



RESEARCH PAPER



Effect of an educational intervention on human papillomavirus (HPV) knowledge and attitudes towards HPV vaccines among healthcare workers (HCWs) in Western China

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ABSTRACT

Background: Healthcare workers (HCWs) play a key role in the recommendation of HPV vaccination. Our study aimed to understand to what extent a structured health intervention could change the knowledge and attitudes toward HPV and its vaccines among HCWs in Western China.

Methods: This was a multi-center, questionnaire-based interventional study conducted across 12 cities of seven provinces in Western China, from November 2018 to July 2019. Participants were recruited from local health systems by e-invitation. Questionnaires were administered to participants before and after the intervention.

Results: A total of 1448 HCWs attended the educational lectures and 1354 participants completed both pre- and post-study questionnaires. In general, HCWs had satisfactory baseline knowledge regarding HPV and its vaccines compared with other populations, and a significantly higher knowledge level was observed after the intervention. However, some more specific knowledge on the vaccination procedures, other HPV-related diseases and whether HPV testing was required before vaccination was relatively poor. Following the educational intervention, the correct responses to the above questions increased ($P < .001$). However, it was still lower compared with answers to other questions. Change was also detected regarding HCWs' willingness to recommend HPV vaccines to the appropriate population ($P < .001$).

Conclusion: Educational intervention on HPV and its vaccines is effective in improving HCWs' knowledge levels and willingness to recommend HPV vaccines. Future educational interventions should focus more on knowledge regarding HPV-related diseases and HPV vaccination. Education campaigns targeting rural HCWs are urgently needed in the near future.

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Introduction

With an estimated 570,000 cases and 311,000 deaths in 2018 worldwide, cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer deaths in women.¹ Cervical cancer is the second most common cancer among females in developing countries such as China, where the incidence of the disease increased from 6.78 per 100,000 in 2008 to 10.31 per 100,000 in 2013.^{1,2} The increasing trend was obvious especially in young women, which increased the overall disease burden in China, especially in central and western China, the less developed areas of the country.^{3,4} Persistent infection with high-risk human papillomavirus (hr-HPV) has been established as the primary cause for cervical cancer and vaccinating girls against HPV before they become sexually active is the key for cervical cancer prevention in the future.^{5,6}

After being licensed by the US Food and Drug Administration in 2006, prophylactic HPV vaccines have been proven to result in safe, effective, and long-lasting immunization against infection.^{7–9} The introduction of prophylactic vaccines against high-risk HPV represents the primary prevention in reducing disease burden. To date, over 100 countries in the world have approved one or more HPV vaccines and over 80 countries have established national HPV vaccination programs.¹⁰ The benefits of HPV vaccine uptake have been shown by reductions in high-risk HPV infection and the incidence of high-grade cervical abnormalities^{11,12} as well as external genital lesions related to HPV 6/11/16/18 in males.¹³ China is far behind from many other countries in the world in terms of introduction and access to HPV vaccines due to the lack of knowledge on HPV, high cost, shortage in HPV vaccine supply, and negative events attributed to vaccination.¹⁴ The bivalent vaccines for HPV 16 and 18 (Cervarix[®], GlaxoSmithKline

Biologicals, Rixensart, Belgium) and the quadrivalent vaccines for HPV 6, 11, 16, and 18 (Gardasil®, Merck and Co., Whitehouse Station, NJ), have been licensed by the China Food and Drug Administration in July 2016 and May 2017, respectively, while the nine-valent vaccine has also been conditionally approved by the Chinese National Medical Products Administration through a fast track in April 2018.^{15–17} Chinese females aged 9–45 years old were recommended for the bivalent vaccines, while females aged 20–45 years old for quadrivalent vaccines and 16–26 years old for nine-valent vaccines.¹⁸ However, the vaccination uptake was relatively low in mainland China.¹⁹ In addition, HPV vaccination is only recommended for females and has not been included into the EPI (Expanded program on immunization), which poses a great challenge to promote HPV vaccination in mainland. The successful use and promotion of HPV vaccines depends on many factors, among all, HCWs play a key role in the recommendation of HPV vaccination.^{20–25} Therefore, it is of vital importance to ensure that HCWs are well informed so that they are able to provide complete and accurate information to the public, which could in turn promote HPV vaccination in China. Studies conducted abroad have demonstrated that educational intervention could improve HPV-related knowledge and change attitudes toward HPV vaccines among HCWs.^{21,22} However, few studies have explored the effectiveness of HPV-related educational interventions for HCWs in China, especially Western China.

Therefore, the objective of this study was to understand the knowledge and attitudes toward HPV and its vaccines, and to assess the short-term effectiveness of a brief-structured presentation on HPV and HPV vaccines among HCWs in Western China. If this intervention proves to be effective in raising the knowledge of HPV and its vaccines among healthcare workers, the promotion of HPV vaccines in China could be promising in the future.

