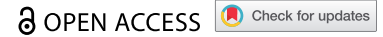


RESEARCH PAPER



Knowledge of HPV, its vaccines, and attitudes toward HPV vaccines among obstetrician-gynecologists, pediatricians and immunization services providers in Western China

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ABSTRACT

Background: In mainland China, HPV vaccines have been available to the public. However, only a few related studies among health care providers, as the key information providers, were reported although public concerns on HPV vaccines still exist. In this study, we aim to assess the knowledge of HPV, its vaccines, and attitudes toward HPV vaccines among the three most important groups of health care providers in Western China.

Method: This was a cross-sectional questionnaire-based study. Health care providers including obstetrician-gynecologists (OB-GYNs), pediatricians, and immunization service providers in Western China were investigated regarding their knowledge of HPV and its vaccines and their attitudes toward HPV vaccines.

Results: Of 1079 health care providers completing the survey, 1015 (94.1%) knew HPV infection is the primary cause of cervical cancer. However, lower knowledge levels of other HPV-related diseases were also found (43.2%). About three-quarters (74.1%) of practitioners interviewed would be willing to recommend HPV vaccination, which was found to be lower among the OB-GYNs (69.6%) and the pediatricians (73.2%). "Lack of relevant knowledge," "concerns on safety and efficacy" and price were the three most important concerns surrounding HPV vaccination.

Conclusion: The interviewed practitioners did not have adequate knowledge of HPV and its vaccines in depth. Education interventions are highly recommended to the health care providers, especially for OB-GYNs and pediatricians, to increase the coverage of HPV vaccination among the population. For the currently high price of vaccines, a future co-sharing mechanism between the government, the providers, and the individuals might be a solution.

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Introduction

Cervical cancer is the second most commonly diagnosed cancer among females in developing countries,¹ due to the lack of effective screening and preventative programs.² In Eastern Asia, the incidence of cervical cancer was 10.9/100,000 in 2018, higher than in Western Asia.³ Persistent high-risk HPV infection has been shown to be involved in the increased risk of high-grade cervical intraepithelial neoplasia (CIN) and cancer.⁴

Prophylactic HPV vaccines have been demonstrated to be effective and safe at preventing the development of high-grade cervical neoplasias since the vaccines were first approved in 2006.^{5,6} In China, the bivalent vaccine for HPV 16 and 18

(Cervarix[®], GlaxoSmithKline Biologicals, Rixensart, Belgium) and the quadrivalent vaccine for HPV 6, 11, 16, and 18 (Gardasil[®], Merck and Co., Whitehouse Station, NJ) were approved in 2016 and 2017, respectively.^{7,8} The nonavalent vaccine has also been commercially available in mainland China.⁹ In December 2019, the China-made bivalent vaccine for HPV 16 and 18 (Cecolin[®]) has been approved by the China Food and Drug Administration.¹⁰

However, public concerns surrounding HPV vaccines, especially their safety and efficacy, still exist in some areas.^{11–13} In mainland China, a few studies have been conducted among junior middle school students,¹⁴ their parents,¹⁵ and women who attended cervical cancer screening¹⁶ to explore their

knowledge and attitudes toward HPV and its vaccines. Although health care providers are the key information providers for the population to ensure effective vaccination coverage in the future,^{17–21} little is known about the knowledge level and attitudes toward HPV vaccines among obstetrician-gynecologists (OB-GYNs), pediatricians, and immunization services providers, who are considered to be the three most important groups among Chinese health care providers to promote HPV vaccination: pediatricians, as pioneers, play an important role in recommending HPV vaccines to the primary group to be vaccinated; OB-GYNs contribute to catch-up doses for adult women; immunization services providers, play a crucial role in the successful implementation of immunization in China.²²

Our study aims to explore the knowledge of HPV, its vaccines, and attitudes toward HPV vaccines among OB-GYNs, pediatricians, and immunization services providers in the less developed Western China. We hope to understand the current situation of the three groups regarding their ability to deliver accurate information on HPV and its vaccines and to make sure they help the target population and/or their guardians to make appropriate decisions. Our study also aims to provide a reference of a tailored evidence-based health education intervention targeting health care providers from different specialties in the future with the purpose to eventually increase the uptake of HPV vaccines in China.

