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# Trust in HPV Vaccine Effectiveness and Safety and Willingness to Initiate HPV Vaccination Among Unvaccinated Female College Students Recruited Through University-Based Online Networks in China: A Cross-Sectional Study

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## Abstract

# Background

Human papillomavirus (HPV) vaccination is an important strategy for preventing cervical cancer and other HPV-related diseases. Vaccine trust may encompass distinct perceptions of effectiveness and safety. This study examined cross-sectional associations of trust in HPV vaccine effectiveness and safety with HPV vaccination willingness among unvaccinated female college students recruited through university-based online networks in China.

# Methods

This cross-sectional online survey recruited female college students from 24 universities located in 12 provincial-level administrative regions of China between January 2025 and March 2026. The primary analysis included participants who reported no prior HPV vaccination. High willingness was defined as reporting being somewhat willing or very willing to receive HPV vaccination. Trust in HPV vaccine effectiveness, the safety of domestically produced bivalent HPV vaccines, and the safety of imported HPV vaccines were modeled as categorical variables. Multivariable logistic regression was used to estimate adjusted odds ratios (aORs) and 95% confidence intervals (CIs).

# Results

Among 2,215 unvaccinated participants, 818 (36.9%) reported high HPV vaccination willingness. Higher categories of effectiveness trust and safety trust were associated with greater odds of reporting high willingness. Compared with participants who were very distrustful of HPV vaccine effectiveness, those who were very trustful had an aOR of 5.397 (95% CI 3.246–8.973). The corresponding aORs for being very trustful of the safety of domestically produced bivalent HPV vaccines and imported HPV vaccines were 3.307 (95% CI 1.930–5.665) and 5.022 (95% CI 2.741–9.201), respectively. Associations were directionally consistent after excluding participants reporting uncertain willingness.

# Conclusions

Among unvaccinated female college students recruited through university-based online networks in 12 provinces in China, higher self-reported trust in HPV vaccine effectiveness and safety was associated with greater reported willingness to initiate HPV vaccination. Longitudinal and intervention studies are needed to examine whether approaches addressing effectiveness and safety concerns improve HPV vaccine uptake.

## Background

Cervical cancer remains an important public health burden among women worldwide[1]. Persistent infection with high-risk human papillomavirus (HPV) is a necessary cause of most cervical cancer cases, and prophylactic HPV vaccination can prevent vaccine-type HPV infection and related precancerous lesions[2]. Female college students constitute a relevant population for HPV prevention[3]. During the transition to adulthood, reproductive health knowledge, preventive health practices, and decisions about self-funded health services are often still developing[4]. Students may also be making vaccination decisions independently for the first time, while balancing perceived health benefits against cost, access, family views, peer influence, and information encountered online[5]. In China, previous studies have documented variation in HPV vaccine uptake and willingness among university students[6–8]. These findings indicate that willingness should be considered in relation to the social and informational context in which young women assess vaccination, rather than as a simple reflection of knowledge alone[9–11]. Estimates from online convenience samples should nevertheless not be interpreted as population-level estimates of HPV vaccination coverage or willingness[12, 13].

Vaccine confidence is widely recognized as an important correlate of vaccination decisions, and trust is one of its central dimensions[14]. Trust in HPV vaccine effectiveness and trust in vaccine safety are related but conceptually distinct perceptions[15]. A student may accept that vaccination can reduce the risk of cervical cancer while remaining uncertain about adverse effects, product quality, or the reliability of safety information[16]. Conversely, a student may report few safety concerns yet question whether vaccination is personally necessary or sufficiently effective[17, 18]. Examining these dimensions separately may therefore provide a more precise account of how vaccine-related beliefs are associated with willingness among unvaccinated students[19].

Safety perceptions may also differ between domestically produced and imported HPV vaccines[12, 20]. Such distinctions can be shaped by product reputation, price, supply and appointment access, prior media coverage, and exposure to information from health professionals, family members, peers, and online sources[21]. These perceptions need not correspond directly to objective differences in clinical performance; instead, they may reflect how individuals interpret available vaccine-related information in a particular market and social context[22]. Few studies have examined effectiveness trust alongside product-specific safety trust in the same model among unvaccinated female college students in China[23].

This study therefore examined cross-sectional associations of trust in HPV vaccine effectiveness, trust in the safety of domestically produced bivalent HPV vaccines, and trust in the safety of imported HPV vaccines with HPV vaccination willingness among unvaccinated female college students in China. By modelling the three trust measures categorically and simultaneously, the analysis aimed to describe whether each measure retained a conditional association with affirmative vaccination willingness after accounting for measured participant characteristics and other vaccine-related perceptions. Given the cross-sectional design and convenience sampling, the study was intended to characterize associations rather than determine causal effects or produce nationally representative estimates.