Materials and methods

Study design and participants

This was a multi-center, questionnaire-based interventional study across seven provinces in Western China, from November 2018 to July 2019. Convenience sampling was used to invite 12 collaborative hospitals from 12 cities/counties of seven provinces, including Chongqing Cancer Hospital, Chengdu Maternal and Children's Hospital, Meishan Maternal and Children's Hospital, Neijiang Center of Disease Control, Deyang Maternal and Children's hospital, Kunming Maternal and Children's Hospital, Dali Maternal and Children's Hospital, Yuxi Chinese Medicine Hospital, Zunyi Medical University Hospital, Northwestern Maternal and Children's Hospital, Xinjiang Medical University and Gansu Cancer Hospital. Participants were recruited by sending e-invitation. Firstly, a paper conference invitation and an e-invitation were sent to the collaborative hospitals, and then the e-invitation was forwarded to subordinate units/hospitals, such as community hospitals, maternity, and child care centers. Later, the e-invitation would be sent to healthcare workers so that they could understand the purpose of the study. If they

were willing to attend free health education regarding cervical cancer prevention, they were asked to fill in registration information in the e-invitation.

Educational intervention

The educational intervention mainly consisted of three parts, including a one and half hour PowerPoint (PPT) presentation given by three experts, followed by a Q&A section and scenario simulations. Topics addressed included advances in HPV vaccine research and the etiological prevention of cervical cancer in China, current cervical cancer disease burden and HPV vaccination in local areas, the application of HPV vaccine and cervical cancer screening in clinical settings.

Research instrument

Two self-administered questionnaires were developed to explore the knowledge of healthcare workers on HPV and HPV vaccines before and after the educational session, and to investigate the effectiveness of the intervention in improving knowledge levels. A unique study ID was assigned to each participant and was printed in both the pre- and post-intervention questionnaires before delivering them. The participants were asked to finish the baseline questionnaire before lectures began and then research staff collected the completed questionnaires on-site. At the end of the lecture, post-intervention questionnaires were given to the attendees. After the Q&A section, the participants were asked to complete these post-intervention questionnaires. Both pre- and post-intervention questionnaires consisted of 15 questions on HPV-related diseases, including the epidemiology of HPV and cervical cancer, as well as HPV vaccines, and detailed questions are shown in Table 2. A score was calculated by adding the scores to the correct answers. Correct statements were designated to receive 1 point while incorrect answers were given 0. The total knowledge score ranged from 0 to 15. Sociodemographic information including age, gender, region, current employment, level of education, and working years was collected in the pre-intervention questionnaires. One additional question regarding the choice of access to HPV-related knowledge in the future was included in the post-intervention questionnaires.

Data collection and quality control

Two graduate students were assigned to double-enter data from the paper questionnaires to a computer-based database (EpiData 3.1) independently after training. All completed double-entry databases were validated by running EpiData. Any inconsistency found between the two databases was adjusted based on the original paper-based questionnaires until the databases agreed. As a final check, one database was chosen and underwent a final consistency check. Logic errors (e.g. a participant who responded as being willing to recommend HPV vaccines to the public chose the reasons, they were unwilling to recommend HPV vaccines) were again double-checked and revised. After the consistency and logic checks, the database was ready for final analysis.

Ethical considerations

The study was approved by the Ethical Review Committee (ERC) of the West China School of Public Health, Sichuan University. Written informed consent was obtained from each participant prior to our study.

Statistical analyses

Statistical analysis was performed utilizing SPSS (Statistical Package for the Social Sciences) version 20.0. Frequency and percentages were used to describe the characteristics of participants, knowledges on HPV and its vaccines, as well as attitudes toward HPV vaccination. Chi-squared test or Fisher's exact test was used to analyze the differences before and after the intervention. Comparison of knowledge scores between groups was analyzed with Kruskal–Wallis test and Mann–Whitney U test, as the data were non-normally distributed. Statistical significance was assessed by two-tailed tests with a level of 0.05.

Results

Participants profile

A total of 1448 HCWs attended the educational lectures and responded to the survey. Of these, 1354 completed both the pre-intervention questionnaire and the post-intervention questionnaire (93.5%). The mean age of the participants was 37.1 years (SD = 9.7 years), with the youngest being 19 years and the oldest being 63 years. Most participants (82.5%, 1187/1448) were female and the majority (80%, 1159/1448) were from urban areas. 408(28.2%) participants were working at community hospitals, 328 (22.7%) at maternity and child care centers, and 328(22.7%) at general hospitals. Nearly half of the participants (41.2%, 595/1448) worked at gynecology departments, 28.5% (413/1448) worked at planning immunology departments and 21.6% (314/1448) worked at other departments. When the level of education was considered, more than half of the healthcare workers had a bachelor's degree (52.3%, 758/1448), followed by an associate's degree (37.9%, 549/1448) and master's degree (6.0%, 87/1448). More than half of participants (54.6%) had been working for more than 11 years (Table 1).

Effects of education on HCWs' knowledge and attitudes

Change in knowledge about HPV-related diseases

There were significant statistical differences between pre- and post-intervention questionnaires for the question regarding the connection between HPV and cervical cancer (92.2% vs. 95.4%, $P < .001$) and for the question that HPV16 and 18 were the two high-risk types that caused cervical cancer (87.7% vs. 95.2%, $P < .001$). When asked about the connection between HPV and other diseases, 41.6% and 60.6% of participants knew that HPV was related to anal cancer, genital warts, penile cancer, and oropharyngeal cancer correctly in the pre- and post-intervention tests, respectively ($P < .001$). When questioned about prevention, in the pre-intervention questionnaire, 81.9% of the participants thought that HPV vaccination was the most

Table 1. Demographic characteristics of the HCWs at baseline.