Materials and methods

Study design and participants

This was a cross-sectional questionnaire-based study that ran from November 2018 to July 2019. Convenience sampling was used to invite 12 collaborative medical centers from Western China, including Chongqing University Cancer Hospital, Chengdu Women's and Children's Central Hospital, Meishan Maternal and Children's Hospital, Neijiang Center of Disease Control and Prevention, Deyang Maternal and Children's Hospital, Kunming Women and Children's Hospital, Dali Maternal & Child Health Hospital, Yuxi Hospital of Traditional Chinese Medicine, Zunyi Medical University Hospital, Northwest Women's and Children's Hospital, Xinjiang Medical University and Gansu Provincial Cancer Hospital. The collaborative institutions invited local health care providers, including OB-GYNs, pediatricians, immunization services providers, internists, and those from other specialties to attend free health education regarding cervical cancer prevention by sending both paper and electronic invitations. Our surveys were conducted before the health education took place. In this article, the results of OB-GYNs, pediatricians and immunization services providers were selected for analysis.

Research instrument

The anonymous self-completed questionnaires were administered after a detailed explanation by the researchers. The questionnaire contained four parts: (i) the social demographic characteristics (including the gender, age, current employment, education, region, specialty, years in practice, etc.); (ii)

knowledge of HPV and its related diseases, e.g. the primary cause of cervical cancer, the major two subtypes of hr-HPV, other HPV related diseases, etc.; (iii) knowledge of epidemiology in HPV & cervical cancer, e.g., the possibility of being infected by HPV, the age distribution pattern of HPV, etc.; (iv) knowledge of HPV vaccines, e.g. efficacy and safety, possible side effects, whether an HPV test is necessary before vaccination, whether HPV vaccination is still recommended after a positive test result or treatment, whether screening is still necessary after vaccination; (v) attitudes toward HPV vaccines, e.g. willingness to recommend HPV vaccination to the appropriate population.

Data collection and quality control

Two graduate and two undergraduate students were assigned to double-enter the data independently after training. Any inconsistency found between the two databases would be adjusted based on the original questionnaire-based questionnaires until the elimination of the inconsistency. 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 vaccination) were again double-checked and revised. After the consistency and logic checks, the database was ready for the final analysis.

Statistical analysis

SPSS statistical software version 20.0 was used to analyze the data. Frequency and percentages were used to describe the characteristics of participants, related knowledge, as well as attitudes toward HPV vaccines. Chi-squared test or Fisher's exact test was used to analyze the differences among OB-GYNs, pediatricians, and immunization services providers. Logistic regression was used to analyze the influential factors of attitudes toward HPV vaccines. Statistical significance was assessed by two-tailed tests with an α level of 0.05.

Results

Participants profile

There were a total of 1797 health care providers attending the health education. 1459 (81.2%) participants out of 1797 entered our surveys before the educational interventions, with 1448 (99.2%) completed out of 1459. Among the completed 1448 questionnaires, there were 1079 (74.5%) from the three specialties, including 595 OB-GYNs, 71 pediatricians, and 413 immunization services providers from 7 different provinces/autonomous regions in Western China.

The majority of the 1079 participants were females (85.4%) and the mean age was 37.7 years (s.d. = 9.5 years). 21.2% of participants were aged younger than 29 years of age, more than half of them aged between 30–49 years (30–39 yrs (28.0%) and 40–49 yrs (26.7%)). Most (78.8%) of participants came from urban areas, while one-fifth (19.3%) of them were from rural areas. 30.4% of participants were from community hospitals, approximately half (52.2%) of them working at general hospitals or women's and children's hospitals, and only 8.1% of them

working at CDC. Among all participants, 38.8% had graduated from junior colleges, about half of them (52.5%) had bachelor's degrees and very few had master's or doctor's degrees (6.2%). About one-third (36.9%) of participants were from Sichuan Province, followed by Yunnan (25.8%) and Gansu (12.6%). More than a quarter (26.4%) of participants had been working for more than 21 years (Table 1).

Knowledge toward HPV and its vaccines

In our study, 94.1% of participants knew that HPV infection is the primary cause of cervical cancer and 93.3% knew the most important two subtypes of hr-HPV. However, less than half of them (43.2%) knew the other HPV-related diseases, which was found to be higher among OB-GYNs (54.8%). The majority (84.6%) of them knew that HPV vaccination is the most effective way to prevent HPV infection and most of them (65.3%)

were aware that more than 80% of sexually active women could be infected with HPV in their lifetime. About eighty percent (78.0%) of participants knew about the age distribution pattern of hr-HPV among Chinese women. Similarly, about eighty percent (78.3%) of participants knew HPV16 and HPV18 cause about 70% of cervical cancer worldwide. When asked about HPV vaccines, most of them thought the vaccine was safe (90.2%) and effective (84.2%). Around three-quarters (75.1%) knew the correct answers about the side effects. Only half (50.5%) of the health care providers knew that pre-vaccination HPV tests are not necessary. However, most of them (82.4%) would recommend HPV vaccination to their patients with positive HPV tests or even after treatment. For screening, 92.6% of the health care providers were fully aware that cervical cancer screening is recommended even after any of the HPV vaccinations. However, it was much lower (87.9%) among the immunization service providers (Table 2).