## Methods

# Study design, setting, recruitment, and participants

This cross-sectional survey was conducted among female college students in 12 provincial-level administrative regions of China between January 2025 and March 2026. The participating institutions were located in Shandong, Jiangsu, Zhejiang, Shanxi, Guangdong, Hainan, Sichuan, Hebei, Anhui, and Heilongjiang provinces, and in the Xinjiang Uygur Autonomous Region and Tibet Autonomous Region. Convenience sampling was used to recruit students from 24 universities, including nine comprehensive universities, eight medical universities or colleges, and seven vocational or technical colleges. These institutions and participants were not selected through probability sampling. The sample should therefore be interpreted as a multi-province university-based convenience sample and not as representative of female college students nationally or within any participating region[24]. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement[25, 26]. Questionnaire links and Quick Response codes were distributed through university health centres, student affairs offices, and course-based announcements; official university WeChat public accounts supplemented recruitment. Eligible participants were full-time female students enrolled in associate-degree, undergraduate, or postgraduate programmes who could understand the questionnaire. Electronic informed consent was obtained before participation. Questionnaires with more than 10% missing responses or logically inconsistent responses were excluded. The final full survey dataset comprised 6,428 valid questionnaires. Participants who answered “no” to the item asking whether they had ever received an HPV vaccine were classified as having self-reported no history of HPV vaccination and included in the primary analytical sample. Because recruitment was conducted through open online channels without a defined sampling frame, a conventional response rate could not be calculated.

## Questionnaire and measures

Data were collected using Questionnaire Star, a web-based survey platform. Investigators received standardized training before data collection. Participants completed anonymous self-administered questionnaires after scanning a Quick Response code. On-site verification and logic checks were used to identify questionnaires with substantial missing data or internally inconsistent responses[15]. The questionnaire was developed by the research team for this study. It covered demographic characteristics, reproductive health, HPV vaccination history, HPV vaccine trust, information exposure, perceived necessity of HPV vaccination, acceptable vaccine price, and vaccination willingness. The English-language version of the questionnaire is provided in **Supplementary Material S1**. Analytic coding and variable-level completeness in the primary analytical sample are reported in **Supplementary Table S2**.

## Outcome

The primary outcome was HPV vaccination willingness among participants who self-reported no history of HPV vaccination. Willingness was assessed using a five-category item: very willing, somewhat willing, uncertain, somewhat unwilling, and very unwilling. Participants reporting "very willing" or "somewhat willing" were classified as having high willingness. All other responses, including "uncertain," "somewhat unwilling," and "very unwilling," were classified as not having high willingness in the primary binary analysis. This coding did not imply that uncertainty was equivalent to unwillingness. A sensitivity analysis excluding participants who selected "uncertain" was conducted to assess the robustness of the findings. In addition, a three-category multinomial analysis categorized responses as unwilling (very unwilling or somewhat unwilling), uncertain, or willing (somewhat willing or very willing), using unwillingness as the reference category.

## Exposure variables

The primary exposures were three single-item measures of HPV vaccine trust: trust in HPV vaccine effectiveness for preventing cervical cancer; trust in the safety of domestically produced bivalent HPV vaccines; and trust in the safety of imported HPV vaccines. Each item was assessed on a five-category response scale: very trustful, somewhat trustful, neutral, somewhat distrustful, and very distrustful. For regression analyses, each trust measure was modelled as a categorical variable, with “very distrustful” as the reference category. This approach did not assume equal intervals between adjacent Likert-scale response categories or a linear relation between trust and the log odds of high vaccination willingness. These single-item measures were developed for this study to capture self-reported perceptions of vaccine effectiveness and safety. They do not measure clinical vaccine safety or establish construct validity as multi-item scales[27].

## Covariates

Covariates included age, educational level, residence, medical or health-related major, trust in medical recommendations, exposure to media reports of adverse vaccine events, perceived necessity of HPV vaccination, attention to HPV vaccine information, and acceptable HPV vaccine price. Trust in medical recommendations, perceived necessity of HPV vaccination, and attention to HPV vaccine information may overlap conceptually with the trust measures and may lie on pathways between trust and willingness. Model 3 therefore estimates associations conditional on these variables and is not interpreted as a total, direct, or causal effect. Because temporal ordering was unavailable and several covariates may themselves be related to the trust-willingness pathway, none of the sequential models was interpreted as identifying a causal total effect. Acceptable HPV vaccine price was analysed as a six-category variable: 1000 yuan or less, 1000–1999 yuan, 2000–2999 yuan, 3000–3999 yuan, 4000 yuan or more, and uncertain. Participants who selected “uncertain” were retained as a distinct substantive response category and were not treated as having missing data.This variable was interpreted as stated acceptable price, not as a direct measure of household affordability, willingness to pay, or a causal price exposure.

