

Original Research

Human papillomavirus vaccine uptake in South Korea

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Abstract

Background: This study aimed to assess the human papillomavirus (HPV) vaccine uptake rate in South Korean women and to identify factors affecting vaccination rate before initiation of the national HPV vaccination as a National Immunization Program (NIP) in Korea.**Materials and methods:** We conducted online survey in February 2016 with questions to 2000 women aged between 9 and 59 years in South Korea by distribution of age and region, to assess HPV uptake and associated correlates such as age, residential region, education, and socioeconomic status. **Results:** The overall HPV vaccine received at least 1 dose rate was 23.1%, and the highest rate of vaccination was observed in women aged 20–29 years (38.6%), followed by those aged 30–39 years (36.9%), 9–19 years (16.9%), 40–49 years (14.2%), and 50–59 years (12.5%). Factors affecting HPV vaccination included metropolitan cities (odds ratio [OR] = 1.44, 95% confidence interval [CI], 1.15–1.80), university graduate (OR = 1.45, 95% CI, 1.06–2.00), regular influenza vaccination (OR = 2.11, 95% CI, 1.64–2.70), visited clinic within the last 6 months (OR = 1.73, 95% CI, 1.20–2.51) and high family income (OR = 1.55, 95% CI, 1.01–2.37). **Conclusion:** HPV vaccine uptake is low in South Korean women. Correct publicity, education and economic support programs for HPV vaccine could play an important role in increasing HPV vaccine uptake in South Korea.**Keywords:** Human papillomavirus; HPV; Vaccination; Vaccine uptake; Korean

1. Introduction

The fourth most common cancer in worldwide women is cervical cancer which is accounted for 604,127 new cases and 341,831 deaths in 2020 [1]. In South Korean women, cervical cancer is eighth most common cancer which is accounted for 3500 new cancers and 845 deaths in 2018 [2]. Human papillomavirus (HPV) is detected in 99% of all cervical cancer patients, and 70% of the cervical cancer cases are associated with HPV type 16 and 18 [3–5]. HPV vaccination can reduce the cervical cancer by preventing cervical intraepithelial neoplasia (CIN), and long-term clinical efficacy studies in naive populations have shown 90–100% efficacy of the HPV vaccine against CIN2 or CIN3 [6].

The quadrivalent HPV vaccine was approved by the United States Food and Drug Administration in 2006, the bivalent HPV vaccine was licensed in 2009, and the 9-valent HPV vaccine was licensed in 2014. The Advisory Committee on Immunization Practices recommends routine vaccination for girls aged 11–12 years, and “catch-up” vaccination for women aged 13–26 years with these HPV vaccines [7]. In Korea, The Korea Society of Gynecology Oncology has recommended a quadrivalent and bivalent vaccine to 9–26 years old women. In middle-aged women, the followings were recommended. HPV preventive vac-

cine has a preventive effect in middle-aged women (27 to 45 years); before vaccination, a clinical assessment of individual patient risk and state of inoculation should be performed [8]. HPV vaccination was provided through both public and private sector in South Korea. The cost of vaccine was about 150,000–200,000 KRW (about 150 US Dollar) for the 1 dose of vaccination.

Nowadays, the HPV vaccine is covered by national vaccination programs in many developed countries. In some countries, such HPV vaccination programs are offered through schools (e.g., Australia, UK, Portugal), and the coverage rate (3 doses) of HPV vaccination in these countries is 64–81% [9]. HPV vaccination was scheduled to be covered by the National Immunization Program (NIP) in South Korea from the June, 2016. Reliable data on the HPV vaccination rate before NIP remains unavailable. An analysis of the HPV vaccine uptake status and associated factors will be important to implement the National HPV vaccination program successfully.

This study aimed to assess the HPV vaccine uptake rate in South Korean women and to identify factors that affected the vaccine uptake before the NIP began through a sample survey.



Table 1. HPV vaccine uptake by characteristics.

