

Letter to the Editor

**The Changes in the Awareness of Cervical Cancer Prevention and the Acceptability of HPV Vaccines among Women after Their Introduction in China***

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Cervical cancer is a form of malignant tumor that seriously threatens women's health. In China, according to the cancer statistics, 98,900 new cervical cancer cases and 30,500 deaths due to cervical cancer were estimated to have occurred in 2015, and the incidence and mortality rates still exhibited an upward trend^[1]. It has been established that persistent high-risk human papillomavirus (HPV) infection is the primary cause of the development of cervical cancer and its precursors. HPV is the commonest sexually transmitted infection worldwide and can be found in 99.7% of cervical cancer cases, of which HPV16 and HPV18 are responsible for approximately 70%^[2].

Vaccination against HPV is an effective method of preventing cervical cancer. The first vaccine against HPV, namely, Gardasil, was approved by the United States Food and Drug Administration (FDA) in 2006. It is a quadrivalent vaccine against HPV16 and HPV18 and also targets HPV6 and HPV11, which cause 90% of genital warts. In 2009, the bivalent vaccine Cervarix, which targets HPV16 and HPV18, was approved by the FDA. The most recent HPV vaccine, namely, the nine-valent Gardasil 9, which targets HPV6, HPV11, HPV16, HPV18, HPV31, HPV33, HPV45, HPV52, and HPV58, was approved in 2014 and can prevent approximately 90% of all cervical cancers.

In China, Cervarix was approved by the China Food and Drug Administration (CFDA) in 2016, and in May 2017 Gardasil was approved by the CFDA. In July 2017 and December 2017, Cervarix and Gardasil, respectively, were first marketed in mainland China. In April 2018 Gardasil 9 was approved by the Chinese National Medical Products Administration via a fast-track process. At the same time, since the approval of Gardasil, cervical cancer and the HPV vaccines

have been widely reported by the public media *via* television, the internet, and newspapers. The cervical cancer vaccines became well known in 2017 owing to widely disseminated media reports that attracted a great deal of attention.

Currently, in China the main method used for the prevention of cervical cancer is screening. However, government-led cervical cancer screening has limited coverage, and the main form of screening is opportunistic. Although the HPV vaccines have been introduced in China, they are classified as second-class vaccines, which implies that women must make the decision whether to be vaccinated and should pay the full cost. In the absence of legally mandated immunization against HPV and cervical cancer screening, women's participation in opportunistic screening and HPV vaccination is closely related to their knowledge of cervical cancer prevention^[3]. Before the HPV vaccines were introduced in China, studies of awareness of cervical cancer and attitudes toward HPV vaccination were conducted in various regions of China, and the results showed that the knowledge held by Chinese women regarding cervical cancer and HPV vaccines was inadequate^[4,5].

The Cervical Cancer Control Center of Hubei Province undertook work on the prevention and treatment of cervical cancer in Hubei Province. After the HPV vaccines were introduced in China, the center also undertook work on HPV vaccination. Before and after the HPV vaccines were introduced in China, the investigation group conducted surveys at the center to study women's awareness of cervical cancer prevention and the acceptability of HPV vaccination. We wanted to determine whether women's knowledge of cervical cancer prevention had increased as a result of the widespread media reports and education by medical personnel, as well

doi: 10.3967/bes2019.109

*This work was supported by the Natural Science Foundation of Hubei Province, China [Grant No. 2017CKC891]; and the Health Commission Of Hubei Province, China [Grant No. WJ2019H286].

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as what is the current acceptability of the HPV vaccines and what are the main factors that affect women's knowledge. The results could guide the government in developing effective methods for improving women's participation in cervical cancer screening and HPV vaccination.

A total of 16,830 women who first visited the center for regular gynecological examinations or on account of other diseases were enrolled in the study from March 2016 to May 2018. Women who were pregnant or had a history of HPV vaccination were excluded. Participants voluntarily took part in the study on the condition that they were fully informed of the aim and details of the research in advance, and written informed consent was obtained from each participant.