# Statistical analysis

Categorical variables were summarized as frequencies and percentages, and age was summarized using mean and standard deviation. Chi-square tests and Cramer's V were used to examine unadjusted associations between trust measures and high vaccination willingness. The primary analysis included all unvaccinated participants. Binary logistic regression was used to estimate crude and adjusted ORs with 95% CIs. Three hierarchical binary logistic regression models were constructed, and all three primary trust measures were entered simultaneously as categorical variables in each model. Model 1 adjusted for age, educational level, residence, and medical or health-related major. Model 2 additionally adjusted for trust in medical recommendations, exposure to media reports of adverse vaccine events, and acceptable vaccine price. Model 3 additionally adjusted for perceived necessity of HPV vaccination and attention to HPV vaccine information. Model 3 was interpreted as a conditional association model rather than an estimate of a total, direct, or causal effect. Statistical analyses were performed using SPSS version 26.0 and R version 4.2.1. Spearman correlations among trust and perception-related variables are shown in **Supplementary Figure S1**. **Supplementary Table S2** reports correlations with effectiveness trust and collinearity diagnostics based on the Model 3 dummy-variable design matrix; the maximum VIF was 2.855. A sensitivity analysis repeated the binary model after excluding participants who selected uncertain willingness. A multinomial logistic regression estimated the associations of the trust measures with uncertain and willing responses separately, compared with unwilling responses. All tests were two-sided, and $p < 0.05$ was considered statistically significant.

## Results

# Participant flow and analytical sample

After exclusion of questionnaires with more than 10% missing responses or logically inconsistent responses, 6,428 valid questionnaires were retained. Of these respondents, 4,213 answered that they had previously received HPV vaccination and 2,215 answered that they had not. The latter group was classified as having self-reported no history of HPV vaccination; it was not possible to distinguish incomplete from complete vaccination among respondents answering “yes”. All 2,215 participants in the primary group were retained in the descriptive and multivariable analyses. The 86 participants who selected uncertain for acceptable vaccine price were retained as a substantive response category rather than excluded as missing. Participant flow is shown in Fig. 1. The five-category willingness outcome was retained for descriptive and multinomial sensitivity analyses.

# Characteristics of unvaccinated participants

The mean age of the 2,215 unvaccinated participants was 21.97 years (SD 2.92). Undergraduate students comprised the largest educational subgroup (41.2%), followed by vocational-college students (37.6%) and postgraduate students (21.2%). More than half of participants reported rural residence (54.0%) and a medical or health-related major (57.7%). 1,336 participants (60.3%) considered HPV

vaccination necessary, whereas 850 (38.4%) reported having seen media reports of adverse vaccine events. High HPV vaccination willingness was reported by 818 participants (36.9%). The most frequently selected acceptable price category was 1000 yuan or less (25.0%); 86 participants (3.9%) were uncertain about the price they could accept. Table 1 presents descriptive characteristics within each willingness group; percentages in the two willingness columns are column percentages.

Table 1
Sociodemographic characteristics and vaccine-related perceptions of unvaccinated female college students included in the primary analysis (N = 2,215).

| Characteristic | n (%) or mean (SD) |
|---|---|
| **Sociodemographic characteristics** | |
| Age, years | 21.97 (2.92) |
| Educational level: vocational college | 832 (37.6) |
| Educational level: undergraduate | 913 (41.2) |
| Educational level: postgraduate or above | 470 (21.2) |
| Rural residence | 1,196 (54.0) |
| Medical or health-related major | 1,277 (57.7) |
| **Vaccine-related information and perceptions** | |
| Exposure to media reports of adverse vaccine events | 850 (38.4) |
| Perceived HPV vaccination as necessary | 1,336 (60.3) |
| Trust in medical recommendations: very distrustful | 523 (23.6) |
| Trust in medical recommendations: somewhat distrustful | 523 (23.6) |
| Trust in medical recommendations: neutral | 482 (21.8) |
| Trust in medical recommendations: somewhat trustful | 382 (17.3) |
| Trust in medical recommendations: very trustful | 305 (13.8) |
| Attention to HPV vaccine information: very low | 471 (21.3) |
| Attention to HPV vaccine information: low | 533 (24.1) |
| Attention to HPV vaccine information: moderate | 510 (23.0) |
| Attention to HPV vaccine information: high | 378 (17.1) |
| Attention to HPV vaccine information: very high | 323 (14.6) |
| **Acceptable HPV vaccine price** | |
| 1000 yuan or less | 553 (25.0) |
| 1000–1999 yuan | 511 (23.1) |
| 2000–2999 yuan | 426 (19.2) |

*Note: Values are n (%) unless otherwise indicated. High HPV vaccination willingness was defined as reporting being somewhat willing or very willing to receive HPV vaccination. Participants selecting "uncertain" for acceptable HPV vaccine price were retained as a substantive response category.*

| Characteristic | n (%) or mean (SD) |
|---|---|
| **Sociodemographic characteristics** | |
| 3000–3999 yuan | 379 (17.1) |
| 4000 yuan or more | 260 (11.7) |
| Uncertain | 86 (3.9) |
| **Vaccination willingness** | |
| High HPV vaccination willingness | 818 (36.9) |

