informed

about the catch up program and target population in order to recommend HPV vaccine to appropriate population who may benefit from the vaccination. The prophylactic nature, safety and efficacy of HPV vaccine, the catch up vaccination program and target population should be explicitly stated. Increased education of medical students may improve the general knowledge of HPV vaccine and raise society's acceptance of the vaccination.

Several factors were associated with the level of HPV related knowledge. Female students had better knowledge than males, and the students in a more senior year increasingly had better knowledge. As cervical cancer is a female cancer, females may pay more attention on this issue. But it is also important to enhance males' HPV related education since they play an indispensable role in the spread of the virus. Students in a more senior year of study may obtain more comprehensive information from medical teaching, which is consistent to the recognition that school courses were the most selected source of HPV vaccination. Thus, tailored and targeted education programs should be designed incorporating such impacts from gender and medical teaching. Moreover, over 85% of the students were willing to receive more education by experts. An education program showed increased HPV knowledge from 45% to 79% among students at three months after a brief educational intervention (Lambert, 2001). Well-designed educational interventions should be combined with academic curriculum to raise students' awareness of HPV related diseases and prevention (Genc et al., 2013).

There are certain limitations in the study. Firstly, all data were self-reported and response rates to some questions were not very high. Since 83.0% (1660) of survey students completed all questions analyzed in the study, the results based on current analysis may be still reliable. Secondly, because of the cross-sectional nature of this study, findings should be interpreted with caution to avoid the determination of causal relationships. Thirdly, results in our study may not be readily extrapolated to other regions since the survey was carried out only at certain medical schools in Southwest China. There may be regional variation in the level of knowledge. National studies are needed to understand current HPV related education in medical schools.

In conclusion, our study has been the first study on detailed knowledge of HPV infection, cervical cancer and HPV vaccine among medical students in China so far. Most students were aware of HPV, but had limited knowledge of HPV related diseases and HPV vaccine. Since health care providers will play a pivotal role in spreading information and education in future vaccination programs, well-designed and targeted education programs ought to be combined with medical courses to inform medical students.

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