Each participant completed an interviewer-guided questionnaire. The questionnaire consisted of five sections: (1) demographic characteristics; (2) family history of cervical cancer and HPV infection, history of cervical disease, and history of cervical cancer screening; (3) knowledge of cervical cancer, HPV, and HPV vaccines; (4) attitudes toward cervical cancer; and (5) acceptability of HPV vaccination. The third section included three questions: 'Have you ever heard of cervical cancer?',

'Have you ever heard of HPV?', and 'Have you ever heard of HPV vaccines?' Those who said 'Yes' were then asked to answer 10 corresponding open questions, which are listed in Table 1. For these 10 questions, 1 point was given for each correct response, and the total score was regarded as the participant's overall score. We defined an overall score of 6 points or more as 'adequate knowledge'.

The survey was conducted by medical staff at the Cervical Cancer Control Center of Hubei Province. Before the survey was carried out, the explanations for completing the questionnaire were unified, and the participating staff were trained. Two preliminary surveys, each comprising 30 questionnaires, were conducted in advance to ensure that the questions in the questionnaire could be understood clearly by the respondents. During the survey, the quality control group examined 10% of the responses randomly each day to make sure that there were no missing blanks, typographical errors, or logical errors and to correct errors as soon as they were found.

We employed EpiData software to construct a database. Statistical analysis was conducted using SAS 9.1 software (North Carolina State University, Raleigh, NC, USA). We compared and analyzed the following statistics for women before and after the

Table 1. The change in awareness of cervical cancer prevention before and after the HPV vaccines introduction in China

Items	Yes, n (%)		χ^2	p	Total (n = 15,494) n (%)
	Before vaccines introduction (n = 10,837)	After vaccines introduction (n = 4,657)			
Have you heard of cervical cancer?	4,691 (43.29%)	2,619 (56.24%)	219.23	< 0.01	7,310 (47.18%)
Cervical cancer can be diagnosed early	4,093 (37.77)	2,286 (49.09%)	172.29	< 0.01	6,379 (41.17%)
Early cervical cancer is curable	3,651 (33.69)	1,984 (42.60%)	111.80	< 0.01	5,635 (36.37%)
Have you heard of HPV?	2,661 (24.55)	1,320 (28.34%)	24.50	< 0.01	3,981 (25.69%)
High-risk HPV infection is the cause of cervical cancer	1,905 (17.58)	1,036 (22.25%)	46.14	< 0.01	2,941 (18.98%)
HPV spreads primarily through sexual contact	2,103 (19.41)	1,114 (23.92%)	40.36	< 0.01	3,217 (20.76%)
HPV can be cleared	1,337 (12.34)	736 (15.80%)	33.78	< 0.01	2,073 (13.38%)
HPV infection does not necessarily develop into cervical cancer	990 (9.14)	624 (13.40%)	63.46	< 0.01	1,614 (10.42%)
Cytology + HPV test can prevent cervical cancer	2,023 (18.67)	1,088 (23.36%)	44.75	< 0.01	3,111 (20.08%)
Have you heard of HPV vaccines (to prevent cervical cancer)?	2,114 (19.51)	1,772 (38.05%)	596.04	< 0.01	3,886 (25.08%)
HPV vaccines can prevent cervical cancer, CIN, penile cancer, etc.	1,701 (15.70)	1,580 (33.93%)	648.60	< 0.01	3,281 (21.18%)
After HPV vaccination, regular cervical cancer screening is still required	1,609 (14.85)	1,419 (30.47%)	505.62	< 0.01	3,028 (19.54%)
The optimal age for HPV vaccination is before the start of sexual activity	856 (7.90)	862 (18.51%)	371.99	< 0.01	1,718 (11.09%)

HPV vaccines were introduced into China: the knowledge of cervical cancer, HPV, and HPV vaccines; the degree of concern regarding cervical cancer; and attitudes toward HPV vaccines. The Chi-squared test was used to determine whether the differences were statistically significant.

A total of 15,494 valid responses were collected. Among these, the residency status of 7,183 women (46.4%) was rural, and 8,311 women (53.6%) were from city. The average age of the respondents was 34.22 ± 9.63 years, and most women were between 26 and 45 years old (65.8%). Among the respondents, the largest percentages of women were married (80.9%), had at least a high school degree (69.8%), had a monthly income of ¥3,000 or more (43.6%), and were engaged in service industry work (25.7%). The details can be seen in Supplementary Table S1 (available in www.besjournal.com).