Factors	Received ≥ 1 dose		p^\dagger	Received 3 doses		p^\dagger
	N = 2000*	(%)		N = 2000*	(%)	
Age (years)			<0.001			<0.001
9–19	54/319	(16.9)		20/319	(6.3)	
20–29	134/346	(38.6)		101/346	(29.0)	
30–39	151/408	(36.9)		106/408	(25.9)	
40–49	68/477	(14.2)		38/477	(8.0)	
50–59	56/450	(12.5)		18/450	(4.1)	
Area of residence			0.003			0.009
Rural area [‡]	220/1075	(20.5)		132/1075	(12.2)	
Metropolitan city	242/925	(26.2)		151/925	(16.3)	
Educational level			<0.001			<0.001
\leq High school	62/447	(13.9)		23/447	(5.1)	
\geq College	385/1449	(26.6)		252/1449	(17.4)	
Income per month (USD) [§]			<0.001			0.002
<2600	116/585	(19.8)		73/585	(12.5)	
≥ 2600 , <4300	146/707	(20.6)		83/707	(11.7)	
≥ 4300 , <7000	147/535	(27.5)		90/535	(16.9)	
≥ 7000	53/172	(30.8)		36/172	(20.9)	
Family history of cervical cancer			0.222			0.354
No	395/1652	(23.9)		252/1652	(15.3)	
Yes	32/112	(29.0)		13/112	(12.0)	
Visited a clinic in last 6 months			<0.001			0.003
No visits	43/299	(14.2)		26/299	(8.7)	
Once or more	420/1701	(24.7)		257/1701	(15.1)	
Regular influenza vaccination			<0.001			0.006
No	288/1413	(20.4)		180/1413	(12.7)	
Yes	174/587	(29.6)		103/587	(17.5)	

*The numbers do not add up to 2000 due to missing data and rounding.

[†]Chi-square test was used for comparison ($p < 0.05$ considered statistically significant).

[‡]Rural area defined as areas outside metropolitan cities and includes the nine “do” (administrative districts of South Korea).

[§]The average monthly household income in South Korea is approximately 3800 USD (in January 2016, data obtained from the Korean statistical information service).

2. Materials and methods

2.1 Population

We have set the target sample size as 2000. Sample size of about 385 will give a sufficient sample size to draw assumptions of nearly any population size at the 95% confidence level with a 5% margin of error. We were looking to draw comparisons between different five sub-age groups (Table 1), assigned about 400 per subgroup, and set 2000 as the sample size.

We conducted the study with survey agency (Invight Inc., Seoul, <http://www.invight.co.kr>) which has panels of 800,000 registered survey participants. We emailed link to the online survey to 10,000 women, and the data was collected until target sample number for each age and regional group except for samples with less sincerity in the response through verification work by survey agency. A total replies of 2000 South Korean women aged between 9 and 59 years were obtained based on regional and age dis-

tribution of South Korea (Table 1) among panels (Response rate: 20%). The survey subjects were randomly extracted by a panel management program of survey agency according to the age distribution and regional distribution ratio of the Korean population. The regional and age distribution of the study population was based the Korean census data [10].

Details of the panels are as follows. Panels are South Korean who living in South Korea. The survey agency has accumulated panels for over 10 years through systematic probabilistic sampling to achieve the sample representativeness. The survey agency has sent invitation E mails to members of website and portal site asking to participate in particular survey. Then, respondents who completed particular survey and were willing to participate in the next survey were enrolled as panels.

We did not include personally identifiable information in the survey, and our research involved no more than

minimal risk to the subject. The institutional review board waived the need for consent forms for this study. We explained at the beginning of the survey that this survey is for medical research and does not include any personal information.

2.2 Survey

We emailed a link to the online survey to the chosen study population in February 2016. The survey questionnaire included information on HPV vaccination status, age, region of residence, education, monthly family income, visited a clinic in last 6 months, regular influenza vaccination, HPV vaccination doses (initiation or completion), type of vaccination, reasons for HPV vaccine, place of vaccination, and the main reason for remaining unvaccinated against HPV. For the subjects in the 9–16 years age group, survey was administered to mothers who had 9–16-year-old daughters.

2.3 Statistical analysis

A chi-square or a Fisher's exact test was performed to compare categorical variables. Multivariate logistic regression analysis was used to identify correlates of HPV vaccine uptake. The differences were considered statistically significant if the $p < 0.05$. All analyses were performed using the SPSS version 22.0.0.1 (SPSS Inc., IBM corp., Chicago, IL, USA).

