


# Effect of an IMB Model-Based Education on the Acceptability of HPV Vaccination Among College Girls in Mainland China: A Cluster RCT

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## Abstract

**Objective:** Despite the fact that the human papillomavirus vaccine (HPV) has been approved in mainland China since 2016, there is a lack of inoculation among Chinese college women. This multi-center, online interventional RCT based on the information-motivation-behavioral skills (IMB) model intended to investigate if the intervention may improve human papillomavirus vaccine acceptance and awareness among target women.

**Methods:** Participants were selected from comprehensive universities and allocated to 1 of 2 groups: intervention or control. After the baseline survey, participants in the intervention group were given 10-minute online IMB model-based education every day for 7 days. Self-administered questionnaire surveys on Human papillomavirus knowledge, HPVV acceptability, and IMB construct toward HPV vaccination were performed at pre- and post-intervention.

**Results:** The baseline survey was completed by 3739 female university students from the intervention (n = 1936) and control groups (n = 1803) between February and April 2020. The average score of students on 11 HPV-related questions was  $5.225 \pm 2.739$ , and only 32.07% (1199/3739) of them showed a willingness to be vaccinated against HPV. After the intervention, the intervention group had a higher willingness to vaccinate themselves and encourage their friends to get the HPVV compared to the control group (40.39% vs 31.56%, 82.67 vs 73.18%,  $P < .001$ ), and the difference in knowledge scores between the 2 groups was significant ( $7.917 \pm 1.840$  vs  $5.590 \pm 2.859$ ,  $P < .001$ ). In addition, 8 students in the intervention group self-reported receiving HPVV during the research period.

**Conclusions:** This IMB model-based intervention showed positive effects on the participants' knowledge, motivation, and perceived objective skills toward HPV vaccination and has the potential to improve the vaccination among Chinese college women.

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## Keywords

HPV vaccination, education, IMB, college women, China

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## Introduction

Human papillomavirus (HPV) has been confirmed to be the causative agent of fatal cancers in the cervix uteri, vagina, and oropharynx.<sup>1</sup> High HPV infection rate has been found among teenagers shortly after their sexual debut, which emphasizes the importance of increasing HPV vaccination among these populations.<sup>2-4</sup> In mainland China, it was reported that the 15–19-year-old females had the highest infection rate of high-risk HPV, and the average age of sexual debut was 17 years old.<sup>3,5</sup> Young adults at high risk for HPV infection are often lack of awareness on HPV infection, and their intention to accept HPV vaccination might be improved with better awareness on HPV-related diseases, safety, and efficacy of HPV vaccines.<sup>6-9</sup> However, adolescents in China do not have much chance to receive HPV-related education regularly, and reaching them can be difficult since they are barely seen on sites related to HPV education, such as healthcare settings, clinics, and hospitals.<sup>10</sup>

HPV vaccines have been verified effective in preventing cervical cancer and other diseases caused by HPV infection.<sup>11</sup> Female students in college can be the appropriate catch-up population for HPV vaccination, given that the HPV vaccine was only approved in mainland China in 2016, and college-aged students are at increased risk of HPV infection due to possible premarital sex.<sup>12,13</sup> In mainland China, HPV vaccination requires self-appointment and at recipients' expenses, which is currently different from the countries which include HPV vaccination into the National Immunization Program.<sup>14</sup> Over the past several years, propaganda addressing HPV-related knowledge, vaccine safety, and efficacy has been delivered in various forms, such as news, expert interviews, and brochures.<sup>15,16</sup> In addition, the HPV vaccine was strongly recommended by domestic and international healthcare authorities, such as the World Health Organization (WHO), Federation International of Gynecology and Obstetrics (FIGO), and National Health Commission of the people's Republic of China.<sup>15-18</sup> However, despite these efforts, college females still perceived that information was inadequate for them to make decision on the HPV vaccination, and the HPV vaccination rate in this population ranged from only 2.64% to 11.0% in China, which is much lower than in most of the other countries.<sup>7-9</sup>

Therefore, it is essential to understand the attitude and knowledge of college females on HPV, HPV-related diseases, and its vaccines, and hence offer proper educational materials to this population to ensure an effective intervention, and eventually decrease the burden of HPV-related diseases in the future. Apart from the objective causes such as the accessibility and affordability (inadequate supply and relatively high cost) of the HPV vaccination, previous studies also

highlighted some other modifiable issues based on behavioral intervention theories, in which knowledge and awareness of HPV and relevant information among many others are key influencing factors of HPV vaccine acceptance.<sup>6-8</sup> If we can address these modifiable factors to increase the uptake of HPV vaccine in target populations, it would provide an alternative and cost-effective way in the prevention of HPV infection.<sup>19</sup>

Numerous studies have utilized health behavior theories, such as the Health Belief Model, Theory of Planned Behavior, and Information-Motivation-Behavioral Skills (IMB) model, to identify the multifaceted factors and underlying mechanisms of positive health behaviors.<sup>20-23</sup> Programs or interventions built upon a theoretical framework would be easier to achieve desirable effects.<sup>24,25</sup> Compared with other models, the IMB model, which has been widely used in HIV/AIDS and chronic disease interventions in recent years, covers comprehensive and multilevel influencing factors and takes realistic factors into account to predict health behaviors influenced by information/knowledge, motivation, and behavioral skills required to perform the behavior.<sup>23-28</sup>

Given the strengths of model-based intervention, we developed a series of IMB model-based educational materials for improving the acceptability of HPV vaccination among colleges in mainland China and utilized the material in a randomized controlled trial. The primary objective was to observe the effectiveness of IMB model-based interventions on improving HPV vaccination rates and willingness to vaccinate. And if yes, the multivariate predictors of intervention effectiveness would be explored.