Variables	Number (n)	Percentage (%)
Age (years)		
<30	351	24.2
30–39	390	26.9
40–49	372	25.7
≥50	175	12.1
Missing	160	11.0
Gender		
Male	123	8.5
Female	1187	82.5
Missing	138	9.5
Region		
Urban	1159	80.0
Rural	251	17.3
Other	28	1.9
Missing	10	0.7
Current Employment		
Community hospital	408	28.2
Maternity and Child Care Center	328	22.7
The Centers for Disease Control	140	9.7
General hospital	328	22.7
Other	239	16.5
Missing	5	0.3
Departments		
Department of gynecology	595	41.2
Department of pediatrics	71	4.9
Department of planning immunology	413	28.5
Department of Internal Medicine	50	3.5
Other	314	21.6
Missing	5	0.3
Level of education		
Associate	549	37.9
Bachelor	758	52.3
Master	87	6.0
Doctor	7	0.5
Other	42	2.9
Missing	5	0.3
Years of Working		
0–5 years	368	25.4
6–10 years	260	18.0
11–15 years	212	14.6
16–20 years	219	15.1
≥21 years	386	26.7
Missing	3	0.2

effective way to prevent HPV, compared with 91.9% in the post-questionnaire ($P < .001$) (Table 2).

Change in knowledge about the epidemiology of HPV and cervical cancer

When participants were asked about the prevalence of HPV infection, the largest increase could be observed in the answer “80% of women would be infected by HPV in their lifetime,” from 62.9% to 82.9% ($P < .001$). When asked about their awareness of the age distribution of high-risk HPV infection in Chinese women, the proportion of ‘two peaks’ answer also increased significantly after the intervention (72.7% vs. 82.1%, $P < .001$). When questioned which HPV caused 70% of cervical cancer worldwide, the proportion of HCWs with correct responses increased substantially (72.9% vs. 76.4%, $P < .05$) (Table 2).

Change in awareness and attitudes about HPV vaccine

At baseline, the question most correctly answered was “Cervical cancer screening was still required after HPV vaccination,” with 92.4% of the participants providing the correct

Table 2. Changes in knowledge and attitudes toward HPV and its vaccines.

Item	Pre-intervention (N = 1448)		Post-intervention (N = 1354)		Change percentage point difference	P-value
	Number (n)	Percent (%)	Number (n)	Percent (%)		
HPV-Related Diseases						
1.What's the necessary cause of cervical cancer? (HPV infection)	1335	92.2	1292	95.4	↑ 3.2	<0.001 ^a
2.What are the most important two subtypes of high-risk HPV? (HPV 16/18)	1270	87.7	1289	95.2	↑ 7.5	<0.001 ^a
3.What other diseases HPV can cause except for cervical cancer? (Anal cancer/Genital warts/carcinoma of penis/Oropharyngeal cancer)	603	41.6	821	60.6	↑ 19.0	<0.001 ^a
4.What's the most effective prevention from HPV infection? (HPV vaccine)	1186	81.9	1245	91.9	↑ 10.0	<0.001 ^a
Epidemiology of HPV and cervical cancer						
5.What is the possibility that women would be infected by HPV in their lifetime? (Around 80%)	911	62.9	1123	82.9	↑ 20.0	<0.001 ^a
6.What's the age distribution of high-risk HPV among Chinese women? (bimodal distribution)	1053	72.7	1112	82.1	↑ 9.4	<0.001 ^a
7. What are the most important HPV subtypes that cause about 70% of cervical cancer worldwide? (HPV 16/18)	1055	72.9	1034	76.4	↑ 3.5	0.033 ^a
HPV vaccines						
8.Is HPV vaccine safe? (Yes)	1278	88.3	1316	97.2	↑ 8.9	<0.001 ^a
9.Is HPV vaccine effective? (Yes)	1181	81.6	1268	93.6	↑ 12.0	<0.001 ^a
10.What are the possible side effects after vaccination? (Local redness, swelling, heat and pain; fever, headache, vertigo)	1047	72.3	1100	81.2	↑ 8.9	<0.001 ^a
11.Which conditions are not recommended to get HPV vaccination? (during pregnancy and lactation)	778	53.7	886	65.4	↑ 11.7	<0.001 ^a
12.Is HPV test needed before HPV vaccination? (No)	642	44.3	781	57.7	↑ 13.4	<0.001 ^a
13.Is HPV vaccine still recommended even with a positive HPV test or after treatment? (Yes)	1126	77.8	1247	92.1	↑ 14.3	<0.001 ^a
14.Is screening recommended after HPV vaccination? (Yes)	1338	92.4	1309	96.7	↑ 4.3	<0.001 ^a
15.Which HPV vaccines had been approved in Mainland China and what's the vaccination procedures of each vaccine? (2v/4 v/9vHPV vaccines; 0,1,6 months for 2vHPV vaccine and 0,2,6 months for 4 v/9vHPV vaccines)	527	36.4	689	50.9	↑ 14.5	<0.001 ^a
Attitudes						
16.Are you willing to recommend HPV vaccine to the public? (Yes)	1041	71.9	1115	82.3	↑ 10.4	<0.001 ^a

^aχ² test

answer, while the lowest number of participants knew “2 v/4 v/9 vHPV vaccines had been approved in Mainland China and the vaccination procedures for each vaccine” both before and after the educational intervention (36.4%, 50.9%). 88.3% and 81.6% of the participants believed that HPV vaccine was safe and effective before intervention, and the proportion increased significantly to 97.2% and 93.6% following the educational intervention ($P < .001$). When the side effects of HPV vaccination were mentioned, 73.2% responded correctly before intervention compared with 81.2% after the intervention ($P < .001$). Only 53.7% knew that “HPV vaccination was not recommended during pregnancy and lactation” pre-intervention compared to 65.4% post-intervention ($P < .001$). Less than half (44.3%) of the participants provided the correct answer that “HPV testing was not required before vaccination” before the intervention and 57.7% chose the right answer after the intervention ($P < .001$). When questioned about their intention to recommend HPV vaccination to public, a significant increase (71.9% vs. 82.3%, $P < .001$) in participants' willingness was observed (Table 2).