3. Results

3.1 HPV vaccine initiation rate by age group and region

In this survey, the overall HPV vaccine initiation rate was estimated at 23.1%. The HPV vaccine uptake was significantly lower in women aged 9 to 19 years compared to that in women aged 20 to 29 years (16.9% vs. 38.6%, $p < 0.001$) and 30 to 39 years (16.9% vs. 36.9%, $p < 0.001$) (Table 1). Women living in the metropolitan cities were more likely to receive the HPV vaccine than those living in the rural areas (26.2% vs. 20.5%, $p = 0.003$) (Table 1). Proportion of respondents who had taken at least one dose (462) completed the schedule (283) was 61.2%.

3.2 Factors associated with HPV vaccine initiation

Area of residence ($p = 0.003$), education level ($p < 0.001$), monthly income ($p < 0.001$), recently clinic visit ($p < 0.001$), regular vaccination ($p < 0.001$) were associated with high HPV vaccine initiation rate (Tables 1,2).

3.3 Factors affecting the completion of the 3-dose HPV vaccine regimen

Area of residence, educational level, monthly income, clinic visit in the last 6 months, and regular influenza vaccination were all associated significantly with the completion of the 3-dose vaccination regimen in a univariate analysis (Table 1) and multivariate logistic regression analysis (Table 2).

3.4 Characteristics associated with HPV vaccination

Table 3 shows that the most common reason for their unvaccinated status was the cost (24.3%), followed by concern about safety (23.1%).

4. Discussion

To our knowledge, our study is the first report about HPV vaccine uptake in South Korea before the NIP began. Our results showed that the HPV vaccine uptake at least one dose among South Korean women was low (23.1%), especially among women aged 9–19 years (16.9%), compared to the coverage rates reported in countries that have implemented a national HPV vaccination program. In the United States, among the 13–17-year-old women, the HPV vaccination coverage rate (at least 1 dose) was 60.0% and the rate of complete vaccination was 69.3% [11]. In Australia, among girls who turned 15 in the year 2015, the coverage rate of single dose HPV vaccination was 85.6%, while the coverage rate of 3-dose vaccination was 77.4% [12]. Netherlands, Italy, and Denmark offer HPV vaccination through health care providers, and the coverage rate of the 3-dose HPV vaccination in teenage girls from these countries is 45–58% [9,13]. The vaccine delivery strategies employed by the national vaccination programs play a major role in determining the vaccination coverage. HPV vaccination was scheduled to be covered by the NIP for 12 years old girls in South Korea from the June, 2016. HPV vaccination rate of 12 years old girls in South Korea is 83.5% in October, 2019 [14].

HPV vaccine is most effective when administered to adolescent girls before their first sexual contact [7,15]. As vaccination at this age results in higher antibody titers than vaccination at an older age [16], most national HPV vaccination programs target adolescent girls in their early teens. Further, because the non-inferior antibody levels after HPV vaccination were shown in women 27–45 years compared with women 16–26 years of age, HPV vaccine is also important in adult women [17].

In our study, vaccination rate was significantly lower in aged 9–19 years compared with subjects aged 20–39 years. Among unvaccinated 9–19-year-old girls, “concerned about vaccine safety” was the most common reason for remaining unvaccinated (27.1%, data not shown). This result indicates that the availability of accurate information on HPV vaccine safety is important in increasing vaccine uptake. A previous study also suggests that the vaccine uptake in adolescent females may reflect the knowledge and attitude of parents or healthcare providers regarding the HPV vaccine [18]. According to a recent updated review, the risk-benefit profile for HPV vaccines remains highly favorable. There was no consistent evidence of an increased risk of any adverse event of special interest, including demyelinating syndromes or neurological conditions such as complex regional pain or postural orthostatic tachycardia syndrome [19].

Table 2. Multivariate logistic regression analysis to identify factors associated with HPV vaccine uptake.