Table 1. The distribution of social demographics among health care providers.

Social demographics	Total (N = 1079)		OB-GYNs (n = 595)		Pediatricians (n = 71)		Immunization services providers (n = 413)	
	n	%	n	%	n	%	n	%
Gender								
male	57	5.3	20	3.4	8	11.3	29	7.0
female	922	85.4	526	88.4	58	81.7	338	81.8
missing data	100	9.3	49	8.2	5	7.0	46	11.1
Age (years)								
≤29	229	21.2	99	16.6	22	31.0	108	26.2
30–39	302	28.0	165	27.7	15	21.1	122	29.5
40–49	288	26.7	187	31.4	18	25.4	83	20.1
≥50	130	12.0	88	14.8	5	7.0	37	9.0
missing data	130	12.0	56	9.4	11	15.5	63	15.3
Region								
urban	850	78.8	514	86.4	57	80.3	279	67.6
rural	208	19.3	63	10.6	14	19.7	131	31.7
other ^a	15	1.4	14	2.4	0	0.0	1	0.2
missing data	6	0.6	4	0.7	0	0.0	2	0.5
Current Employment								
community hospital	328	30.4	67	11.3	28	39.4	233	56.4
general hospital or women's and children's hospital	563	52.2	465	78.2	36	50.7	62	15.0
CDC	87	8.1	3	0.5	2	2.8	82	19.9
other	98	9.1	59	9.9	5	7.0	34	8.2
missing data	3	0.3	1	0.2	0	0.0	2	0.5
Education								
junior college	419	38.8	146	24.5	43	60.6	230	55.7
bachelor	566	52.5	389	65.4	22	31.0	155	37.5
master or doctor	67	6.2	54	9.1	4	5.6	9	2.2
other	26	2.4	6	1.0	2	2.8	18	4.4
missing data	1	0.1	0	0.0	0	0.0	1	0.2
Province^b								
Sichuan	398	36.9	116	19.5	18	25.4	264	63.9
Yunnan	278	25.8	244	41.0	26	36.6	8	1.9
Gansu	136	12.6	57	9.6	9	12.7	70	16.9
Guizhou	83	7.7	69	11.6	0	0.0	14	3.4
Xinjiang	74	6.9	44	7.4	8	11.3	22	5.3
Shannxi	58	5.4	49	8.2	2	2.8	7	1.7
Chongqing	52	4.8	16	2.7	8	11.3	28	6.8
Years in practice								
≤5	242	22.4	111	18.7	22	31.0	109	26.4
6–10	203	18.8	99	16.6	12	16.9	92	22.3
11–15	169	15.7	101	17.0	11	15.5	57	13.8
16–20	178	16.5	104	17.5	10	14.1	64	15.5
≥21	285	26.4	178	29.9	16	22.5	91	22.0
missing data	2	0.2	2	0.3	0	0.0	0	0.0

a: "other" means the combination zones between urban and rural areas; b: in our study, Sichuan province includes Chengdu (137), Deyang (103), Meishan (34) and Neijiang (124); Yunnan province includes Kunming (155), Dali (83) and Yuxi (40); Guizhou province includes Zunyi (83); Gansu province includes Lanzhou (136); Shannxi province includes Xi'an (58); Xinjiang Autonomous Region includes Urumchi (74); Chongqing (52) is a municipality.

Table 2. Knowledge of HPV, its vaccines and attitudes toward HPV vaccines among health care providers.