## Methods

The reporting of this study conforms to the CONSORT statements.<sup>29</sup> In addition, we had registered the trial in the website of Chinese Clinical Trial Registry (<https://www.chictr.org.cn/>) prior to the study, and the registration number was ChiCTR1900025476.

## Study Design and Population

This study was a school-based intervention conducted from February to April 2020. To ensure representativeness, participants were recruited from different universities located in 7 geographic regions of China, and a minimum of 3360 previously unvaccinated participants was needed in the study to show significance (see [Appendix Table A1](#) and the published protocol for details<sup>30</sup>).

First-year female college students (aged 18 years or more) who agreed to voluntarily participate in the study and agreed to the informed consent were examined for eligibility.

Potential participants who had not been vaccinated against HPV before the study, had no vaccination contraindications, and were not current pregnancy or breastfeeding were required to use their mobile phones to scan the code and participate in subsequent online interventions.

### *Theoretical Framework*

The Information-Motivation-Behavioral skills Model (IMB) was used as a theoretical framework in this study. This model was created by Fisher JD to predict and promote healthy behaviors, and to conceptualize factors that influence the prevention of sexually transmitted infections.<sup>23</sup> IMB includes the following 3 constructs: information (the personal knowledge of health actions), motivation (the personal beliefs regarding health actions, such as perceived susceptibility, perceived severity, beliefs about the benefits and barriers, and subjective norms), and behavioral skills (the ability to make decisions and self-efficacy). According to the IMB model, it assumes that individuals who are well-informed about HPV and HPV vaccination, motivated to vaccinate themselves, and who can self-make decisions and believe that they can successfully uptake the HPV vaccination are likely to successfully overcome barriers to uptake HPV vaccines.<sup>27-31</sup> Furthermore, socio-demographic characteristics, such as age, major in school, ethnicity, monthly living expenses, as well as previous sexual experience are defined as factors that might influence the HPV vaccination.

### *Intervention*

The theory-based intervention was conducted in a smart application called DingTalk (<https://www.dingtalk.com/>). While the control group received some health tips including updated information on COVID-19, which were not relevant with HPV vaccination, the intervention group received tailored HPV health education guided by the IMB model and a quiz at the end of each day during the intervention period to track the actual exposure to educational materials. Different e-education between the intervention group and the control group was uploaded by administrators of each school in 7 consecutive days. The intervention took about 10 minutes per day, and its contents and expected effects were as follows:

- (a) General health education on disease prevention and sexual health, to attract participants with health care knowledge in graphic, short video form.
- (b) Information on HPV infections and their risk factors, to enable participants to understand the susceptibility of HPV infection and its consequences.
- (c) Facts of the HPV prevention including safe sex and HPV vaccination, to make participants well-informed about HPV prevention.
- (d) Examples of celebrity deaths due to cervical cancer, to stimulate participants' perceptions of the severity of HPV infection.
- (e) Narratives of women transitioning from being unaware of HPV to receiving HPV vaccine, the purpose is to eliminate participants' hesitation, further clarify the benefits of vaccination, and finally make it easier for them to make decision on vaccination.
- (f) How to improve self-efficacy, to facilitate the translation of decisions into concrete actions.
- (g) Information on the booking platform, address, and price of the HPV vaccination, to make it easier for participants to uptake the HPV vaccine.

### *Outcome Measures*

Primary outcomes: the rate and intention of HPV vaccination, which were measured by asking participants if they had been vaccinated against HPV, and if they were willing to uptake HPV vaccine in the next 6 months ("Yes" or "No"). Secondary outcomes were the knowledge of HPV ("Agree," "Disagree," or "Do not know") and beliefs toward HPV vaccination including the constructs of motivation and behavioral skills toward prevention of HPV (1 = strongly disagree, 2 = disagree, 3 = neither disagree nor agree, 4 = agree, and 5 = strongly agree)

### *Data Collection and Quality Control*

Before the baseline survey, electronic informed consent was obtained from each participant. After that, the intervention group received 10-minute e-education uploaded in the DingTalk, while the control group received educational materials irrelevant to HPV prevention in 7 consecutive days. After the 7-day online education, both the intervention and control groups were asked to complete a post-intervention questionnaire.

The self-administered questionnaire used in this study included demographic information, health-related beliefs, and 3 constructs of the IMB model. The quality control criteria of the questionnaire were as follows: (a) ID number was filled out under coding rules; (b) individual group was filled in correctly (intervention or control group); (c) questionnaires could be matched before and after the intervention. Only questionnaires that met the above quality requirements were included in the statistical analysis.

### *Statistical Analysis*

For descriptive statistics, categorical data were given as frequencies and percentages, continuous data included age, and the IMB scores were presented as mean and standard deviation (SD). Differences between intervention and control groups before and after the intervention were examined with Chi-square test for categorical variables, Student's independent samples t-test for continuous variables, and a paired sample t-test was used to evaluate pre- and post-intervention IMB construct scores. Binary logistic regression and generalized estimating equations (GEE) were performed to evaluate the

multivariate predictors of intervention effectiveness. Odds ratios (ORs) and adjusted ORs (AORs) with 95% confidence intervals (CIs) were calculated based on Wald Chi-square statistics. IBM SPSS Statistics 23.0 was used to perform all the statistical analyses. Statistical significance was assessed by two-sided tests with a  $P$ -value  $<.05$ .

### Ethical Approval

This study was approved by the Institutional Review Board of Chinese Center for Disease Control and Prevention in Beijing, China on October 24, 2019 (No. 201918-01). Before participating in the study, participants were provided with electronic informed consent regarding the research objectives, requirements, procedures, benefits, and other study-related information, and only those who clicked on “I agreed to join the study” would be linked to the questionnaire and subsequent interventional study.