Factors	Received ≥ 1 dose		<i>p</i>	Received 3 doses		<i>p</i>
	Adjusted OR*	(95% CI)		Adjusted OR*	(95% CI)	
Age (years)						
9–19		Reference			Reference	
20–29	4.12	(2.65–6.42)	<0.001	9.91	(5.12–19.15)	<0.001
30–39	3.62	(2.36–5.57)	<0.001	8.05	(4.21–15.40)	<0.001
40–49	1.04	(0.67–1.64)	0.853	2.15	(1.08–4.28)	0.029
50–59	0.86	(0.54–1.37)	0.529	1.01	(0.47–2.17)	0.973
Area of residence						
Rural area [†]		Reference			Reference	
Metropolitan city	1.44	(1.15–1.80)	0.002	1.44	(1.10–1.90)	0.009
Educational level						
\leq High school		Reference			Reference	
\geq College	1.45	(1.06–2.00)	0.021	2.25	(1.41–3.59)	0.001
Income per month (USD) [‡]						
<2600		Reference			Reference	
≥ 2600 , <4300	1.16	(0.86–1.57)	0.319	1.07	(0.74–1.54)	0.713
≥ 4300 , <7000	1.57	(1.15–2.14)	0.004	1.52	(1.05–2.20)	0.027
≥ 7000	1.55	(1.01–2.37)	0.043	1.81	(1.11–2.96)	0.017
Visited a clinic in last 6 months						
No visits		Reference			Reference	
Once or more	1.73	(1.20–2.51)	0.004	1.57	(0.99–2.48)	0.054
Regular influenza vaccination						
No		Reference			Reference	
Yes	2.11	(1.64–2.70)	<0.001	2.12	(1.57–2.87)	<0.001

*Multivariate logistic regression analysis was used. Family history of cervix cancer was excluded from the multivariate regression model due to univariate $p > 0.200$.

[†]Rural areas include the nine “do” (administrative districts of South Korea), excluding the metropolitan cities.

[‡]Average South Korean monthly household income is approximately 3800 USD (in January 2016, based on data from the Korean statistical information service).

OR, odds ratio; CI, confidence interval.

Previous studies from the United States have reported that rural regions are at a disadvantage as they have fewer health care providers and women have to travel longer distances to access health care [20–22]. In our study, the HPV vaccine uptake rate was higher in the six metropolitan cities than in other regions ($p = 0.003$). Fewer health care providers, public relations, and HPV vaccine related awareness may be the reasons for the low HPV vaccine uptake in the rural regions of the South Korea.

It was reported that vaccine uptake was affected by various factors including race, age, knowledge of HPV vaccination among adolescents and their parents, and health care utilization [9]. In our study, higher educational status and family income were both significantly associated with HPV vaccine uptake. In South Korea, universal health insurance is provided to all people regardless of income level or health risk. However, HPV vaccine is not applicable before the NIP began. So, economic issue may play a role on vaccine uptake rate. In our survey, the cost of the vac-

cine was one of the main reasons for withholding vaccine uptake in the unvaccinated women (24.1%). The NIP of South Korea offer complimentary HPV vaccination by bivalent or quadrivalent vaccine to 11 and 12-year-old girls through health care providers. The complimentary vaccination could solve the effect of economic disparity on vaccine uptake. Preventive health behaviors such as “clinic visit within the last 6 months”, “regular influenza vaccination” were associated with the HPV vaccine coverage rate in our results. These results are consistent with several previous studies [23–25]. Family history of cervical cancer was not associated with uptake of the HPV vaccine in our result. In previous report, family history of cervical cancer was associated with positive attitudes for HPV vaccine [26]. We think that this did not lead to actual vaccination in our study. It would have been affected by the high cost of HPV vaccine, the fear of side effects and lack of knowledge about HPV vaccine as shown in Table 3.

Table 3. Characteristics associated with HPV vaccination.

Characteristics	N	(%)
The type of vaccine	N = 462	
Bivalent vaccine	84	(18.3)
Quadrivalent vaccine	231	(49.9)
Do not know	147	(31.8)
Place of vaccination	N = 462	
Obstetrics and gynecology clinic	205	(44.5)
General hospital	92	(19.8)
Public health care center	51	(11.0)
Other clinic	47	(10.2)
University hospital	42	(9.1)
Pediatric clinic	25	(5.4)
Reasons for vaccination	N = 462	
Internet or television	231	(49.9)
Recommended by physician	101	(21.9)
Group vaccination (school or office)	61	(13.2)
Recommended by acquaintance	39	(8.4)
Promotional material from vaccine manufacturing company	26	(5.7)
Other	4	(0.9)
Reasons reported by women who remaining unvaccinated	N = 1538	
Cost	373	(24.3)
Concerned about safety	355	(23.1)
Did not have a specific chance to obtain vaccination	329	(21.4)
Do not know about vaccine	187	(12.2)
Unconcerned	179	(11.7)
Others (details below)	115	(7.5)
Old age	46	
Having a plan to get vaccine	16	
Thought HPV vaccine was unnecessary	10	
History of a uterine surgery	9	
Concerned about effectiveness	7	
Have regular screening test	6	
Concerned about pain	5	
Virgin	4	
I don't know	4	
Thought hasn't been long since the vaccine approved	1	
Thought I've been vaccinated, but I'm not sure	1	
Uncomfortable going to gynecology clinic	1	
There were several reasons	1	
Planning pregnant soon	1	
I have a lot of knowledge about HPV vaccine	1	
Process of vaccination was difficult	1	
I don't have cervical cancer	1	