*Note: Values are n (%) unless otherwise indicated. High HPV vaccination willingness was defined as reporting being somewhat willing or very willing to receive HPV vaccination. Participants selecting "uncertain" for acceptable HPV vaccine price were retained as a substantive response category.*

# Unadjusted associations between trust and vaccination willingness

High HPV vaccination willingness increased across higher categories of trust in HPV vaccine effectiveness and in the safety of both domestic and imported HPV vaccines. Among participants who were very distrustful of HPV vaccine effectiveness, 7.2% reported high willingness; the corresponding proportion was 78.3% among those who were very trustful. Similar gradients were observed for trust in domestic bivalent vaccine safety, for which the proportion ranged from 7.1% to 73.9%, and for trust in imported vaccine safety, for which the proportion ranged from 5.3% to 78.3%.

The overall associations were statistically significant for effectiveness trust (chi-square = 755.157, Cramer's V = 0.584, $p < 0.001$), domestic vaccine safety trust (chi-square = 676.670, Cramer's V = 0.553, $p < 0.001$), and imported vaccine safety trust (chi-square = 664.415, Cramer's V = 0.548, $p < 0.001$). All expected cell counts exceeded 5. Table 2 and Fig. 2 show the unadjusted associations.

Table 2
High HPV vaccination willingness across categories of HPV vaccine trust among unvaccinated participants (N = 2,215)

| Trust category | Total N | High willingness, n | High willingness, % | Chi-square | *p* | Cramer's V |
|---|---|---|---|---|---|---|
| **Trust in HPV vaccine effectiveness** | | | | | | |
| Very distrustful | 539 | 39 | 7.2 | 755.157 | < 0.001 | 0.584 |
| Somewhat distrustful | 516 | 81 | 15.7 | | | |
| Neutral | 378 | 126 | 33.3 | | | |
| Somewhat trustful | 391 | 266 | 68.0 | | | |
| Very trustful | 391 | 306 | 78.3 | | | |
| **Trust in domestic bivalent vaccine safety** | | | | | | |
| Very distrustful | 464 | 33 | 7.1 | 676.670 | < 0.001 | 0.553 |
| Somewhat distrustful | 497 | 69 | 13.9 | | | |
| Neutral | 471 | 163 | 34.6 | | | |
| Somewhat trustful | 400 | 270 | 67.5 | | | |
| Very trustful | 383 | 283 | 73.9 | | | |
| **Trust in imported vaccine safety** | | | | | | |
| Very distrustful | 453 | 24 | 5.3 | 664.415 | < 0.001 | 0.548 |
| Somewhat distrustful | 512 | 87 | 17.0 | | | |
| Neutral | 545 | 199 | 36.5 | | | |
| Somewhat trustful | 401 | 270 | 67.3 | | | |
| Very trustful | 304 | 238 | 78.3 | | | |

*Note: High willingness was defined as reporting being somewhat willing or very willing to receive HPV vaccination. Percentages represent the proportion with high willingness within each trust category. Chi-square tests compared high willingness across the five response categories for each trust measure. All expected cell counts exceeded 5.*

# Hierarchical adjusted associations

Three sequential models were used to show the change in mutually adjusted associations as prespecified covariate groups were added (Table 3**)**. All three trust measures remained positively associated with high willingness across the three models, although the estimates were attenuated after addition of the perception-related covariates. In Model 3, compared with very distrustful participants, those who were very trustful had aORs of 5.397 (95% CI 3.246–8.973) for effectiveness trust, 3.307 (1.930–5.665) for domestic bivalent safety trust, and 5.022 (2.741–9.201) for imported safety trust. Model 3 estimates are conditional cross-sectional associations among correlated perceptions and should not be interpreted as independent causal effects or used to rank trust dimensions.

Table 3
Hierarchical logistic regression: very trustful versus very distrustful categories (N = 2,215)

| **Comparison** | **Model 1 aOR (95% CI)** | **Model 2 aOR (95% CI)** | **Model 3 aOR (95% CI)** |
|---|---|---|---|
| Effectiveness trust | 7.986 (4.992–12.777) | 6.572 (4.026–10.729) | 5.397 (3.246–8.973) |
| Domestic bivalent safety trust | 6.119 (3.723–10.057) | 4.367 (2.596–7.345) | 3.307 (1.930–5.665) |
| Imported safety trust | 9.326 (5.294–16.429) | 6.561 (3.655–11.778) | 5.022 (2.741–9.201) |
| Model likelihood-ratio chi-square | 1096.129 | 1148.748 | 1201.188 |
| Model degrees of freedom | 17 | 27 | 32 |
| Nagelkerke R-squared | 0.533 | 0.553 | 0.572 |

*Note: aOR, adjusted odds ratio; CI, confidence interval. Each estimate compares the very trustful with the very distrustful category. Model 1 adjusted for age, educational level, residence, and medical or health-related major, with all three trust measures entered simultaneously. Model 2 additionally adjusted for trust in medical recommendations, exposure to media reports of adverse vaccine events, and acceptable vaccine price. Model 3 additionally adjusted for perceived necessity of HPV vaccination and attention to HPV vaccine information. These are conditional cross-sectional associations, not causal effects. The full category-specific Model 3 estimates are shown in* Fig. 3; *complete estimates for all covariates are presented in* **Supplementary Table S3**.