HCWs' knowledge scores in relation to demographic characteristics pre-and post-intervention

We performed an analysis to establish a relationship between knowledge scores and demographic characteristics (Table 3). The median (P25, P75) knowledge score after

intervention was 12.0 (11.0–14.0), a significant increase from 11.0 (9.0–13.0) pre-intervention ($P < .001$). At baseline, those who were older than 30 years old, were female, worked at maternity and child care centers, worked for departments of gynecology and planning immunology, got a better education and had worked for more than 5 years were more knowledgeable ($P < .001$). After the intervention, the significant relationships between knowledge scores and regions and education levels emerged ($P < .05$). It also showed that the improvement of knowledge scores was significantly higher among participants who were less than 30 years old, were hired by other employers and worked for an internal medicine department.

Changes in reasons for being unwilling to recommend HPV vaccines

Table 4 presents the reasons for being unwilling to recommend HPV vaccination before and after the intervention. Before the intervention, insufficient knowledge of HPV and HPV vaccines (67.9%, 265/390) was the leading reason for being unwilling to recommend HPV vaccination, followed by concerns about vaccine safety and efficacy (54.4%, 212/390) and the high cost of HPV vaccines (44.9%, 175/390). Other reasons included the fear of offending patients and lack of privacy (18.5%, 72/390) and the belief that cancer screening was enough for cervical cancer prevention (6.9%, 27/390). 10.8% and 15.1% reduction

in “insufficient knowledge of HPV and HPV vaccines” and “concerns about vaccine safety and efficacy” were observed after the intervention ($P < .05$), respectively.

The choice of access to HPV-related knowledge in the future

When questioned about HCWs’ future choice of access to information about cervical cancer and HPV vaccines, 90.9% preferred expert lectures, followed by online media (82.8%) and guidance manuals (82.1%).

Discussion

Healthcare workers play an important role in the prevention of cervical cancer. Previous studies have found that suggestions from HCWs were important in influencing decisions about whether or not to be vaccinated.^{20–25} Thus, it is crucial that HCWs are knowledgeable about and maintain a positive attitude toward HPV vaccines. This study is the first to evaluate the short-term effectiveness of a brief structured presentation on HPV and HPV vaccines among HCWs in Western China

regarding their knowledge and attitudes toward HPV and its vaccines.

Healthcare workers included in our study seem to be more knowledgeable at baseline regarding HPV and its vaccines compared with studies conducted among other populations^{20,26–28} and a higher knowledge level could be noticed after an education intervention. However, some more specific knowledge was insufficient. Only 36.4% of participants knew that “2 v/4 v/9 vHPV vaccines had been approved in Mainland China and the vaccination procedures for each vaccine”. Although the correct proportion increased to be 50.9% after the intervention, it still remained low. A study conducted in the US reported that 53.2% and 95.1% of HCWs knew the recommended dosing intervals for the 3 doses of 4v/9v HPV vaccines in pre-and posttests, respectively,²² which was much higher than in our study. One reason for low awareness of HPV vaccines may be that China is further behind many other countries in the world in terms of the introduction and access to HPV vaccines,¹⁴ which may result in lower awareness of HPV vaccines. Another reason was possibly because that the content about the vaccination procedures of 2 v/4 v/9vHPV vaccines in the intervention was easily confused, which may

Table 3. HCWs’ knowledge scores in relation to demographic characteristics pre-and post-intervention.