Total (N = 1079)		OB-GYNs (n = 595)		Pediatricians (n = 71)		Immunization services providers (n = 413)		χ^2 test
N	%	n	%	n	%	n	%	P value
Knowledge of HPV-Related Diseases								
1. What is the primary cause of cervical cancer? (HPV infection) ^b								
1015	94.1	564	94.8	69	97.2	382	92.5	.183 ^a
2. What are the most important two subtypes of high risk HPV? (HPV 16/18) ^b								
1007	93.3	570	95.8	61	85.9	376	91.0	<.001 ^a
3. What other diseases HPV can cause except for cervical cancer? (Anal cancer/Genital warts/carcinoma of the penis/Oropharyngeal cancer) ^b								
466	43.2	326	54.8	18	25.4	122	29.5	<.001
4. What is the most effective prevention from HPV infection? (HPV vaccine) ^b								
913	84.6	471	79.2	61	85.9	381	92.3	<.001
Knowledge of Epidemiology in HPV & Cervical Cancer								
5. What is the possibility that sexual active women would be infected by HPV in their lifetime, although 90% of the infection would be spontaneously regress within 12–24 months (Around 80%) ^b								
705	65.3	409	68.7	42	59.2	254	61.5	.031
6. What is the age distribution pattern of high risk HPV among Chinese women? (Bimodal distribution) ^b								
842	78.0	473	79.5	54	76.1	315	76.3	.438
7. What are the most important HPV subtypes that cause about 70% of cervical cancer worldwide? (HPV 16 and 18) ^b								
845	78.3	480	80.7	53	74.7	312	75.5	.112
Knowledge of HPV Vaccines								
8. Is HPV vaccine safe? (Yes)								
973	90.2	530	89.1	58	81.7	385	93.2	.004
9. Is HPV vaccine effective? (Yes)								
909	84.2	479	80.5	57	80.3	373	90.3	<.001
10. What are the possible side effects after HPV vaccination? (Local redness, swelling, heat and pain; fever, headache, vertigo) ^b								
810	75.1	439	73.8	50	70.4	321	77.7	.234
11. Is HPV test needed before HPV vaccination? (No) ^b								
545	50.5	258	43.4	31	43.7	256	62.0	<.001
12. Is HPV vaccine still recommended even with a positive HPV test or after treatment? (Yes) ^b								
889	82.4	490	82.4	58	81.7	341	82.6	.983
13. Is screening recommended after HPV vaccination? (Yes) ^b								
999	92.6	570	95.8	66	93.0	363	87.9	<.001
Attitudes toward HPV vaccines								
14. Are you willing to recommend HPV vaccination to your patients?								
799	74.1	414	69.6	52	73.2	333	80.6	<.001

a: Fisher's exact test; b: referential answer. Boldface reflects statistical significance.

Attitudes toward HPV vaccines

Of all, 74.1% of the health care providers would recommend HPV vaccination to their patients, and the immunization service providers (80.6%) were the most likely to do this (Table 2). When the remaining 25.9% were questioned about the reasons why they were not willing to recommend HPV vaccination, "Lack of relevant knowledge" (62.1%), "concerns on the efficacy and safety regarding HPV vaccines" (53.6%), and "do not want to be regarded as hard-selling because of its high price" (45.0%) were the top three obstacles (Table 3).

Influential factors of attitudes toward HPV vaccines

For social demographics, logistic regression revealed that education and specialty are the major influential factors of attitudes toward HPV vaccines. Health care providers with a bachelor's degree (OR = 2.97, $P = .043$), as well as a master's or doctor's degree (OR = 5.16, $P = .012$), were more likely to recommend HPV vaccination, compared with those with "other degree." OB-GYNs, according to our study, showed less willingness to recommend HPV vaccination (OR = 0.44, $P = .002$), compared with immunization services providers.

Guizhou Province was less likely to recommend HPV vaccination (OR = 0.30, $P = .021$), compared with Chongqing (Table 4).

Discussion

This is the first questionnaire-based evaluation on related knowledge, attitudes, and the reasons for not willing to recommend HPV vaccination among OB-GYNs, pediatricians, and immunization services providers in Western China. Therefore, our study aims to understand the current situation of the three groups regarding their ability to deliver accurate information on HPV and its vaccines, and provide a reference of a tailored evidence-based health educational intervention aimed at health care providers from different specialties.