# Participant characteristics according to vaccination willingness

Table 4 provides descriptive, unadjusted characteristics by willingness group. These comparisons are included as sample context and are not interpreted as independent associations; the multivariable estimates are reported in Table 3 and **Supplementary Table S3**. Percentages in the two willingness columns are column percentages; the within-price-category proportions reporting high willingness, together with the corresponding fully adjusted associations, are presented in **Supplementary Table S4**.

Table 4
Characteristics of unvaccinated participants according to high HPV vaccination willingness (N = 2,215)

| Characteristic | Overall | Not high willingness (n = 1,397) | High willingness (n = 818) | *p* value |
|---|---|---|---|---|
| Age, years, mean (SD) | 21.97 (2.92) | 22.05 (2.85) | 21.85 (3.04) | 0.124 |
| Educational level: vocational college | 832 (37.6) | 487 (34.9) | 345 (42.2) | < 0.001 |
| Educational level: undergraduate | 913 (41.2) | 577 (41.3) | 336 (41.1) | |
| Educational level: postgraduate or above | 470 (21.2) | 333 (23.8) | 137 (16.7) | |
| Rural residence | 1,196 (54.0) | 724 (51.8) | 472 (57.7) | 0.008 |
| Medical or health-related major | 1,277 (57.7) | 815 (58.3) | 462 (56.5) | 0.418 |
| Exposure to adverse vaccine-event reports | 850 (38.4) | 443 (31.7) | 407 (49.8) | < 0.001 |
| Perceived HPV vaccination as necessary | 1,336 (60.3) | 717 (51.3) | 619 (75.7) | < 0.001 |
| Acceptable price: 1000 yuan or less | 553 (25.0) | 256 (18.3) | 297 (36.3) | < 0.001 |
| Acceptable price: 1000–1999 yuan | 511 (23.1) | 331 (23.7) | 180 (22.0) | |
| Acceptable price: 2000–2999 yuan | 426 (19.2) | 286 (20.5) | 140 (17.1) | |
| Acceptable price: 3000–3999 yuan | 379 (17.1) | 284 (20.3) | 95 (11.6) | |
| Acceptable price: 4000 yuan or more | 260 (11.7) | 195 (14.0) | 65 (8.0) | |
| Acceptable price: uncertain | 86 (3.9) | 45 (3.2) | 41 (5.0) | |

*Note: Values are n (%) unless otherwise indicated. High willingness was defined as reporting being somewhat willing or very willing to receive HPV vaccination. For price categories, percentages in the not-high-willingness and high-willingness columns use the respective willingness group as the denominator.*

# Sensitivity analysis

After exclusion of 432 participants who reported uncertain willingness, 1,783 participants remained for the sensitivity analysis. The direction and overall gradient of associations between the three trust

measures and vaccination willingness were consistent with those observed in the primary analysis. Compared with very distrustful participants, those who were very trustful had adjusted odds ratios of 5.694 (95% CI 3.077–10.538) for trust in HPV vaccine effectiveness, 3.940 (95% CI 2.079–7.466) for trust in domestic bivalent vaccine safety, and 6.924 (95% CI 3.344–14.336) for trust in imported vaccine safety. Full category-specific results from the sensitivity analysis are presented in **Supplementary Table S5**.

In the three-category multinomial model using unwillingness as the reference category, very trustful effectiveness, domestic safety, and imported safety were associated with willing responses, with relative risk ratios of 5.637 (95% CI 3.122–10.177), 4.485 (2.432–8.268), and 7.148 (3.559–14.359), respectively. For uncertain versus unwilling responses, the corresponding relative risk ratios were 1.211 (0.676–2.170), 2.302 (1.291–4.103), and 2.638 (1.364–5.102), respectively (**Supplementary Table S6**). Thus, the principal findings were not solely attributable to combining uncertain and unwilling responses in the primary binary outcome.

# Discussion

Trust in vaccine effectiveness showed a clear association with stated willingness[28]. The observed association between trust in HPV vaccine effectiveness and willingness is conceptually consistent with previous research on perceived benefit and vaccine confidence. However, the present single-item measure of effectiveness trust does not capture the broader, multidimensional construct of perceived benefit[27]. In the present study, the proportion reporting high willingness rose from 7.2% among participants who were very distrustful of vaccine effectiveness to 78.3% among those who were very trustful. The difference is substantial, although it reflects reported attitudes measured at one point in time rather than a demonstrated change in subsequent vaccination behavior.