We compared the knowledge of cervical cancer, HPV, and HPV vaccines among women before and after the HPV vaccines were introduced. We found that between January 2016 and May 2017, 43.29%, 24.55%, and 19.51% of women had heard of cervical cancer, HPV, and HPV vaccines, respectively, and these percentages increased to 56.24%, 28.34%, and 38.05%, respectively, after the vaccines were introduced into China ($P < 0.01$). As for specific items, Table 1 shows that the knowledge of cervical cancer and HPV vaccines increased significantly.

This is the first study to compare women's awareness of cervical cancer prevention and the acceptability of HPV vaccination before and after the HPV vaccines were introduced in China. According to the results, after the HPV vaccines were introduced in China the percentages of women who had heard of cervical cancer, HPV, and HPV vaccines all increased, among which the percentage of women who had heard of HPV vaccines increased by 18.54%. As for the specific items, there were different levels of improvement and, in comparison with previous studies carried out in China, the awareness rates significantly increased^[4,5]. The increases in awareness indicated that not only did the introduction of the HPV vaccines provide an effective measure for the primary prevention of cervical cancer in China, but also, more importantly, women's awareness of cervical cancer prevention had been further improved as a result of the massive public media campaigns and education by medical personnel. However, in comparison with those in many other countries, the awareness rates of Chinese women were still low^[6,7].

We analyzed the research results further and found some problems. Although the percentages of women who had heard of cervical cancer and HPV vaccines had significantly increased, the percentage of women who had heard of HPV was still low. This low rate reflects a lack of clarity in terms of women's understanding of HPV vaccines and may reflect a lack of knowledge that most women have regarding the mechanism by which HPV vaccination may prevent cervical cancer. For example, after the HPV vaccines were introduced, only 18.51% of women knew that the best time for HPV vaccination is before first sexual intercourse. In fact, the 'Guidelines for Comprehensive Prevention and Control of Cervical Cancer' explicitly mention that the target population for HPV vaccination in China is 13–15-year-old girls. If most women do not know this, it will cause the target population to miss the optimal time for vaccination. It is also important to note that only 30.47% of women knew that they still need to regularly participate in cervical screening after vaccination, which might result in failure to undergo cervical screening once vaccination has been administered. In summary, the lack of awareness of the mechanism of HPV vaccines may lead to a series of problems. Therefore, educational campaigns could highlight the prophylactic nature and mechanism of HPV vaccines.

This study compared the rates of awareness of cervical cancer prevention among different populations before and after the HPV vaccines were introduced. As can be seen from Supplementary Table S2 (available in www.besjournal.com), the groups whose awareness rates did not significantly increase after the introduction of the HPV vaccines were older women, rural women, women with low educational attainment and incomes, and women engaged in farming. A common feature of these groups is that they are less likely to have access to a network, whereas current information from the media is mainly disseminated through a network. Their degrees of understanding and acceptance were also lower. Therefore, we can improve TV-based and community-based publicity to achieve better outcomes for these populations^[3]. Moreover, women who have participated in cervical cancer screening have relatively higher awareness rates, because they receive relevant education from medical staff when they visit hospitals. In Yangcheng County, Shanxi Province, an educational intervention study was designed to assess the short-term effectiveness of a brief hospital-based session that focused on HPV on rural Chinese women's

knowledge and attitudes. It was found that following the intervention significant increases were detected in awareness of HPV (from 5.9% to 59%) and cervical cancer (from 63.0% to 89.2%)^[8].

In China, facilities for free screening and HPV vaccination centers are mainly located in community hospitals, which are not fully staffed with professional gynecologists. Even if women go to a community hospital for screening or HPV vaccination, it is difficult for them to obtain adequate education and guidance. Rosenthal et al. found that the strength of a physician's recommendation had a significant effect on the decision to be vaccinated, which resulted in a fourfold greater likelihood of vaccination when women received a strong recommendation in comparison with one that was not strong^[9]. It is possible for the government to organize special training for community doctors so that they can provide relevant education and recommendations for women visiting clinics.

This study also compared women's concerns regarding cervical cancer before and after the vaccines were introduced. As can be seen from Table 2, the introduction of the HPV vaccines did not increase women's concerns regarding cervical cancer as a result of the massive media campaign, as the percentages of women with concerns regarding cervical cancer were 59.10% before and 60.40% after the introduction of the HPV vaccines. However, women's concerns regarding cervical cancer were still strong overall. Although there is great fear of cervical cancer in China, this is a type of cancer that can be successfully prevented. Basically, this situation is due to women's lack of a correct understanding of cervical cancer.