### Results

3968 female students participated in the study. Among them, 102 had received the HPV vaccine before the survey; thus, they were not included in the subsequent intervention study. The remaining 3866 participants were divided into the intervention group or control group according to the random number. At the baseline survey, 137 questionnaires failed to meet the requirements of quality control were removed, and a total of 3739 female college students were finally included in the baseline analysis, and 3224 completed the questionnaires both before and after the intervention, and the response rate was 86.23% (3224/3739).

### Demographic Characteristics

The mean age of the participants was 19.14 years; more than a half (52.80%) majored in science. The majority (87.70%) of respondents was Han ethnicity. 64.24% had lived in urban areas for more than 1 year, and 71.17% had living expenses between 1000 and 2000 Yuan a month. Only 25.22% of the participants had parents with college degrees or more, and less than a quarter (24.15%) had family members or friends with cancer. 17.14% were currently in romantic relationships, and 106 (2.83%) of the respondents had sex intercourse before the survey. In addition, only 7.01% of participants were not convinced of the effectiveness of general vaccines in preventing diseases, and 64.27% had ever received vaccines at their own expenses. 79.09% of respondents self-reported had received sexual education, and 38.09% thought premarital sex was acceptable. In addition, the intervention group and the control group were balanced in other variables except for the significant difference at baseline regarding previous sexual intercourse (3.46% vs 2.16%) (Table 1).

### Effect of the Intervention

**Knowledge on HPV and HPV-Related Diseases.** At baseline, a total of 3739 female students from intervention ( $n = 1936$ ) and

control groups ( $n = 1803$ ) completed the questionnaire survey. Among them, about 60% had heard of HPV, HPV-related diseases, and HPV vaccine before the survey, which were similar in both intervention and control groups. In addition, there was no significant difference between the intervention group and the control group at baseline in the mastery of the 11-item HPV-related information, which is one of the three components of the IMB model (Figure 1). 70.02% of participants were aware that HPV was related to the development of cervical cancer, 72.35% understood that HPV vaccine cannot protect against all types of cervical cancer, and 76.33% agreed that regular cervical cancer screening was necessary after HPV vaccination. However, only 8.37% of respondents knew that HPV infection was often asymptomatic, and 9.44% were aware that most HPV infections would disappear on their own.

After the IMB model-based education about HPV and cervical cancer, respectively, 1662 and 1562 participants in intervention group and control group received post-intervention survey, and significant differences on HPV-related knowledge were identified both between the two groups and in pre–post comparison of the intervention group (Figure 1). At post-intervention, 95.67%, 91.64%, and 93.74% of students in the intervention group reported having heard of HPV, HPV-related diseases, and HPV vaccines, respectively. Compared with those in the control group, participants in the intervention group were more likely to be aware of HPV-related information regarding the following 11 items: (1) “HPV infection causes cervical cancer” (95.07% vs 71.64%,  $P < .001$ ), (2) “Regular cervical cancer screening is necessary even after getting HPV vaccines” (94.46% vs 77.59%,  $P < .001$ ), (3) “Males can get HPV infections” (91.76% vs 69.14%,  $P < .001$ ), (4) “The ideal time for HPV vaccination is prior to sexual debut” (91.03% vs 55.06%,  $P < .001$ ), (5) “the HPV vaccine does not prevent all HPV infections” (89.95% vs 70.68%,  $P < .001$ ), (6) “HPV infection may result in oral and anal cancer” (88.63% vs 63.00%,  $P < .001$ ), (7) “HPV is related to sexual contact” (78.94% vs 55.57%,  $P < .001$ ), (8) “HPV infection is very common” (71.24% vs 32.65%,  $P < .001$ ), (9) “condoms prevent HPV infection” (47.17% vs 39.31%,  $P < .001$ ), (10) “most HPV infections get resolved without treatment” (24.43% vs 13.76%,  $P < .001$ ), and (11) “HPV infections are almost asymptomatic” (19.01% vs 10.63%,  $P < .001$ ).

**IMB Construct Scores.** At baseline, there were no significant differences between the intervention group and the control group on all 7 variables except the perceived barriers ( $3.000 \pm .706$  vs  $3.059 \pm .700$ ,  $P = .011$ ). After the IMB model-based education, significant differences were found between the intervention and control groups in all 7 variables except perceived severity ( $3.380 \pm .804$  vs  $3.385 \pm .766$ ,  $P = .853$ ). Among these variables, scores for information, perceived susceptibility, perceived barriers, subjective norms, and self-efficacy increased, while scores for perceived severity, perceived barriers, and decision-making decreased (Table 2).