The two product-specific safety-trust measures, namely trust in the safety of domestically produced bivalent HPV vaccines and trust in the safety of imported HPV vaccines, were both positively associated with reported willingness. Higher trust in the safety of domestically produced bivalent vaccines and imported vaccines was associated with higher odds of reporting high willingness after adjustment for demographic characteristics and other perception-related variables[29]. Concerns about adverse events, manufacturing quality, regulatory oversight, and the reliability of vaccine information are well-recognized features of vaccine hesitancy[30]. For students who have not yet initiated HPV vaccination, safety concerns may be particularly influential because vaccination is a preventive intervention received while individuals are generally healthy[31]. Information on vaccine authorization, safety surveillance, evaluation of adverse events, and post-marketing monitoring may therefore be relevant when communicating with students who remain uncertain about vaccination[31]. However, the present findings do not demonstrate that changing such trust will increase actual vaccine uptake[32].

The results should not be interpreted as evidence that domestically produced bivalent and imported HPV vaccines differ in clinical safety. The survey assessed participants' perceptions of safety, not

comparative safety outcomes[33]. Trust in domestically produced bivalent and imported vaccines may reflect broader beliefs about manufacturing standards, quality control, product availability, price, previous media coverage, and confidence in health institutions[20]. These perceptions are likely to overlap. The correlation coefficients among the three trust measures ranged from 0.613 to 0.625, indicating that effectiveness trust and the two product-specific safety-trust measures were related, although the variance inflation factors did not indicate severe statistical multicollinearity. Accordingly, the mutually adjusted estimates should be interpreted as associations between correlated perceptions and reported willingness. They do not establish fully separable causal effects, and the adjusted odds ratios should not be used to rank the relative importance of effectiveness trust and safety trust[34].

The strong unadjusted associations also warrant careful interpretation. Trust and vaccination willingness were measured using the same self-administered questionnaire at the same time. Students with a generally favorable orientation toward HPV vaccination may have been more likely to report both higher trust and greater willingness. Common-method bias and conceptual overlap may therefore have contributed to the magnitude of the observed associations. Reverse causation is also possible[35]. Students who already intend to receive HPV vaccination may subsequently evaluate the vaccine as more effective or safer[23]. The temporal ordering of trust and willingness cannot be established from this cross-sectional design.

The association between acceptable vaccine price and vaccination willingness was less straightforward. Compared with students who considered 1000 yuan or less acceptable, participants selecting several higher price categories had lower adjusted odds of high willingness. This finding was not anticipated. It should not be interpreted as evidence that a greater willingness or ability to pay reduces willingness to vaccinate[36]. The price item may capture several considerations simultaneously, including preferences for particular vaccine products, expected value for money, uncertainty about future costs, local vaccine availability, and barriers to accessing vaccination services[37]. Restricting the analysis to students who had not yet been vaccinated may also have influenced this association[38]. The variable should therefore not be interpreted as a pure measure of affordability or willingness to pay, and its cross-sectional association with willingness should not be given a causal interpretation[39]. Further research should distinguish household economic resources, perceived affordability, willingness to pay, preferred vaccine type, appointment accessibility, and actual vaccine supply.

Several limitations should be acknowledged. First, the study used online convenience sampling. Students who were more connected to university-based networks, more engaged with health information, or more willing to complete web-based questionnaires may have been more likely to participate. The sample should therefore not be regarded as representative of all female college students in China. Neither the reported prevalence of prior HPV vaccination nor the proportion of students with high willingness should be interpreted as a national estimate. The study was also not designed to compare provinces, institutions, or educational settings. A conventional response rate could not be calculated because recruitment occurred through open online channels without a defined sampling frame. Second, and importantly, university, province, and class-level identifiers were not

retained in the de-identified analytical dataset. Potential clustering of responses within universities, classes, or regions could not be modeled using multilevel techniques, generalized estimating equations, or cluster-robust standard errors. Students within the same university may share health education exposure, vaccine access, local policy contexts, campus publicity, and social networks[40]. The reported standard errors may therefore be underestimated and confidence intervals overly narrow. This limitation is not corrected by school-type adjustment, the three hierarchical covariate models, or stronger limitation wording. Third, questionnaire-completion dates were not retained in the de-identified analytical dataset. Potential temporal variation in vaccine supply, appointment access, local initiatives, media coverage, public discussion, or actual vaccine costs could not be examined or adjusted for. Fourth, the primary trust measures were based on single items developed for this study. Although the items addressed conceptually important aspects of HPV vaccine confidence, they may not capture the full range of beliefs underlying trust. Perceptions of vaccine safety may include concerns about adverse effects, manufacturing quality, regulation, supply, cost, and information credibility. These elements could not be separated in the present survey. The English-language version of the questionnaire is provided as **Supplementary Material S1**. Future studies should use culturally appropriate multi-item measures and assess their reliability and validity among Chinese university students.