In our study, the knowledge level about other HPV-related diseases excluding cervical cancer was quite low (43.2%), similar to some other studies that found significant gaps in knowledge regarding HPV protection against diseases other than cervical cancer.^{23,24} The low knowledge level regarding other HPV-related diseases was quite obvious among pediatricians (25.4%) and immunization services providers (29.5%), which may be because these groups do not have as much access to HPV-related training as OB-GYNs. However, even among OB-GYNs,

Table 3. Main reasons for health care providers not to recommend HPV vaccination.^a

	Total (N = 280)		OB-GYNs (n = 181)		Pediatricians (n = 19)		Immunization services providers (n = 80)		χ^2 test P value
	N	%	n	%	n	%	n	%	
1	Lack of relevant knowledge about HPV vaccines.								
	174	62.1	110	60.8	13	68.4	51	63.8	.759
2	Concerns on the efficacy and safety.								
	150	53.6	102	56.4	12	63.2	36	45.0	.163
3	Do not want to be regarded as hard-selling because of the high price.								
	126	45.0	81	44.8	8	42.1	37	46.3	.942
4	It is not convenient to talk about because it is sexual related.								
	40	14.3	19	10.5	5	26.3	16	20.0	.030^b
5	Patients are not knowledgeable about HPV, so it is a waste of time to talk to them.								
	33	11.8	16	8.8	4	21.1	13	16.3	.078 ^b
6	Screening is enough, so there is no need for HPV vaccination.								
	23	8.2	13	7.2	1	5.3	9	11.3	.585 ^b

a: "not to recommend HPV vaccination" including "not to recommend" and "not clear"; b: Fisher's exact test. Boldface reflects statistical significance.

Table 4. Logistic Regression for social demographics of attitudes toward HPV vaccines.

Characteristics	OR	95%CI	P value	
Gender				
male	0.66	0.32	1.34	.245
female	1			
Age (years)				
≤29	0.78	0.26	2.35	.664
30–39	1.06	0.44	2.54	.904
40–49	1.11	0.63	1.94	.727
≥50	1			
Region				
urban	0.20	0.03	1.60	.129
rural	0.19	0.02	1.55	.120
other ^a	1			
Current Employment				
community hospital	1.20	0.65	2.23	.557
general hospital or women's and children's Hospital	1.77	1.00	3.13	.050
CDC	2.34	0.79	6.90	.124
other	1			
Education				
junior college	2.10	0.75	5.91	.158
bachelor	2.97	1.04	8.52	.043
master or doctor	5.16	1.43	18.59	.012
other	1			
Province				
Sichuan	0.71	0.28	1.76	.457
Yunnan	0.44	0.18	1.11	.081
Gansu	0.40	0.15	1.02	.054
Guizhou	0.30	0.11	0.83	.021
Xinjiang	2.41	0.56	10.34	.235
Shannxi	0.39	0.14	1.11	.076
Chongqing	1			
Years in practice				
≤5	1.50	0.53	4.25	.448
6–10	1.29	0.54	3.10	.571
11–15	1.21	0.56	2.63	.631
16–20	1.38	0.78	2.46	.272
≥21	1			
Specialty				
OB-GYNs	0.44	0.26	0.74	.002
pediatricians	0.65	0.31	1.36	.254
immunization services providers	1			

a: "other" means the combination zones between urban and rural areas. Boldface reflects statistical significance.

the knowledge level was not high, as only about half (54.8%) were aware of the added protection that the vaccine provides against other diseases, which is similar to another study.²³

Increasing coverage of HPV vaccination in females at the routine age of 11 or 12 and catch-up vaccination through age 26 will contribute to a further reduction in cervical precancers,²⁵ which highlights the importance of OB-GYNs and pediatricians.

However, in our study, only nearly eighty percent of OB-GYNs (79.2%) and pediatricians (85.9%) knew that HPV vaccination is the most effective way to prevent HPV infection. Additionally, only around seventy percent of OB-GYNs (69.6%) and pediatricians (73.2%) were willing to recommend HPV vaccination. According to the influential factors, although there was no significant association between pediatricians and attitudes toward

HPV vaccines, it may be caused by insufficient samples of pediatricians. Therefore, it is suggested that pediatricians and OB-GYNs, whose practice mainly deals with children including teenagers, as well as women, held particularly negative attitudes toward HPV vaccines. This finding poses an alarming signal to the Chinese government if the World Health Organization (WHO) recommends that the target population is to be significantly covered by vaccination. Fortunately, in our study, we also explored the reasons why they were not willing to recommend the vaccination, on which basis we proposed the possible solutions. The primary reason not to recommend HPV vaccination was the lack of relevant knowledge, for 60.8% of OB-GYNs and 68.4% of pediatricians among the unwilling population admitted to this. Therefore, we recommend that more tailored health education aimed at health care providers, especially for OB-GYNs and pediatricians, should be one of the interventions to eliminate their false beliefs and to, therefore, increase the vaccination coverage.