Characteristics	Pre-intervention			Post-intervention			Change		
	n	Knowledge scores Median (P25, P75)	P-value	n	Knowledge scores Median (P25, P75)	P-value	n	Knowledge scores Median (P25, P75)	P-value
Overall	1448	11.0 (9.0,13.0)		1354	12.0(11.0,14.0)				
Age			<0.001 ^a			0.001 ^a			0.012 ^a
<30	351	10.0(8.0,12.0)		305	12.0(11.0,13.0)		305	2.0 (0,3.0)	
30–39	390	11.0(9.0,13.0)		333	13.0(11.0,14.0)		333	1.0(0,3.0)	
40–49	372	11.0(9.0,13.0)		328	13.0(11.0,14.0)		328	1.0(0,2.0)	
≥50	175	11.0(9.0,13.0)		149	13.0(11.0,13.0)		149	1.0(0,2.5)	
Gender			<0.001 ^d			<0.001 ^d			0.515 ^d
Male	123	10.0(8.0,12.0)		99	12.0(10.0,13.0)		99	1.0(0,3.0)	
Female	1187	11.0(9.0,13.0)		1038	13.0(11.0,14.0)		1038	1.0(0,3.0)	
Regions			0.681 ^a			0.005 ^a			0.443 ^a
Urban	1159	11.0(9.0,13.0)		991	13.0(11.0,14.0)		991	1.0(0,3.0)	
Rural	251	11.0(9.0,12.0)		225	12.0(11.0,13.0)		225	1.0(0,3.0)	
Other	28	11.5(9.0,13.0)		24	12.5(11.0,13.8)		24	1.0(0,3.0)	
Current Employment			<0.001 ^a			<0.001 ^a			0.013 ^a
Community hospital	408	11.0(9.0,13.0)		357	13.0(11.0,14.0)		357	1.0(0,3.0)	
Maternity and Child Care Center	328	12.0(10.0,13.0)		291	13.0(11.0,14.0)		212	1.0(0,2.0)	
The Centers for Disease Control	140	11.5(9.0,14.0)		117	13.0(12.0,14.0)		117	1.0(0,3.0)	
General hospital	328	11.0(9.0,13.0)		292	13.0(11.0,14.0)		292	1.0(0,2.8)	
Other	239	9.0(7.0,11.0)		186	12.0(11.0,13.0)		186	2.0(0,3.0)	
Departments			<0.001 ^a			<0.001 ^a			<0.001 ^a
Department of gynecology	595	11.0(10.0,13.0)		523	13.0(11.0,14.0)		523	1.0(0,2.0)	
Department of pediatrics	71	11.0(9.0,13.0)		61	12.0(11.0,13.5)		61	1.0(0,3.0)	
Department of planning immunology	413	12.0(10.0,13.0)		348	13.0(12.0,14.0)		348	1.0(0,2.0)	
Department of internal medicine	50	9.0(7.8,13.0)		44	12.0(10.0,13.0)		44	1.5(0,4.0)	
Other	314	9.0(7.0,11.0)		268	12.0(10.0,13.0)		268	2.0(0,4.0)	
Level of education			0.139 ^a			0.045 ^a			0.079 ^a
Associate	549	11.0(9.0,13.0)		491	12.0(11.0,14.0)		491	1.0(0,3.0)	
Bachelor	758	11.0(9.0,13.0)		632	13.0(11.0,14.0)		632	1.0(0,3.0)	
Master	87	12.0(9.0,13.0)		77	13.0(11.5,14.0)		77	1.0(0,3.0)	
Doctor	7	13.0(9.0,13.0)		7	13.0(10.0,14.0)		7	1.0(0,1.0)	
Other	42	10.0(7.0,12.0)		36	12.5(11.0,13.0)		36	2.0(1.0,4.0)	
Work years			<0.001 ^a			0.002 ^a			0.051 ^a
0–5 years	368	10.0(8.0,12.0)		312	12.0(11.0,13.0)		312	2.0(0,3.0)	
6–10 years	260	11.0(9.0,13.0)		223	13.0(11.0,14.0)		223	1.0(0,2.0)	
11–15 years	212	11.0(9.0,13.0)		187	13.0(11.0,14.0)		187	1.0(0,3.0)	
16–20 years	219	11.0(9.0,13.0)		190	12.0(11.0,14.0)		190	1.0(0,3.0)	
≥21 years	386	11.0(9.0,13.0)		333	13.0(11.0,14.0)		333	1.0(0,2.0)	

*Pre-intervention analyses only conducted in participants who provided demographic information;

Post-intervention analysis only conducted in participants who numbered the post-intervention questionnaires.

^c Kruskal-Wallis Test; ^d Mann-Whitney U Test

The total number is not added up to 1448 and 1354 due to missing data

Table 4. Changes in reasons for unwilling to recommend HPV vaccines.

Reasons for unwilling to recommend HPV vaccines	Pre-intervention (n = 390)		Post-intervention (n = 224)		Change percentage point difference	P-value
	n	Percent (%)	n	Percent (%)		
1. Insufficient knowledge on HPV and HPV vaccines	265	67.9	128	57.1	↓10.8	0.007^a
2. Concerns about vaccine safety and efficacy	212	54.4	88	39.3	↓15.1	<0.001^a
3. High cost of HPV vaccines	175	44.9	109	48.7	↑ 3.8	0.365 ^a
4. The fear of offending patients and lack of privacy	72	18.5	44	19.6	↑ 1.1	0.719 ^a
5. It's a waste of time because of the low awareness of the public	45	11.5	40	17.9	↑ 6.4	0.029^a
6. Cervical cancer screening is enough and no more vaccinations are needed	27	6.9	17	7.6	↓0.7	0.758 ^a

The analysis was conducted among those who chose "not recommend" and "not clear"; ^aχ² test; ^bFisher's exact test

lead to low acceptance of knowledge. After intervention, we found that the correct responses of "other HPV related diseases" and "HPV testing was not required before vaccination" were still relatively low compared with other specific questions. The above findings suggest that intervention may be effective in increasing HCWs' knowledge in general, and future intervention should focus more on other HPV-related diseases and HPV vaccination, including procedures for different vaccines. Future education should also provide clear and impressive content for healthcare workers to remember and understand better, so that they are able to provide complete and accurate recommendations to women.

Compared with other educational interventions,^{22,26,29} the improvement of knowledge in our study seems to be low, with the largest increase observed in the answer "80% of women would be infected by HPV in their lifetime," from 62.9% to 82.9% ($P < .001$). A possible reason may be that HCWs' baseline knowledge was adequate in general. For example, 92.2% knew that HPV infection was the primary cause of cervical cancer at baseline, which was much higher than employed women (20.7%) and female undergraduate students (7.3%) in China.²⁹

Among the participants, only 17.3% were from rural areas of Western China. Since our educational sessions were held in the main cities of seven provinces, HCWs working at rural areas were less likely to attend such an educational session due to barriers of time and distance. However, it was reported that rural women were more than twofold likely to be infected by high-risk HPV than urban women in China,³⁰ and cervical cancer still remains a major health problem for women (especially women living in rural areas of central and western China).⁴ Therefore, such health education should be done in more rural areas in the future if it is effective thus to provide better resources to rural women.