**Table 1.** Demographic characteristics of participants (n = 3739).

Variables	All N (%)	Intervention Group n = 1936	Control Group n = 1803	P-Value
<b>Socio-Demographics</b>				
Age (years, mean ± SD)	19.14 ± .73	19.12 ± .72	19.11 ± .73	.566
<b>Major</b>				
Science	1975 (52.82)	906 (46.80)	858 (47.59)	.629
Liberal art	1764 (47.18)	1030 (53.20)	945 (52.41)	
<b>Ethnicity</b>				
Han	3279 (87.70)	1693 (87.45)	1586 (87.96)	.631
Other	460 (12.30)	243 (12.55)	217 (12.04)	
<b>Permanent residence place (for more than 1 year)</b>				
Urban	2402 (64.24)	1270 (65.60)	1132 (62.78)	.073
Rural	1337 (35.76)	666 (34.40)	671 (37.22)	
<b>Living expenses (RMB/month)</b>				
<1000 Yuan	767 (20.51)	421 (21.75)	346 (19.19)	.070
1000–2000 Yuan	2661 (71.17)	1346 (69.52)	1315 (72.93)	
>2000 Yuan	311 (8.32)	69 (8.73)	142 (7.88)	
<b>Parental education</b>				
Junior high school or below	1682 (44.99)	880 (45.45)	802 (44.48)	.809
Senior high school (including vocational high school)	1114 (29.79)	569 (29.39)	545 (30.23)	
College (including technical college) and above	943 (25.22)	487 (25.15)	456 (25.29)	
<b>Previous sexual intercourse</b>				
Yes	106 (2.83)	67 (3.46)	39 (2.16)	.017 <sup>a</sup>
No	3633 (97.17)	1869 (96.54)	1764 (97.84)	
<b>Currently in romantic relationship</b>				
Yes	641 (17.14)	324 (16.74)	317 (17.58)	.493
No	3098 (82.86)	1612 (83.26)	1486 (82.42)	
<b>Family/friends with any cancer</b>				
Yes	903 (24.15)	460 (23.76)	443 (24.57)	.563
No	2836 (75.85)	1476 (76.24)	1360 (75.43)	
<b>Health-related variables</b>				
Vaccination is effective in preventing disease				
Yes	3477 (92.99)	1815 (93.75)	1662 (92.18)	.060
No	262 (7.01)	121 (6.25)	141 (7.82)	
Received self-paid vaccines (e.g., hepatitis B, influenza)				
Yes	2403 (64.27)	1242 (64.15)	1161 (64.39)	.878
No	1336 (35.73)	694 (35.85)	642 (35.61)	
Ever received sexual education				
Yes	2957 (79.09)	1537 (79.39)	1420 (78.76)	.634
No	782 (20.91)	399 (20.61)	383 (21.24)	
Attitude toward premarital sex				
Pro	1424 (38.09)	749 (38.69)	675 (37.44)	.431
Con	2315 (61.91)	1187 (61.31)	1128 (62.56)	

<sup>a</sup>Significant P < .05.

**Willingness to be Vaccinated Against HPV.** At baseline, there was no significant difference between the intervention group and the control group on the willingness to be vaccinated. After the IMB model-based education, the willingness to vaccinate themselves and willingness to encourage friends to uptake the HPV vaccine was higher in the intervention group compared to the control group (40.39% vs 31.56%, 82.67 vs 73.18%,  $P < .001$ ). In addition, compared with the control group (n = 3), the

number of women in the intervention group (n = 8) who received HPV vaccine was twice as that in the control group, although the proportions were not significantly different (.19% vs .48%,  $P = 1.159$ ) (Figure 2).

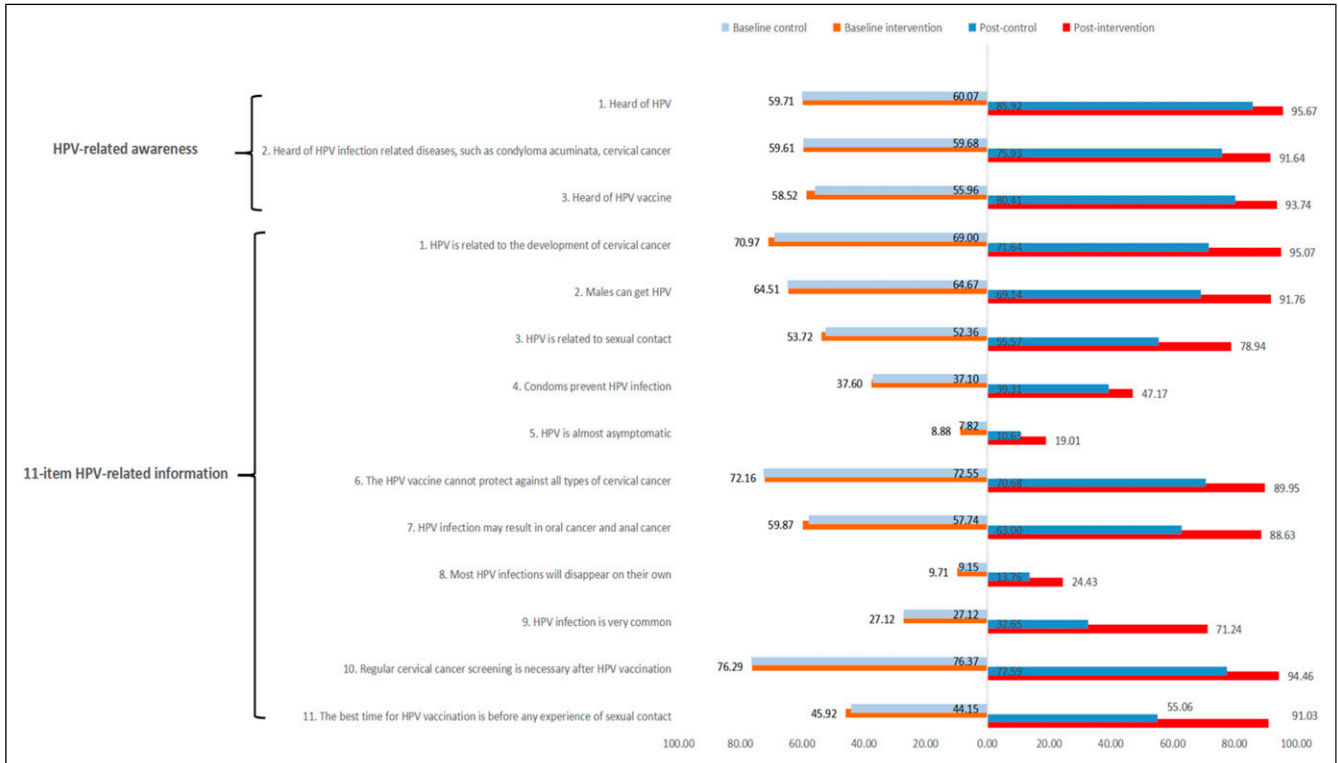
\* The total number after the intervention is 3213 due to the removal of the participants who have been vaccinated (8 in the intervention group and 3 in the control group) during the study period.