The efficacy and safety of the HPV vaccines have been already confirmed.^{5,6,26} Moreover, even when inadvertently administered in pregnancy or during the preconception period, HPV vaccines were not associated with adverse pregnancy or birth outcomes.²⁷ However, such information has not been delivered efficiently to the public or even to some health care providers. On the one hand, for the public, a previous study has reported that when parents were asked about their most pressing concerns about HPV vaccines from their children's health care providers, their answers were safety and side effects.²⁸ For health care providers from our study, on the other hand, insufficient knowledge level (75.1%) regarding side effects and "concerns on the efficacy and safety" (which was the second important reason not to recommend, as half (53.6%) of the unwilling population indicated), indirectly led to the reduced acceptance of HPV vaccination by the public. Therefore, our study suggests that health care providers in Western China need to be better informed regarding HPV vaccine-related knowledge in the future process of health education, especially about the efficacy and safety.

The age distribution of HPV prevalence among Chinese women is bimodal, with one peak around 20 years and the other around 45 years,²⁹ which poses great challenges for HPV prevention in the Chinese population as well as in other populations that share a similar distribution pattern. Currently, no HPV vaccine on the market covers all types of hr-HPV that cause cervical cancer, which means that screening after vaccination is still necessary. In our study population, 22% of practitioners reported to have never heard about the "bimodal distribution," and 7.4% thought that "screening is no longer needed after HPV vaccination" which was even worse among the immunization services providers (12.1%). Therefore, primary prevention via vaccination plus secondary prevention via screening should both be taken into consideration in the future for cervical cancer-related training.

Apart from the lack of knowledge and concerns on efficacy and safety, price is the third most important reason that led to the unwillingness to recommend vaccination among the practitioners. Therefore, a two-dose schedule should be considered,³⁰ or a novel co-sharing price mechanism as well as an expanded EPI

(Expanded Program on Immunization), should also be thought about to reduce the price. Additionally, more cost-effective vaccines, such as domestic or bivalent vaccines, are recommended to stakeholders if decent vaccination coverage is expected.

There were some limitations to our study. First, to ensure feasibility, this study was conducted in only one or two local hospitals, which may result in a lack of representation by our study. Second, there was a small sample size of pediatricians involved in our study, which may also reduce our persuasiveness.

One of the major strengths of this study is that this is the first study to investigate the knowledge of HPV, its vaccines, and attitudes toward HPV vaccines among OB-GYNs, pediatricians, and immunization services providers in Western China. This study helps to provide important information to policymakers on how important health education is if future decent coverage of HPV vaccination is expected, and it also provides the reference of a tailored evidence-based health educational intervention aimed at health care providers from different specialties.

Conclusion

Our results indicated that the health care providers in Western China did not have adequate knowledge of HPV and its vaccines in depth. Our results also showed that around 30% of OB-GYNs and pediatricians were not willing to recommend HPV vaccination due to lack of knowledge, as well as doubts on safety and efficacy, posing a great challenge for cervical cancer control in less developed areas. Therefore, more tailored and specific health educations targeting health care providers to eliminate their prejudices and false beliefs are of great importance.³¹ Price is another issue that should be taken into consideration by stakeholders if decent vaccination coverage is to be expected in the future, especially in resource-limited areas of China.

Contribution to authorship

This was a nationwide study conducted by Professor YLQ. JL was responsible for the west China study. JL helped with the writing and revision of this manuscript. JQM collected data, performed the statistical analysis and drafted the manuscript. XZ, WW, RZ, LS, YCL, XHW, YJL, WZ, XLL, MNW, HC, JZ participated in data collection. And HC also helped to revise the manuscript.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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References

- Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin*. 2015;65(2):87–108. doi:10.3322/caac.21262.
- Shi JF, Qiao YL, Smith JS, Dondog B, Bao YP, Dai M, Clifford GM, Franceschi S. Epidemiology and prevention of human papillomavirus and cervical cancer in China and Mongolia. *Vaccine*. 2008;26(Suppl 12):M53–9. doi:10.1016/j.vaccine.2008.05.009.
- Arbyn M, Weiderpass E, Bruni L, de Sanjose S, Saraiya M, Ferlay J, Bray F. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob Health*. 2020;8(2):e191–e203. doi:10.1016/S2214-109X(19)30482-6.
- Kjaer SK, Frederiksen K, Munk C, Iftner T. Long-term absolute risk of cervical intraepithelial neoplasia grade 3 or worse following human Papillomavirus infection: role of persistence. *JNCI J National Cancer Inst*. 2010;102(19):1478–88. doi:10.1093/jnci/djq356.
- Medeiros LR, Rosa DD, Da RM, Bozzetti MC, Zanini RR. Efficacy of human papillomavirus vaccines: a systematic quantitative review. *Int J Gynecol Cancer*. 2009;19(7):1166–76. doi:10.1111/IGC.0b013e3181a3d100.
- Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Wheeler CM, Perez G, Brown DR, Koutsky LA, Tay EH, Garcia P. A pooled analysis of continued prophylactic efficacy of quadrivalent human Papillomavirus (Types 6/11/16/18) vaccine against high-grade cervical and external genital lesions. *Cancer Prev Res*. 2009;2(10):868–78. doi:10.1158/1940-6207.CAPR-09-0031.
- Li W, Nowak G, Jin Y, Cacciatore M. Inadequate and incomplete: Chinese Newspapers' Coverage of the First Licensed Human Papillomavirus (HPV) Vaccine in China. *J HEALTH COMMUN*. 2018;23(6):581–90. doi:10.1080/10810730.2018.1493060.
- Li K, Li Q, Song L, Wang D, Yin R. The distribution and prevalence of human papillomavirus in women in mainland China. *Cancer*. 2019;125(7):1030–37. doi:10.1002/cncr.32003.
- Wang R, Pan W, Jin L, Huang W, Li Y, Wu D, Gao C, Ma D, Liao S. Human papillomavirus vaccine against cervical cancer: opportunity and challenge. *Cancer Lett*. 2020;471:88–102. doi:10.1016/j.canlet.2019.11.039.
- China Food and Drug Administration. The license of human papillomavirus bivalent(types 16, 18) vaccine was approved by CFDA. <https://www.nmpa.gov.cn/directory/web/nmpa/yaowen/ypjgw/20191231160701608.html>.
- Zhang Y, Wang Y, Liu L, Fan Y, Liu Z, Wang Y, Nie S. Awareness and knowledge about human papillomavirus vaccination and its acceptance in China: a meta-analysis of 58 observational studies. *BMC Public Health*. 2016;16:216. doi:10.1186/s12889-016-2873-8.
- Abou El Ola M, Rajab A, Abdallah D, Fawaz I, Awad L, Tamim H, Ibrahim A, Mugharbil A, Moghnieh R. Low rate of human papillomavirus vaccination among schoolgirls in Lebanon: barriers to vaccination with a focus on mothers' knowledge about available vaccines. *Ther Clin Risk Manage*. 2018;14:617–26. doi:10.2147/TCRM.S152737.
- Gidengil C, Chen C, Parker AM, Nowak S, Matthews L. Beliefs around childhood vaccines in the United States: a systematic review. *VACCINE*. 2019;37(45):6793–802. doi:10.1016/j.vaccine.2019.08.068.
- Liu CR, Liang H, Zhang X, Pu C, Li Q, Li QL, Ren F-Y, 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):488. doi:10.1186/s12889-019-6823-0.
- Yu Y, Xu M, Sun J, Li R, Li M, Wang J, Zhang D, Xu A. Human Papillomavirus infection and vaccination: awareness and knowledge of HPV and acceptability of HPV vaccine among mothers of teenage daughters in Weihai, Shandong, China. *Plos One*. 2016;11(1):e0146741. doi:10.1371/journal.pone.0146741.
- Li J, Kang LN, Li B, 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;15:691. doi:10.1186/s12885-015-1682-2.
- Santhanes D, Wong CP, Yap YY, San SP, Chaiyakunapruk N, Khan TM. Factors involved in human papillomavirus (HPV) vaccine hesitancy among women in the South-East Asian Region (SEAR) and Western Pacific Region (WPR): a scoping review. *Hum Vacc Immunother*. 2017;14(1):124–33. doi:10.1080/21645515.2017.1381811.