At baseline, 71.9% of the HCWs were willing to recommend HPV vaccine to the public, which was lower than Korean health teachers (79.5%) and English nurses (98.9%).^{31,32} The leading reason for an unwillingness to recommend HPV vaccines was lack of related knowledge (68.2%, 266/390), followed by doubts regarding the efficacy and safety of HPV vaccines (54.4%, 212/390). Concerns regarding safety and efficacy were also the main reasons for the low acceptance of HPV vaccines in the general Chinese population.³³ After the education, the willingness increased to 82.3% and the proportion of the participants who chose the above two reasons decreased significantly. It demonstrated

that educational intervention could enhance knowledge levels and remove doubts about vaccines, thus increasing recommendation willingness and the provision of correct information to the public.

The high price of vaccines became the second most important reason for the unwillingness to recommend in the post-intervention tests. The HPV vaccines are usually regarded as too expensive for the general public uptake in China,¹⁴ costing about 260, 340, and 567 dollars for three doses of 2 v/4 v/9v HPV vaccines, respectively, while a modeling study suggested that HPV vaccination is cost effective across all income groups when the cost is less than 50 USD per vaccinated girl.³⁴ Previous studies found that very few Chinese women would pay more than 15 dollars for vaccination.^{20,26} At the current price, HPV vaccination is not affordable for many women and families in China. According to a recent meta-analysis, HPV 16 and 18 are responsible for 78.2% of invasive cervical cancers in China,³⁵ which indicated that vaccination with 2 vHPV may protect against as many as 78.2% of cervical cancers in Chinese women. Therefore, the recommendation of 2vHPV, which may be less expensive and more feasible for widespread use, would be more cost-effective at the population level for cervical cancer prevention. Of course, HCWs should offer different suggestions according to the characteristics of individuals.

Results showed that lectures given by experts are the preferred way among HCWs to learn about HPV-related knowledge in the future, followed by online media and guidance manuals. Previous studies conducted among English practice nurses revealed that there was a requirement for continued HPV education and the majority of the respondents stated that the development of an online e-learning program could be a way of achieving this.³² Travel distance and lack of time were stated as key barriers to attending educational sessions. It was believed that online resources would be easier to access and would, therefore, be more likely to increase participation.³⁶ In addition, web-based educations regarding cervical cancer, HPV, and HPV vaccines have shown positive results in increasing knowledge levels among nurses and female university students.^{37,38} Thus, online media might be a cost-effective and time-saving way to increase knowledge levels among HCWs in China, and educational lectures combined with online media and guidance manuals will be necessary to guarantee a long-term impact.

There are several limitations in our study. First, the study was undertaken in Western China and our results may not reflect the knowledge and attitudes of HCWs in other regions

of China. Secondly, the lack of a matched control group may weaken the ability to ascertain the effectiveness of the intervention. Thirdly, short-term effectiveness does not necessarily guarantee a long-term impact and a follow up study was not conducted to evaluate the duration of effect as well as to help decide the interval for a 'booster' session in future education campaigns. Finally, HCWs' actual behavioral changes (recommending the HPV vaccine) were not measured in our study.

One of the major strengths of the present study is that this is the first study to evaluate a brief structured health education to change knowledge and attitudes toward HPV and its vaccines among HCWs in Western China, the less developed region of China. Additionally, the educational intervention provided specialized and in-depth HPV knowledge in diversified forms, such as scenario simulation, which can help to strengthen understanding and memory of related knowledge.

Conclusion

In conclusion, this is the first study to evaluate the short-term effectiveness of a brief structured presentation combined with a Q&A and followed by a series of scenario simulations on HPV and its vaccines among HCWs in Western China. Our results showed that educational intervention on HPV and its vaccines is effective in improving HCWs' knowledge levels and changing their attitudes toward HPV vaccines, which may help improve the quality or quantity of their counseling and future services regarding HPV vaccines. In addition, our findings suggest that such educational intervention should focus more on knowledge regarding other HPV-related diseases and HPV vaccination, and that education campaigns, particularly targeting rural HCWs, are needed in the near future, to provide better healthcare information to individuals.

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Declaration of interest statement