# The baseline excluded females who had been vaccinated before the study, and the figure only shows the number of vaccinated women after the intervention.

**Multivariate Predictors of Intervention Effectiveness**

After intervention, eleven variables were found to be associated with the behavior or willingness to be vaccinated against HPV with statistical significance by using binary

logistic regression analysis and GEE. After eliminating the confounding effects of time, the intervention group (AOR: 1.533, 95CI%: 1.102–1.439) was more willing to be vaccinated than the control group. Regarding background variables, participants whose ethnicity were a minority (AOR: 1.394, 95CI%: 1.136–1.711), who were from urban (AOR: 1.291, 95CI%: 1.100–1.516), those living on more than 2000 Yuan a month (AOR: 1.812, 95CI%: 1.356–2.422), who had parents with college degrees or more (AOR: 1.291, 95CI%: 1.064–

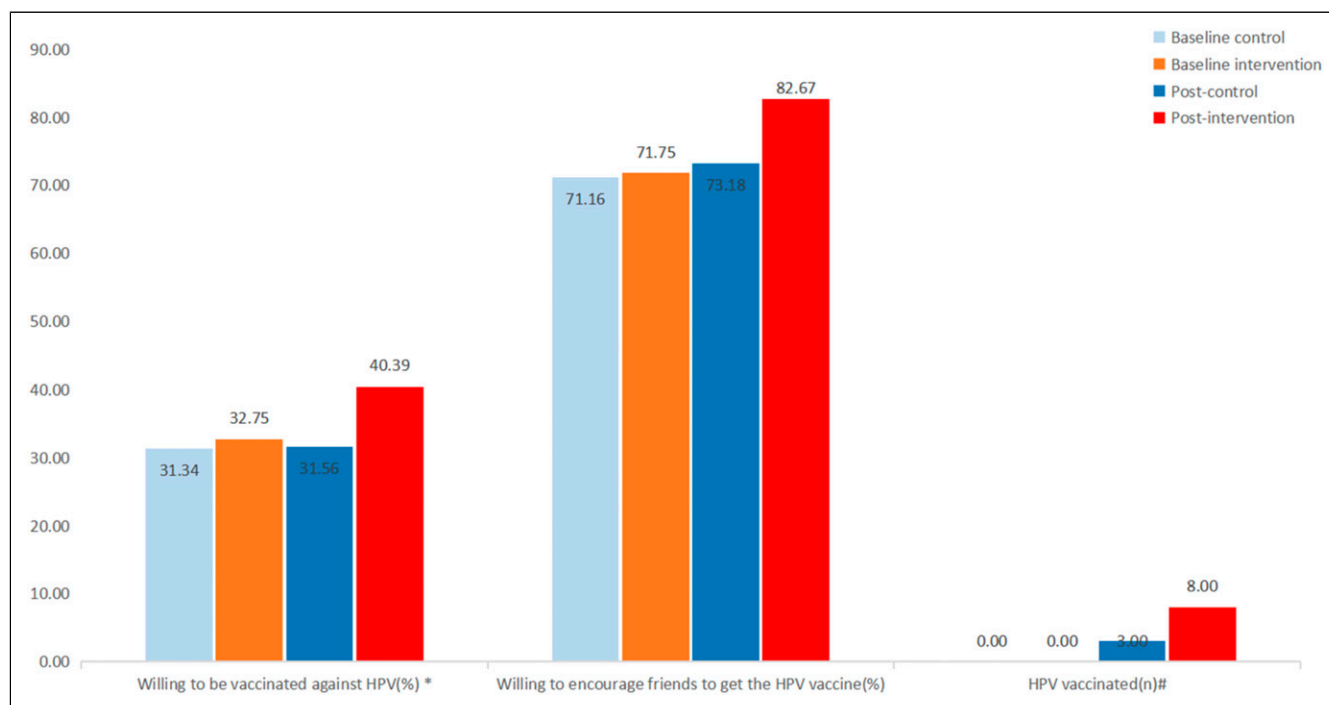


**Figure 1.** Comparison between baseline and post-intervention data on HPV-related knowledge.

**Table 2.** Information/knowledge, motivation, and behavioral skills scores among participants before and after intervention.

Variables	Baseline		T	P-Value	Post-intervention		T	P-Value
	Intervention (n = 1936)	Control (n = 1803)			Intervention (n = 1662)	Control (n = 1562)		
<b>Information</b>	5.268 ± 2.754	5.180 ± 2.722	.974	.330	7.917 ± 1.840	5.590 ± 2.859	27.641	.000 <sup>a</sup>
<b>Motivation</b>								
Perceived susceptibility	2.429 ± .886	2.455 ± .889	-.889	.374	2.860 ± .963	2.609 ± .855	7.835	.000*
Perceived severity	3.529 ± .740	3.537 ± .756	-.326	.744	3.380 ± .804	3.385 ± .766	-.185	.853
Perceived benefits	3.920 ± .617	3.927 ± .600	-.359	.720	4.107 ± .569	3.883 ± .591	10.983	.000 <sup>a</sup>
Perceived barriers	3.000 ± .706	3.059 ± .700	-.255	.011*	2.870 ± .780	3.088 ± .694	-8.391	.000*
Subjective norms	3.082 ± .561	3.077 ± .560	.261	.794	3.162 ± .636	3.090 ± .568	3.421	.001*
<b>Behavioral skills</b>								
Decision-making	3.981 ± .556	3.949 ± .556	1.77	.077	3.867 ± .588	3.816 ± .588	2.481	.013*
Self-efficacy	3.640 ± .642	3.633 ± .621	.320	.749	3.684 ± .652	3.5850 ± .648	4.307	.000 <sup>a</sup>

<sup>a</sup>Significant P < .05.