- Galbraith KV, Jenerette CM, Moore LAD, Palmer MH, Hamilton JB. Parental acceptance and uptake of the HPV vaccine among African-Americans and Latinos in the United States: a literature review. *Soc Sci Med*. 2016;159:116–26. doi:10.1016/j.socscimed.2016.04.028.
- Romaguera J, Caballero-Varona D, Tortolero-Luna G, Marrero E, Suárez E, Pérez CM, Muñoz C, Palefsky J, Ortiz AP. Factors associated with HPV vaccine awareness in a population-based sample of hispanic women in puerto rico. *J Racial Ethnic Health Disparities*. 2016;3(2):281–90. doi:10.1007/s40615-015-0144-5.
- Unger Z, Maitra A, Kohn J, Devaskar S, Stern L, Patel A. Knowledge of HPV and HPV vaccine among women ages 19 to 26. *Women's Health Issues*. 2015;25(5):458–62. doi:10.1016/j.whi.2015.06.003.
- Maier C, Maier T, Neagu CE, Vlădăreanu R. Romanian adolescents' knowledge and attitudes towards human papillomavirus infection and prophylactic vaccination. *Eur J Obstet Gyn R B*. 2015;195:77–82. doi:10.1016/j.ejogrb.2015.09.029.
- Chang J, Hou Z, Fang H, Meng Q. Are providers' recommendation and knowledge associated with uptake of optional vaccinations among children? A multilevel analysis in three provinces of China. *Vaccine*. 2019;37(30):4133–39. doi:10.1016/j.vaccine.2019.05.070.
- Saraiya M, Rosser JJ, Cooper CP, Cancers That US. Physicians believe the HPV vaccine prevents: findings from a physician survey, 2009. *J Women's Health*. 2012;21(2):111–17. doi:10.1089/jwh.2011.3313.
- Tolunay O, Celik U, Karaman SS, Celik T, Resitoglu S, Donmezer C, Aydin F, Baspinar H, Mert MK, Samsa H. Awareness and attitude relating to the human papilloma virus and its vaccines among pediatrics, obstetrics and gynecology specialists in Turkey. *Asian Pac J Cancer Prev*. 2015;15(24):10723–28. doi:10.7314/APJCP.2014.15.24.10723.
- McClung NM, Gargano JW, Park IU, Whitney E, Abdullah N, Ehlers S, Bennett NM, Scahill M, Niccolai LM, Brackney M, et al. Estimated number of cases of high-grade cervical lesions diagnosed among Women-United States, 2008 and 2016. *MMWR Morb Mortal Wkly Rep*. 2019;68(15):337–43. doi:10.15585/mmwr.mm6815a1.
- Zhu F, Chen W, Hu Y, Hong Y, Li J, Zhang X, Zhang Y-J, Pan Q-J, Zhao F-H, Yu J-X, et al. Efficacy, immunogenicity and safety of the HPV-16/18 AS04-adjuvanted vaccine in healthy Chinese women aged 18–25 years: results from a randomized controlled trial. *Int J Cancer*. 2014;135(11):2612–22. doi:10.1002/ijc.28897.
- Lipkind HS, Vazquez-Benitez G, Nordin JD, Romitti PA, Naleway AL, Klein NP, Hechter RC, Jackson ML, Hambidge SJ, Lee GM, et al. Maternal and infant outcomes after human papillomavirus vaccination in the periconceptional period or during pregnancy. *Obstet Gynecol*. 2017;130(3):599–608. doi:10.1097/AOG.0000000000002191.
- Shah PD, Calo WA, Gilkey MB, Boynton MH, Alton DS, Todd KG, Robichaud MO, Margolis MA, Brewer NT. Questions and Concerns About HPV Vaccine: a Communication Experiment. *PEDIATRICS*. 2019;143(2):e20181872. doi:10.1542/peds.2018-1872.
- Zhao F, Lewkowitz AK, Hu S, Chen F, Li L, Zhang Q, Wu R-F, Li C-Q, Wei L-H, Xu A-D, et al. Prevalence of human papillomavirus and cervical intraepithelial neoplasia in China: a pooled analysis of 17 population-based studies. *International Journal of Cancer*. 2012;131(12):2929–38. doi:10.1002/ijc.27571.
- Mariani L, Preti M, Cristoforoni P, Stigliano CM, Perino A. Overview of the benefits and potential issues of the nonavalent HPV vaccine. *Int J Gynecol Obstet*. 2017;136(3):258–65. doi:10.1002/ijgo.12075.
- Abi Jaoude J, Khair D, Dagher H, Saad H, Cherfan P, Kaafarani MA, Jamaluddin Z, Ghattas H. Factors associated with Human Papilloma Virus (HPV) vaccine recommendation by physicians in Lebanon, a cross-sectional study. *Vaccine*. 2018;36(49):7562–67. doi:10.1016/j.vaccine.2018.10.065.