The authors declare that they have no conflicts of interest to disclose.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394–424. doi:10.3322/caac.21492.
2. Chen WQ, Zheng RS, Zhang SW, Zeng HM, Zou TT, Xia CF, Yang ZX, He J. Cancer incidence and mortality in China in 2013: an analysis based on urbanization level. *Chin J Cancer Res.* 2017;29(1):1–10. doi:10.21147/j.1000-9604.2017.01.01.
3. Zhao FH, Hu SY, Zhang SW, Chen WQ, Qiao YL. Cervical cancer mortality in 2004–2005 and changes during last 30 years in China. *Chin J Prev Med (Article in Chinese).* 2010;44(5):408–12. doi:10.3760/cma.j.0253-9624.2010.05.009.
4. Li J, Kang LN, Qiao YL. Review of the cervical cancer disease burden in Mainland China. *Asian Pacific J Cancer Prev.* 2011;12:1149–53. doi:10.1097/01.cad.0000390767.85658.83.
5. Bosch FX, Muñoz N. The viral etiology of cervical cancer. *Virus Res.* 2002;89(2):183–90. doi:10.1016/S0168-1702(02)00187-9.
6. Erickson BK, Landers EE, Huh WK. Update on vaccination clinical trials for HPV-related disease. *Clin Ther.* 2014;36(1):8–16. doi:10.1016/j.clinthera.2013.11.003.
7. Lehtinen M, Lagheden C, Luostarinen T, Eriksson T, Apter D, Harjula K, Kuoritti M, Natunen K, Palmroth J, Petäjä T, et al. Ten-year follow-up of human papillomavirus vaccine efficacy against the most stringent cervical neoplasia three cohorts from randomized trials. *BMJ Open.* 2017;7(8):1–8. doi:10.1136/bmjopen-2017-015867.
8. Kjaer SK, Nygård M, Dillner J, Marshall JB, Radley D, Li M, Munk C, Hansen BT, Sigurdardottir LG, Hortlund M, et al. A 12-year follow-up on the long-term effectiveness of the quadrivalent human papillomavirus vaccine in 4 Nordic countries. *Clin Infect Dis.* 2018;66(3):339–45. doi:10.1093/cid/cix797.
9. Huh WK, Joura EA, Giuliano AR, Iversen O, De ARP, Ault KA, Bartholomew D, Cestero RM, Fedrizzi EN, Hirschberg AL, et al. Final efficacy, immunogenicity, and safety analyses of a nine-valent human papillomavirus vaccine in women aged 16 – 26 years: a randomised, double-blind trial. *Lancet.* 2017;390(10108):2143–59. doi:10.1016/S0140-6736(17)31821-4.
10. Gallagher KE, Lamontagne DS, Watson-jones D. Status of HPV vaccine introduction and barriers to country uptake. *Vaccine.* 2018;36(32):4761–67. doi:10.1016/j.vaccine.2018.02.003.
11. Drolet M, Bénard É, Boily M, Ali H, Baandrup L, Bauer H, Beddows S, Brisson J, Brotherton JML, Cummings T, et al. Population-level impact and herd effects following human papillomavirus vaccination programmes: a systematic review and meta-analysis. *Lancet Infect Dis.* 2016;15(5):565–80. doi:10.1016/S1473-3099(14)71073-4.
12. Joura EA, Giuliano AR, Iversen OE, Bouchard C, Mao C, Mehlsen J, Moreira ED, Ngan JY, Petersen LK, Lazcano-Ponce E,