Our study has several limitations. The survey agency accumulated the panels over a period of more than 10 years through a systematic probabilistic sampling to achieve sample representativeness. However, owing to the self-reported online nature of the survey, the representativeness of the survey panels and the reliability of replies may be limiting.

As our study population included a wide age range, some of the age-based subgroups comprised a very small number of samples, and this may have decreased the statistical reliability of some of our results.

5. Conclusions

Based on our results, the HPV vaccine uptake rate in South Korean women is low, especially in adolescent girls or women living in the rural regions. Our study identified various demographic, socioeconomic, preventive health behavioral factors, cost to vaccination and concerning about vaccine side effect were affected the HPV vaccine uptake rate in South Korean women. The national HPV vaccination program will improve the vaccine uptake rate by overcoming barriers to costs. Therefore, it seems necessary to promote and educate parents, health care providers, as well as women, about effect of HPV vaccination, NIP, correct information about side effect of HPV vaccine. This could solve the problem of situation that people are hesitant to vaccinate due to the concerns about side effects and difference of vaccine uptake by region. This study is the first to report data on HPV vaccination rate by distribution of age and region in South Korean women before the NIP began. And our data could help to lay essential groundwork for future research on HPV vaccination in South Korea.

Author contributions

CJY, KMS, KBS, JSJ, SDH, and NJH conceived and designed the study. CJY, SDH, NJH, KKD, and KYB collected the data, and all authors analyzed and interpreted the data. CJY, JSJ, SDH, and NJH reviewed all statistical analysis. CJY and NJH wrote the manuscript; all authors approved the final version of the submitted manuscript.

Ethics approval and consent to participate

This retrospective study was granted ethical approval by the Institutional Review Board approval (IRB number: X-1601/332-9021), and the study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments. We did not include personally identifiable information in the survey, and our research involved no more than minimal risk to the subject. The institutional review board waived the need for consent forms for this study.

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Conflict of interest

The authors declare no conflict of interest.

References

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al.* Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in