**Figure 2.** Comparison of baseline and post-intervention regarding willingness to be vaccinated.

1.565), and who had family members or friends with cancer (AOR: 1.369, 95CI%: 1.176–1.593) were more willing to be vaccinated. In addition, participants who self-reported had received sexual education (AOR: 1.427, 95CI%: 1.202–1.696), who had previous sexual intercourse (AOR: 1.654, 95CI%: 1.074–2.547), who thought premarital sex was acceptable (AOR: 1.310, 95CI%: 1.137–1.509), and who believed the effectiveness of general vaccines in preventing diseases (AOR: 1.310, 95CI%: 1.016–1.787) were also predictors of behavior or willingness to be vaccinated against HPV among participants (Table 3).

## Discussion

The results of the current IMB model-based RCT using online education materials among female college students showed a significant increase in knowledge, motivation, and self-efficacy toward HPV vaccination in the intervention group. Such changes, in turn, predicted a greater likelihood of willingness to be vaccinated against HPV. In the post-intervention survey, more female students in the intervention group self-reported had received HPV vaccine and indicated positive willingness to vaccinate themselves compare to the control group, controlling the confounding effect of time. However, we did not find significant differences in the actual number of HPV vaccination between the intervention group and the control group. The possible reasons might be as follows: (a) During the study period, the COVID-19 outbreak in China coincided with the policy requirements of traffic control and

home isolation, which made it difficult for most students to complete the HPV vaccination.<sup>32-34</sup> (b) The price of HPV vaccination was relatively high for most of the students, and they cannot afford the cost of vaccination with a limited monthly expenses.<sup>6-9</sup> (c) It has been only 4 years since the HPV vaccine was approved in mainland China, the shortage of HPV vaccine supply caused many females still in waiting list even though they made appointments on vaccination.<sup>35</sup> However, more weight should be given to the finding that 8 students in the intervention group chose to have themselves vaccinated shortly after the intervention. In addition, although the willingness to get the HPV vaccination in the intervention group increased, it was lower at both pre- and post-intervention than in other similar studies.<sup>6-9</sup> However, it is worth noting that our restriction of willingness to receive HPV vaccine in the following 6 months in the study may be responsible for this difference in some certain extent.<sup>7</sup>

Before the IMB model-based education, the average score for the correct knowledge related to HPV was less than half of the total, which indicated that college females had limited sources in acquiring HPV-related knowledge and information. In the present study, it is demonstrated that the HPV-related knowledge among the intervention group can be significantly improved (from 5.268 points to 7.917 points) in a short period by offering tailored educational materials. The content highlights of educational materials included some facts the participants may not know before the study, such as “Most HPV infections would disappear on their own” and “Effective treatment in the early stages of cervical cancer may be

**Table 3.** Multivariate predictors of behavior or willingness to be vaccinated against HPV among participants.

Variables	All N (%)	Behavior or Willingness to be Vaccinated		Unadjusted odds ratio (95%CI) <sup>a</sup>	Adjusted odds ratio (95%CI) <sup>b</sup>	P
		Yes (%)	No (%)			
Time						
Baseline	3224 (50.00)	1061 (32.91)	2163 (67.09)			
Post-intervention	3224 (50.00)	1171 (36.32)	2053 (63.68)	1.163 (1.049, 1.289)	1.173 (1.094, 1.257)	.000*
Group						
Control	3124 (48.45)	999 (31.98)	2125 (68.02)			
Intervention	3324 (51.55)	1233 (37.09)	2091 (62.91)	1.254 (1.132, 1.390)	1.260 (1.102, 1.439)	.001 <sup>c</sup>
Ethnicity						
Han	5632 (87.34)	1918 (34.06)	3714 (65.93)			
Other	816 (12.66)	314 (38.48)	502 (61.52)	1.211 (1.041, 1.409)	1.394 (1.136, 1.711)	.001*
Permanent residence (for more than 1 year)						
Rural	2356 (36.54)	632 (26.83)	1724 (73.17)			
Urban	4092 (63.46)	1600 (39.10)	2492 (60.90)	1.751 (1.568, 1.956)	1.291 (1.100, 1.516)	.002*
Living expenses (RMB/month)						
<1000 Yuan	1330 (20.63)	355 (26.69)	975 (73.31)			
1000–2000 Yuan	4580 (71.03)	1595 (34.83)	2985 (65.17)	2.062 (1.722, 2.468)	1.134 (.945, 1.360)	.178
>2000 Yuan	538 (8.34)	282 (52.42)	256 (47.58)	3.025 (2.457, 3.726)	1.812 (1.356, 2.422)	.000*
Parental education						
Junior high school or below	2968 (46.03)	856 (28.84)	2112 (71.16)			
Senior high school (including vocational high school)	1902 (29.50)	688 (36.17)	1214 (63.83)	1.364 (1.190, 1.564)	1.140 (.968, 1.342)	.116
College (including technical college) and above	1578 (24.47)	688 (43.60)	890 (56.40)	1.907 (1.679, 2.166)	1.291 (1.064, 1.565)	.009*
Family/friends with any cancer						
No	4870 (75.53)	1567 (32.18)	3303 (67.82)			
Yes	1578 (24.47)	665 (42.14)	913 (57.86)	1.535 (1.366, 1.725)	1.369 (1.176, 1.593)	.000*
Currently in romantic relationship						
No	5362 (83.16)	1789 (33.36)	3573 (66.64)			
Yes	1086 (16.84)	443 (40.79)	643 (59.21)	1.376 (1.204, 1.573)	1.158 (.969, 1.383)	.106
Ever received sexual education						
No	1358 (21.06)	352 (25.92)	1006 (74.08)			
Yes	5090 (78.94)	1880 (36.94)	3210 (63.06)	1.674 (1.464, 1.914)	1.427 (1.202, 1.696)	.000 <sup>c</sup>
Previous sexual intercourse						
No	6274 (97.30)	2131 (33.97)	4143 (66.03)			
Yes	174 (2.70)	101 (58.05)	73 (41.95)	2.690 (1.982, 3.651)	1.654 (1.074, 2.547)	.022*
Attitude toward premarital sex						
Con	4016 (62.28)	1215 (30.25)	2801 (69.75)			
Pro	2432 (37.72)	1017 (41.82)	1415 (58.18)	1.657 (1.492, 1.840)	1.310 (1.137, 1.509)	.000*
Vaccination is effective in preventing disease						
No	468 (7.26)	118 (25.21)	350 (74.79)			
Yes	5980 (92.74)	2114 (35.35)	3866 (64.65)	1.622 (1.308, 2.011)	1.347 (1.016, 1.787)	.039*
Received self-paid vaccines (e.g., hepatitis B, influenza)						
No	2262 (35.08)	739 (32.67)	1523 (67.33)			
Yes	4186 (64.92)	1493 (35.67)	2693 (64.33)	1.143 (1.025, 1.273)	1.031 (.895, 1.188)	.671