A contribution of this study is the simultaneous examination of trust in HPV vaccine effectiveness and two product-specific safety perceptions among a large multi-province convenience sample of unvaccinated female college students in China. Rather than treating safety trust as a single undifferentiated construct, the analysis retained perceived safety of domestically produced bivalent and imported HPV vaccines as separate variables. Because these perceptions were correlated and were measured simultaneously with willingness, the findings characterize conditional associations and do not establish comparative importance, causal effects, or clinical differences between vaccine products.

The study also has several strengths. It included a large sample of unvaccinated female college students and focused the primary analysis on participants for whom willingness to initiate HPV vaccination was directly relevant. The analysis distinguished trust in vaccine effectiveness from trust in the safety of domestic and imported products. In addition, the “uncertain” response to acceptable vaccine price was retained as a substantive category rather than treated as missing. Both the binary sensitivity analysis excluding uncertain willingness and the three-category multinomial analysis yielded patterns consistent with the primary analysis.

Taken together, these findings suggest that communication concerning HPV vaccination among college students should address both its role in cervical cancer prevention and concerns about vaccine safety[17]. However, the present data do not show that changing trust will increase vaccination uptake. Longitudinal studies are needed to determine whether trust precedes willingness and whether willingness predicts subsequent vaccination. Prospective studies should retain institutional and time identifiers, account for clustering, and assess actual vaccine initiation and completion.

# Conclusions

Among unvaccinated female college students recruited through university-based online networks in 12 provincial-level administrative regions of China, higher self-reported trust in HPV vaccine effectiveness and the perceived safety of domestic bivalent and imported HPV vaccines was associated with greater reported willingness to initiate HPV vaccination. Because the study used a cross-sectional convenience sample, measured correlated beliefs and willingness simultaneously, and could not account for institutional or regional clustering, these findings should not be interpreted as causal estimates, evidence of vaccine safety differences, or nationally representative estimates.

## Declarations

# Ethics approval and consent to participate

The study protocol was reviewed and approved by the Institutional Review Boards of Shenzhen Pingshan District Central Hospital (PSZX-EC-AP-020) and Heze Municipal Hospital (2024-KY003-06). Electronic informed consent was obtained from all participants before completion of the questionnaire. The study was conducted in accordance with the Declaration of Helsinki.

# Consent for publication

Not applicable.

# Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request, subject to institutional and ethical restrictions.

# Competing interests

No competing interests.

# Funding

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# Authors' contributions

WB conceived and designed the study, performed the statistical analysis, drafted the manuscript, and was responsible for the publication fee. WS, HC, YL, BY, SX, JC, MW, and YZ contributed to data acquisition and investigation. WC conceived and designed the study, provided supervision, and critically revised the manuscript for important intellectual content. All authors interpreted the data, critically reviewed the manuscript, and approved the final version.