- 185 Countries. *CA: A Cancer Journal for Clinicians*. 2021; 71: 209–249.
- [2] Hong S, Won Y, Lee JJ, Jung K, Kong H, Im J, *et al.* Cancer Statistics in Korea: Incidence, Mortality, Survival, and Prevalence in 2018. *Cancer Research and Treatment*. 2021; 53: 301–315.
- [3] Scheurer ME, Tortolero-Luna G, Adler-Storthz K. Human papillomavirus infection: biology, epidemiology, and prevention. *International Journal of Gynecological Cancer*. 2005; 15: 727–746.
- [4] Schiffman M, Kjaer SK. Chapter 2: Natural History of Anogenital Human Papillomavirus Infection and Neoplasia. *JNCI Monographs*. 2003; 2003: 14–19.
- [5] zur Hausen H. Papillomaviruses in human cancers. *Proceedings of the Association of American Physicians*. 1999; 111: 581–587.
- [6] Angioli R, Lopez S, Aloisi A, Terranova C, De Cicco C, Scaletta G, *et al.* Ten years of HPV vaccines: State of art and controversies. *Critical Reviews in Oncology/Hematology*. 2016; 102: 65–72.
- [7] Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER. Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR. Recommendations and Reports*. 2007; 56: 1–24.
- [8] Min K, Kwon S, Kim S, Kim HJ, Seong SJ, Song YJ, *et al.* Preventive vaccination against cervical cancer: Korean Society of Gynecologic Oncology Guideline. *Journal of Gynecologic Oncology*. 2016; 27: e30.
- [9] Kessels SJM, Marshall HS, Watson M, Braunack-Mayer AJ, Reuzel R, Tooher RL. Factors associated with HPV vaccine uptake in teenage girls: a systematic review. *Vaccine*. 2012; 30: 3546–3556.
- [10] Ministry of the Interior of South Korea. Population census statistical database. 2015. Available at: https://kosis.kr/eng/statisticsList/statisticsListIndex.do?menuId=M_01_01&vwcd=MT_ETITLE&parmTabId=M_01_01&statId=1962001&themald=#A_4.2 (Accessed: 18 November 2004).
- [11] Reagan-Steiner S, Yankey D, Jeyarajah J, Elam-Evans LD, Singleton JA, Curtis CR, *et al.* National, Regional, State, and Selected Local Area Vaccination Coverage among Adolescents Aged 13–17 Years—United States, 2014. *MMWR. Morbidity and Mortality Weekly Report*. 2015; 64: 784–792.
- [12] Tung ILY, Machalek DA, Garland SM. Attitudes, Knowledge and Factors Associated with Human Papillomavirus (HPV) Vaccine Uptake in Adolescent Girls and Young Women in Victoria, Australia. *PLoS ONE*. 2016; 11: e0161846.
- [13] Dorleans F, Giambi C, Dematte L, Cotter S, Stefanoff P, Mereckiene J, *et al.* The current state of introduction of human papillomavirus vaccination into national immunisation schedules in Europe: first results of the VENICE2 2010 survey. *Euro Surveillance*. 2010; 15: 19730.
- [14] Korea Centers for Disease Control & Prevention. National immunization program. 2019. Available at: <https://nip.cdc.go.kr/irgd/index.html> (Accessed: 12 October 2019).
- [15] Hildesheim A, Herrero R. Human papillomavirus vaccine should be given before sexual debut for maximum benefit. *The Journal of Infectious Diseases*. 2007; 196: 1431–1432.
- [16] Seyferth ER, Bratic JS, Bocchini JA. Human papillomavirus epidemiology and vaccine recommendations. *Current Opinion in Pediatrics*. 2016; 28: 400–406.
- [17] Joura EA, Ulied A, Vandermeulen C, Rua Figueroa M, Seppä I, Hernandez Aguado JJ, *et al.* Immunogenicity and safety of a nine-valent human papillomavirus vaccine in women 27–45 years of age compared to women 16–26 years of age: an open-label phase 3 study. *Vaccine*. 2021; 39: 2800–2809.

- [18] Taylor LD, Hariri S, Sternberg M, Dunne EF, Markowitz LE. Human papillomavirus vaccine coverage in the United States, National Health and Nutrition Examination Survey, 2007–2008. *Preventive Medicine*. 2011; 52: 398–400.
- [19] Phillips A, Patel C, Pillsbury A, Brotherton J, Macartney K. Safety of Human Papillomavirus Vaccines: an Updated Review. *Drug Safety*. 2018; 41: 329–346.
- [20] Arcury TA, Gesler WM, Preisser JS, Sherman J, Spencer J, Perin J. The Effects of Geography and Spatial Behavior on Health Care Utilization among the Residents of a Rural Region. *Health Services Research*. 2005; 40: 135–155.
- [21] Centers for Disease Control and Prevention. FDA licensure of bivalent human papillomavirus vaccine (HPV2, Cervarix) for use in females and updated HPV vaccination recommendations from the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report*. 2010; 59: 626–629.
- [22] Katz ML, Wewers ME, Single N, Paskett ED. Key informants' perspectives prior to beginning a cervical cancer study in Ohio Appalachia. *Qualitative Health Research*. 2007; 17: 131–141.
- [23] Dempsey A, Cohn L, Dalton V, Ruffin M. Patient and clinic factors associated with adolescent human papillomavirus vaccine utilization within a university-based health system. *Vaccine*. 2010; 28: 989–995.
- [24] Laz TH, Rahman M, Berenson AB. An update on human papillomavirus vaccine uptake among 11–17 year old girls in the United States: National Health Interview Survey, 2010. *Vaccine*. 2012; 30: 3534–3540.
- [25] Reiter PL, Cates JR, McRee A, Gottlieb SL, Shafer A, Smith JS, *et al.* Statewide HPV vaccine initiation among adolescent females in North Carolina. *Sexually Transmitted Diseases*. 2010; 37: 549–556.
- [26] He J, He L. Knowledge of HPV and acceptability of HPV vaccine among women in western China: a cross-sectional survey. *BMC Women's Health*. 2018; 18: 130.