Significant  $P < .05$ .<sup>a</sup>Binary logistic regression analysis.<sup>b</sup>Generalize estimating equations.



promising," which may reduce adolescents' perceptions of the severity of HPV infection. Thus, adolescents' partial interpretation of this information may undermine the conclusion of previous studies that increased knowledge promotes the willingness to vaccinate against HPV, and maybe the reason for the lack of a significant increase in perceived severity of HPV infection.<sup>7,8</sup> In this respect, college women need more in-depth health education, such as the symptoms, treatment, prognosis, and outcomes of HPV-related diseases, which can increase their perceived severity of HPV infection and thus increase their willingness to get vaccinated.

In addition, the changes from baseline to post-intervention on the scores of perceived susceptibility to HPV infection were higher among intervention groups, which means they were aware of the more risks after the education. Puberty is a time in life with an increased risk of sexually transmitted infection, while adolescents including the early stage university students generally lack awareness of sexual protection and rarely seek medical check-ups until it is pressingly needed.<sup>35-39</sup> This reminds us that in future health education, we should pay more attention to developing content that can easily arouse students' susceptibility to disease. Only when students realize that they are at risk of contracting HPV, will they personally want to take healthy behaviors to protect themselves.

Aligning with previous findings, a higher perceived benefit may be one of the contributing factors to the behavior or willingness to take the HPV vaccine,<sup>8</sup> while perceived barriers toward HPV vaccination may be main reasons for unwillingness of receiving the HPV vaccine, which included price, possible needle hurts, and concerns about the safety, efficacy, and side effects of the HPV vaccine.<sup>8,37</sup> Based on the findings of this study, it is suggested that education should continue to highlight the established effectiveness and safety of the HPV vaccine, simplify the vaccination process and improve the vaccination experience, and more focuses should be taken on reducing the price of HPV vaccination from the government perspective and emphasizing the importance of HPV vaccination in general.

One's decisions are generally a combination of personal needs and social norms, and adolescents' decisions and behaviors may be easily influenced by family, friends, and social norms, since the independent decision-making ability of adolescents is developing.<sup>38,39</sup> In addition, because the HPV vaccine is self-paid and relatively expensive currently, it makes sense that students will likely need the support of family or friends to complete the vaccination. In our education, there is a session specifically teaching how to introduce participants' newly gained knowledge on prevention and treatment of HPV infection to family and friends, for sake of obtaining their support for HPV vaccination. This inspires us that the obtained HPV-related knowledge may work together to increase the willingness of HPV vaccination by persuading the surrounding people and gaining support from family/friends. This finding also suggests that in future public-funded vaccinations such as those in Juungar Banner in the

Ordos, Inner Mongolia autonomous region of China, we should pay more attention to the power of social norms from family and surrounding communities rather than just educating the targeted women.<sup>40</sup> Furthermore, in line with previous studies, by displaying the practical skills required for HPV vaccination, such as the booking platform, different types of the HPV vaccine, applicable conditions, price, and vaccination process, the convenience of HPV vaccination will be increased for the target audience, to strengthen the determination of female students to vaccinate themselves against HPV.<sup>39-41</sup>

In the current study, it is surprised that participants from ethnic minorities were more likely to be vaccinated against HPV. The possible reason is that one of our research centers is located in Xinjiang, so there are more participants from the Uighur population, which has a high HPV infection rate and a strong awareness of preventing HPV infection.<sup>42,43</sup> Previous studies have demonstrated a regional variation on HPV vaccination rate and have identified a need for ongoing efforts to decrease the gap between the urban and rural areas.<sup>8-44</sup> In the current study, wealthier students were more likely to have been vaccinated against HPV than students living on less than 1000 Yuan a month, which was consistent with the former studies.<sup>7,8</sup> It is not surprising that people living in remote areas with low household income and limited health resources cannot afford to pay for vaccination. In addition, it is worth noting that Juungar Banner, as the first county in Ordos City to offer free HPV vaccination to female students aged 13 to 18, has completed the first dose of 8351 HPV vaccines by February 19, 2021.<sup>40</sup> This reminds us that the government-supported HPV vaccination plan in remote areas is very promising. In the future, the introduction of HPV vaccination into the national program will likely make successful practices for the prevention of cervical cancer in China.