The percentage of women willing to receive HPV vaccination was high and exceeded 67%, as shown in Table 3, which is consistent with findings of previous research. Although women lacked sufficient knowledge, they still had a strong willingness to receive vaccination against cervical cancer^[10]. After the vaccines were introduced, the proportion of women who were willing to pay the full cost of vaccination increased from 4.23% to 23.04%, which is still relatively low. Many women hope that the government will provide a certain degree of subsidy. Before the vaccines were introduced into China, some researchers proposed that one of the greatest barriers to the introduction of HPV vaccines was price, and the current study has verified this conclusion. Currently, some coastal cities in China have considered offering free HPV vaccination to the

Table 2. The change in the degree of concern for cervical cancer before and after the HPV vaccines introduction in China

Item	Before vaccines introduction (n = 10,837)				After vaccines introduction (n = 4,657)				P	χ^2	Total (n = 15,494)			
	Worry n (%)	General n (%)	Do not worry n (%)	Unsure n (%)	Worry n (%)	General n (%)	Do not worry n (%)	Unsure n (%)			Worry n (%)	General n (%)	Do not worry n (%)	Unsure n (%)
The degree of concern For cervical cancer	6,405 (59.10)	2,174 (20.06)	735 (6.78)	1,523 (14.05)	2,813 (60.40)	943 (20.25)	605 (12.99)	296 (6.36)	< 0.01	310.57	9,218 (59.49)	3,117 (20.12)	1,340 (8.65)	1,819 (11.74)

Table 3. The change in the acceptability of HPV vaccination before and after the HPV vaccines introduction in China

Item	Yes, n(%)		P	χ^2	Total (n = 15,494) n (%)
	Before vaccines introduction (n = 10,837)	After vaccines introduction (n = 4,657)			
Willing to receive HPV vaccination?	7,316 (67.51)	3,139 (67.40)	0.91	0.02	10,455 (67.48)
Willing to let children and partner be vaccinated?	7,623 (70.34)	3,660 (78.59)	< 0.01	111.99	11,283 (72.82)
Willing to pay the full cost, 2,600 Yuan?	458 (4.23)	1,073 (23.04)	< 0.01	1294.80	1,531 (9.88)

target population of 13–15-year-old girls.

This study has found that the continuous appearance of new vaccines on the market, together with the massive media campaign and education by medical staff, has significantly improved women's awareness, even if there is still a large gap in awareness between Chinese women and those in many other countries. In general, Chinese women have a strong willingness to receive HPV vaccination, but the high cost of the vaccines is still a major factor affecting their final decision. It is necessary for educational campaigns targeting different populations to be ongoing, especially in the cases of those women who do not have good access to current media networks, namely, older women, low-income women, low-education women, and rural women. The number of women living in rural areas included in this study was relatively small. Because of this, our center plans to carry out relevant research and educational work in rural areas. It also suggests that the government can improve the coverage of free cervical screening and related educational campaigns in rural areas and provide a certain degree of subsidy for HPV vaccination.

The authors declare that they have no competing interests.

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Received: April 30, 2019;

Accepted: September 17, 2019

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Supplementary Table S1. The characteristics of 15,494 respondents

Items	Before vaccine introduction		After vaccine introduction		Total	
	<i>n</i>	%	<i>n</i>	%	<i>N</i>	%
Age (years)						
18-25	2,124	19.6	826	17.7	2,950	19.0
26-35	4,547	42.0	1,940	41.7	6,487	41.9
36-45	2,627	24.2	1,078	23.1	3,705	23.9
≥ 46	1,539	14.2	813	17.5	2,352	15.2
Residency status						
Rural	4,908	45.3	2,275	48.9	7,183	46.4
City	5,929	54.7	2,382	51.1	8,311	53.6
Marital status						
Unmarried	1,706	15.7	825	17.7	2,531	16.3
Married	8,853	81.7	3,675	78.9	12,528	80.9
Divorce/Widowed/Remarried	278	2.5	157	3.4	435	2.8
Education						
Secondary school and below	3,264	30.2	1,418	30.4	4,682	30.2
High school	3,104	28.6	1,221	26.2	4,325	27.9
College	4,047	37.3	1,772	38.1	5,819	37.6
Masters degree and above	422	3.9	243	5.2	665	4.3
Occupation						
Institutions and enterprises	1,063	9.8	541	11.6	1,604	10.4
Professional technicians	1,343	12.4	430	9.2	1,773	11.4
Service industry	2,753	25.4	1,230	26.4	3,983	25.7
Farmers	156	1.4	84	1.8	240	1.5
Unemployed and retired	1,281	11.8	735	15.8	2,016	13.0
Students	320	3.0	146	3.1	466	3.0
Others	3,921	36.2	1,491	32.0	5,412	34.9
Monthly income (CNY)						
< 1,000	1,781	16.4	908	19.5	2,689	17.4
1,000-3,000	4,675	43.1	1,376	29.5	6,051	39.1
3,000-5,000	3,214	29.7	1,541	33.1	4,755	30.7
> 5,000	1,167	10.8	832	17.9	1,999	12.9