- et al. A 9-valent HPV vaccine against infection and intraepithelial Neoplasia in women. *N Engl J Med.* 2015;372(8):711–23. doi:10.1056/NEJMoa1405044.
13. Giuliano AR, Palefsky JM, Goldstone S, Moreira EDJ, Penny ME, Aranda C, Vardas E, Moi H, Jessen H, Hillman R, et al. Efficacy of quadrivalent HPV vaccine against HPV Infection and disease in males. *N Engl J Med.* 2011;364(5):401–411. doi:10.1056/NEJMoa0909537.
 14. Wong LP, Han L, Li H, Zhao J, Zhao Q, Zimet GD. Current issues facing the introduction of human papillomavirus vaccine in China and future prospects. *Hum Vaccin Immunother.* 2019;15(7–8):1533–40. doi:10.1080/21645515.2019.1611157.
 15. National Medical Products Administration. The license of human papillomavirus bivalent(types 16, 18) vaccine was approved by CFDA. Beijing: National Medical Products Administration; 2016. [accessed 2020 May 13July18]. <http://www.nmpa.gov.cn/WS04/CL2168/329384.html>.
 16. Deng HN, Wang B The license of human papillomavirus quadrivalent (Types6,11, 16, 18) Vaccine was approved by CFDA. The Xinhua News Agency. 2017 Jun 20. accessed 2020 May 13. http://www.xinhuanet.com/2017-06/20/c_1121179041.htm.
 17. National Medical Products Administration. Nine-valent HPV vaccine has been conditionally approved for marketing. Beijing: National Medical Products Administration; 2018. [accessed 2020 May 13Apr29]. <http://www.nmpa.gov.cn/WS04/CL2094/227881.html>.
 18. National Medical Products Administration. The vaccine to prevent cervical cancer is suitable for women of which age? Beijing: National Medical Products Administration; 2019. [accessed 2020 May 13July18]. <http://www.nmpa.gov.cn/WS04/CL2056/338922.html>.
 19. Liu Y, Di N, Tao X. Knowledge, practice and attitude towards HPV vaccination among college students in Beijing, China[J]. *Hum Vaccin Immunother.* 2020;16(1):116–23. doi:10.1080/21645515.2019.1638727.
 20. Li J, Li LK, Ma JF, Wei LH, Niyazi M, Li CQ, Xu AD, Wang JB, Liang H, Belinson J, et al. Knowledge and attitudes about human papillomavirus (HPV) and HPV vaccines among women living in metropolitan and rural regions of China. *Vaccine.* 2009;27(8):1210–15. doi:10.1016/j.vaccine.2008.12.020.
 21. Pampena E, Vanucci R, Johnson LB, Bind MA, Tamayo I, Welch K, Lind E, Wagner R, Villa A. Educational interventions on human papillomavirus for oral health providers. *J Cancer Edu.* 2019. doi:10.1007/s13187-019-01512-7.
 22. Berenson AB, Rahman M, Hirth JM, Rupp RE, Sarpong KO. A brief educational intervention increases providers' human papillomavirus vaccine knowledge A brief educational intervention increases providers' human papillomavirus vaccine knowledge. *Hum Vaccin Immunother.* 2015;11(6):1331–36. doi:10.1080/21645515.2015.1022691.
 23. Ylitalo KR, Lee H, Mehta NK. Health care provider recommendation, human papillomavirus vaccination, and race/ethnicity in the US national immunization survey. *Am J Public Health.* 2013;103(1):164–69. doi:10.2105/AJPH.2011.300600.
 24. Hswen Y, Gilkey MB, Rimer BK, Brewer NT. Improving physician recommendations for human papillomavirus vaccination: the role of professional organizations. *Sex Transm Dis.* 2017;44(1):43–48. doi:10.1097/OLQ.0000000000000543.
 25. Rahman M, Laz TH, Mcgrath CJ, Berenson AB. Provider recommendation mediates the relationship between parental human papillomavirus (HPV) vaccine awareness and HPV vaccine initiation and completion among 13- to 17-Year-Old US adolescent children. *Clin Pediatr (Phila).* 2015;54(4):371–75. doi:10.1177/0009922814551135.
 26. Li J, Kang LN, Li BY, Pang Y, Huang R, Qiao YL. Effect of a group educational intervention on rural Chinese women' s knowledge and attitudes about human papillomavirus (HPV) and HPV vaccines. *BMC Cancer.* 2015;15(1):1–11. doi:10.1186/s12885-015-1682-2.
 27. Liu CR, Liang H, Zhang X, Pu C, Li Q, Li QL, Ren FY, Li J. Effect of an educational intervention on HPV knowledge and attitudes towards HPV and its vaccines among junior middle school students in Chengdu, China. *BMC Public Health.* 2019;19(1):1–9. doi:10.1186/s12889-019-6823-0.
 28. Pu C, Liu CR, Zhang X, Li J. Knowledge and attitudes toward HPV and its vaccines among parents of middle school students in Chengdu. *Mod Preventive Med.* 2018;45(2):299–303. Article in Chinese.
 29. Chang IJ, Huang R, He W, Zhang SK, Wang SM, Zhao FH, Smith JS, Qiao YL. Effect of an educational intervention on HPV knowledge and vaccine attitudes among urban employed women and female undergraduate students in China : a cross-sectional study. *BMC Public Health.* 2013;13(1):916. doi:10.1186/1471-2458-13-916.
 30. Zhao FH, Lin MJ, Chen F, Hu SY, Zhang R, Belinson JL, Sellors JW, Franceschi S, Qiao YL, Castle PE, et al. Performance of high-risk human papillomavirus DNA testing as a primary screen for cervical cancer : a pooled analysis of individual patient data from 17 population-based studies from China. *Lancet Oncol.* 2010;11(12):1160–71. doi:10.1016/S1470-2045(10)70256-4.
 31. Kim HW. Knowledge about human papillomavirus (HPV), and health beliefs and intention to recommend HPV vaccination for girls and boys among Korean health teachers. *Vaccine.* 2012;30(36):5327–34. doi:10.1016/j.vaccine.2012.06.040.
 32. Patel H, Austin-Smith K, Sherman SM, Tincello D, Moss EL. Knowledge, attitudes and awareness of the human papillomavirus amongst primary care practice nurses: an evaluation of current training in England. *J Public Health (Bangkok).* 2016:1–8. doi:10.1093/pubmed/fdw063.
 33. Zhang YR, Wang Y, Liu L, Fan YZ, Liu ZH, Wang YY, Nie SF. Awareness and knowledge about human papillomavirus vaccination and its acceptance in China: a meta-analysis of 58 observational studies. *BMC Public Health.* 2016;16(1):216. doi:10.1186/s12889-016-2873-8.
 34. Levin C, Sharma M, Olson Z, Verguet S, Shi JF, Wang SM, Qiao YL, Jamison DT, Kim JJ. An extended cost-effectiveness analysis of publicly financed HPV vaccination to prevent cervical cancer in China. *Vaccine.* 2013;33(24):295–306. doi:10.1016/j.vaccine.2015.02.052.
 35. Xu HH, Wang K, Feng XJ, Dong SS, Lin A, Zheng LZ, Yan WH. Prevalence of human papillomavirus genotypes and relative risk of cervical cancer in China: a systematic review and meta- analysis. *Oncotarget.* 2018;9(20):15386–97. doi:10.18632/oncotarget.24169.
 36. Choules AP. The use of e-learning in medical education: a review of the current situation. *Postgrad Med J.* 2007;83(978):212–16. doi:10.1136/pgmj.2006.054189.
 37. Choma K, Mckeever WAE. Cervical cancer screening in adolescents: an evidence-based internet education program for practice improvement among advanced practice nurses. *Worldviews on Evidence-Based Nurs.* 2015;12(1):51–60. doi:10.1111/wvn.12071.
 38. Bennett AT, Patel DA, Carlos RC, Zochowski MK, Pennewell SM, Chi AM, Dalton VK. Human papillomavirus vaccine uptake for female university students: a randomized controlled trial. *J Women's Health.* 2015;24(11):950–57. doi:10.1089/jwh.2015.5251.