Consistent with previous studies,<sup>8,44</sup> parents with higher education are more likely to understand health knowledge and provide material and psychological support for their children's health. Additionally, in the course of HPV infection prevention education, participants with a relative or friend who suffers from cancer were prone to identify the severity and fear of the consequences of infection, and thus they were more likely to take proactive steps to protect themselves. Similarly, findings also highlight the importance of trust in vaccines and having previously received vaccines borne by out-of-pocket money in determining future willingness to receive HPV vaccines. In conclusion, participants with parental support and/or personal value and trust in disease prevention were more likely to make an appointment for the HPV vaccine as soon as possible after receiving health education.

In terms of the sexually transmitted nature of HPV infection, we have found that having received sexual education, previous sexual intercourse, and acceptance about premarital sex had significant associations with behavior or willingness to receive the HPV vaccine, which is in line with previous studies.<sup>7,8</sup> Therefore, the research results remind us that only

when participants realize that sexual behavior may bring sexually transmitted diseases, they will have the willingness or behavior to get HPV vaccine. This finding suggests that future educational campaigns should pay close attention to risks of potential HPV infection, rather than only focusing on the importance of getting vaccinated before sexual intercourse.

To our knowledge, this is the first multi-center, randomized, online educational, school-based intervention study among female college students in mainland China to improve the acceptability of HPV vaccination. The contents of the intervention were tailor-made based on the characteristics of the target audience and carefully validated and monitored by the research team. And the current study achieved a relatively high response rate after the 7-day intervention: 86.23% completed the entire study. It is also a convincing design to use a theoretical framework such as the IMB model when organizing behavioral intervention with preventive aims, and such theory-based measures can be used for interventions addressing vaccine hesitancy in future government-supported HPV vaccination projects. IMB model is a well-validated practical theory widely used in the prediction and promotion of health behaviors, and therefore this theory-based intervention could clarify more accurately on influencing factors of HPV vaccination.<sup>26-31</sup> What is more, the simultaneous distribution of the same set of educational materials to students from different backgrounds not only ensured the uniformity of the intervention but also made the research with a fair degree of representativeness and generalizability.

There were several limitations of our study. First, for management purposes, we randomized on a class level rather than on an individual level, and contamination may occur even though it was an online intervention. Secondly, the period of our study coincided with the COVID-19 epidemic, when the epidemic control in China required home isolation and traffic control measures, as well as psychological states such as anxiety and depression that students may have, would inevitably affect the target outcomes, namely, the HPV vaccination rate and vaccination intention.<sup>32-46</sup> Also, it is worth noting that self-reported HPV vaccination rates and willingness may not match the actual situation. Finally, although our study covered a representative sample of college females in 7 geographic regions, it would have been even better if we had been able to enroll more participants and add a follow-up period.

## Conclusions

Our IMB model-based educational online intervention was specially tailored for Chinese college female students and showed positive effects on the participants' knowledge, motivation, and perceived objective skills toward HPV vaccination. The improvement in these factors contributed to an increased number of female students who intended to uptake the HPV vaccine after the intervention. In addition, the future promotion of the HPV vaccine should pay more attention to students living in rural areas and with low living expenses.

## Appendix

**Table A1** Respondent recruitment source, overall and by region, 2020.

Multi-Center	Geographic Regions of China	Province	City	University	Recruitment(n)	Unvaccinated (n)	Qualified(n)	Baseline survey(n)		Post-intervention survey(n)	
								Intervention	Control	Intervention	Control
1	Ease	Shandong	Jinan	Jinan university	920	904	884	440	444	367	345
2	South	Guangdong	Guangzhou	Sun yat-sen University	481	429	407	213	194	200	187
3	Central	Henan	Zhengzhou	Henan institute of engineering	462	457	438	238	200	220	182
4	North	Shanxi	Changzhi	Shanxi University of finance and economics	534	530	503	263	240	196	192
5	Northwest	Xinjiang uygur autonomous region	Urumqi	Xinjiang agricultural University	611	610	589	296	293	285	286
6	Southwest	Sichuan	Chengdu	Sichuan University	453	437	431	256	175	212	141
7	Northeast	Liaoning	Dalian	Dalian University of technology	507	499	487	242	245	182	229

## Abbreviations

HPV, human papillomavirus; IMB, the Information-Motivation-Behavior Skills Model; WHO, World Health Organization; FIGO, Federation International of Gynecology and Obstetrics; SD, Standard deviation; OR, Odds Ratio; AOR, Adjusted Odds Ratio; CI, Confidence Interval; COVID-19, Coronavirus Disease 2019; P, Probability.

## Authors' contributions

Mingyu Si and Xiaoyou Su prepared the first draft

Yu Jiang, Xiaoyou Su, and Ming-Yu Si managed the overall project

Xi Zhang, Wenjun Wang, Xiaofen Gu, Li Ma, Jing Li, Shaokai Zhang, and Zefang Ren were responsible for the questionnaire survey in seven geographical regions of China

Yu Jiang and Yuanli Liu finalized the manuscript on the basis of comments from other authors

Youlin Qiao provided overall guidance

All authors read and approved the final manuscript.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Ethics approval and consent to participate

This study has been approved by the Institutional Review Board of Chinese Center for Disease Control and Prevention on October 24, 2019. (approval number: 201 918-01).

## TRIAL registration

Chinese clinical trial registry (ChiCTR), ChiCTR1900025476.

## Informed Consent Statement

Informed consent was obtained from all subjects involved in the study

## Data Availability Statement

The original data generated from this study and the analyzed results will be available from the corresponding author upon reasonable request

## Institutional Review Board Statement

This study has been approved by the Institutional Review Board of Chinese Center for Disease Control and Prevention on October 24, 2019. (approval number 201 918-01)

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