Supplementary Table S2. The awareness change among different groups before and after HPV vaccine introduction in China

Items	Before vaccine introduction		After vaccine introduction		χ^2	<i>P</i>
	<i>n</i>	adequate knowledge (%)	<i>N</i>	adequate knowledge (%)		
Age (years)						
18-25	2,124	233 (10.97)	826	164 (19.85)	40.31	< 0.01
26-35	4,547	628 (13.81)	1,940	463 (23.87)	98.27	< 0.01
36-45	2,627	385 (14.66)	1,078	232 (21.52)	25.96	< 0.01
≥ 46	1,539	191 (12.41)	813	102 (12.55)	0.009	0.92
Residency Status						
Rural	4,908	427 (8.70)	2,275	284 (12.48)	24.95	< 0.01
City	5,929	1,010 (17.03)	2382	677 (28.42)	136.18	< 0.01
Marital status						
Unmarried	1,706	237 (13.89)	825	211 (25.58)	52.10	< 0.01
Married	8,853	1,169 (13.20)	3,675	719 (19.56)	82.07	< 0.01
Divorce/Widowed/Remarried	278	31 (11.15)	157	31 (19.75)	6.06	0.01
Education						
Secondary school and below	3,264	252 (7.72)	1,419	117 (8.24)	4.07	0.04
High school	3,104	349 (11.24)	1,221	201 (16.46)	21.50	< 0.01
College and above	4,047	711 (17.57)	1,774	549 (30.98)	130.70	< 0.01
Master and above	422	125 (29.62)	243	94 (38.68)	5.73	0.02
Occupation						
Institutions and enterprises	1,063	224 (21.07)	541	181 (33.46)	29.13	< 0.01
Professional technicians	1,343	229 (17.05)	430	135 (31.40)	41.07	< 0.01
Service industry	2,753	338 (12.28)	1,230	231 (18.78)	29.36	< 0.01
Farmers	156	12 (7.69)	84	3 (3.57)	1.58	0.21
Unemployed and retired	1,281	131 (10.22)	735	83 (11.29)	7.42	< 0.01
Students	320	65 (20.31)	146	43 (29.45)	4.70	0.03
Others	3,921	438 (11.17)	1,491	285 (19.11)	58.90	< 0.01
Monthly income (Yuan)						
< 1,000	1,781	164 (9.21)	908	117 (12.89)	8.69	< 0.01
1,000-3,000	4,675	520 (11.12)	1,376	213 (15.48)	18.95	< 0.01
3,000-5,000	3,214	482 (15.00)	1,541	356 (23.10)	47.13	< 0.01
> 5,000	1,167	271 (23.22)	832	275 (33.05)	23.64	< 0.01
Family history of cervical cancer/HPV infection						
Yes	227	57 (25.11)	123	33 (26.83)	0.123	0.72
No	10,610	1,380 (13.01)	4,534	928 (20.47)	136.88	< 0.01
History of cervical disease						
Yes	3,648	708 (19.41)	1,799	514 (28.57)	58.14	< 0.01
No	7,189	729 (10.14)	2,858	447 (15.64)	59.85	< 0.01
History of cervical cancer screening						
Yes	4,771	875 (18.34)	2,039	553 (27.12)	66.47	< 0.01
No	6,066	562 (9.26)	2,618	408 (15.58)	73.61	< 0.01