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# Figures

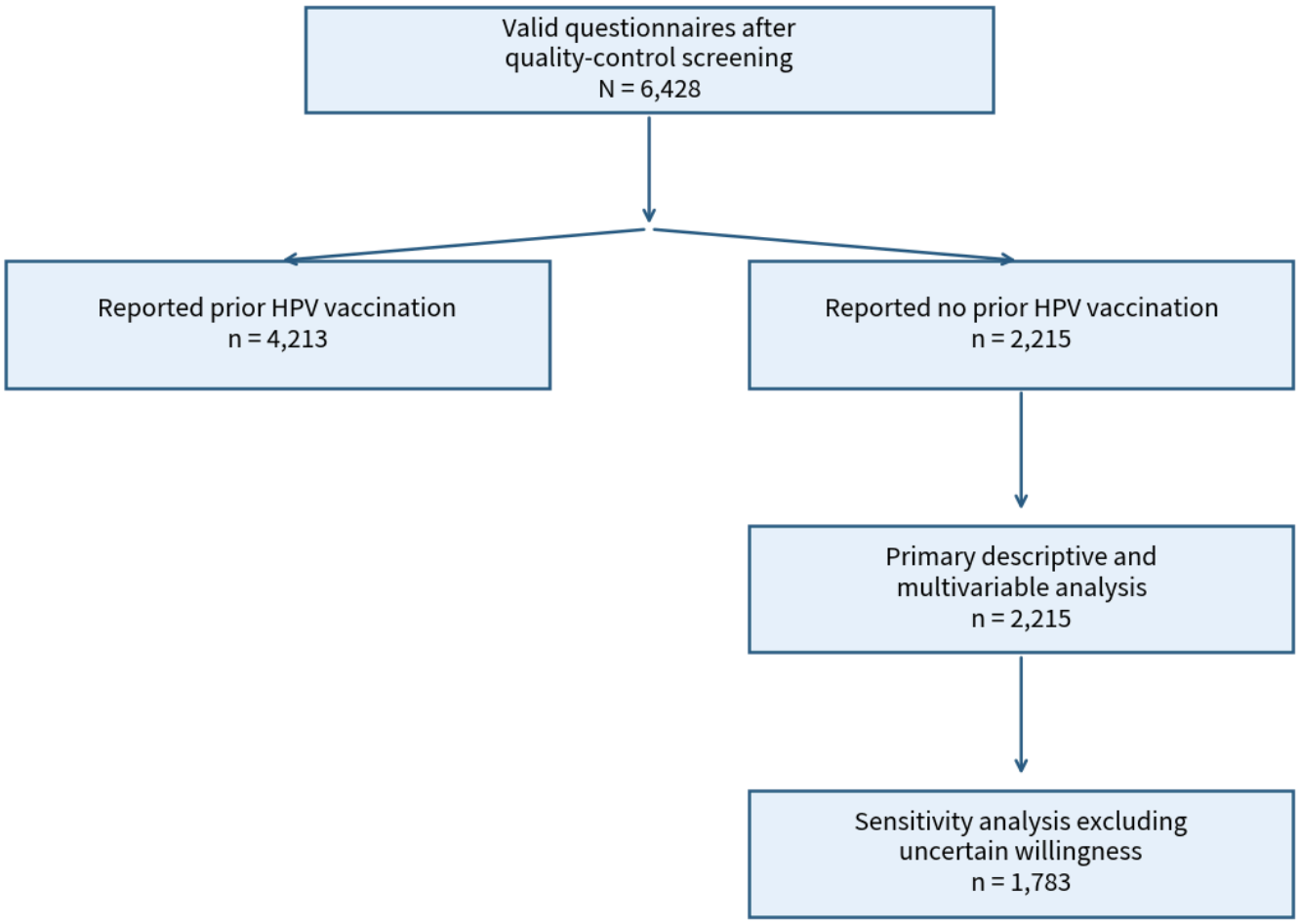
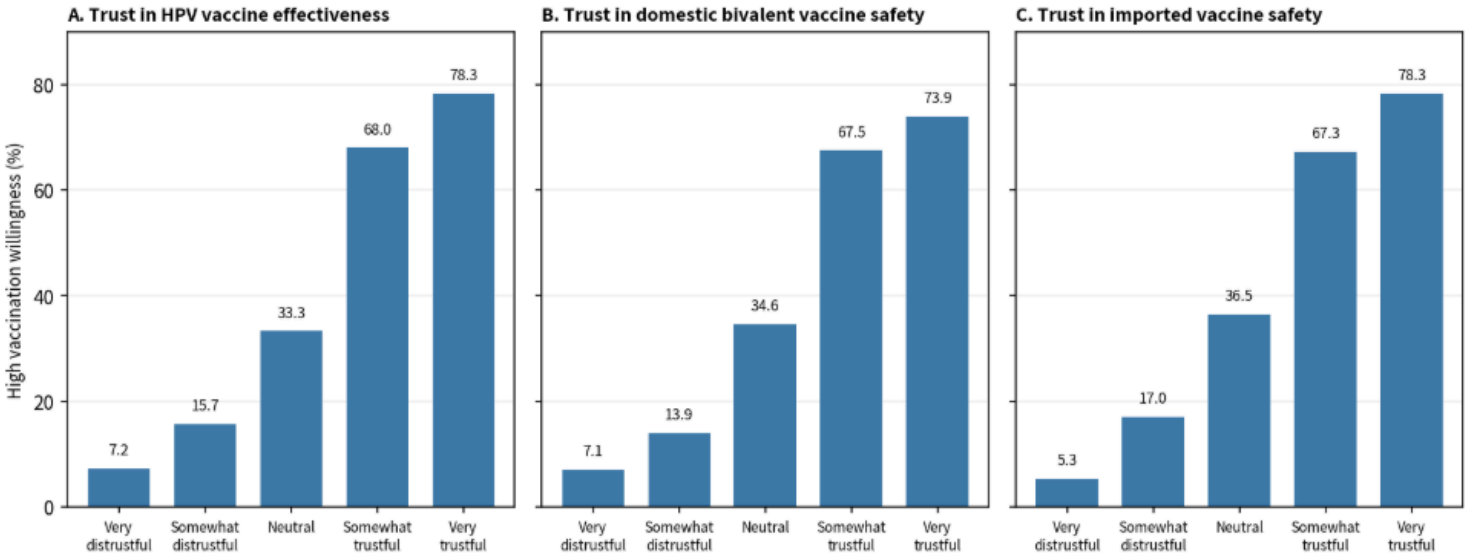



**Figure 1**

**Flow diagram of survey participants and analytical samples.** The primary analysis included all participants reporting no previous HPV vaccination (n=2,215). Participants selecting "uncertain" for acceptable HPV vaccine price were retained as a substantive response category. The sensitivity analysis excluded 432 participants who reported uncertain HPV vaccination willingness. Because recruitment

occurred through open online channels, the underlying sampling frame and conventional response rate were unavailable.




## Figure 2

**Proportion of unvaccinated participants reporting high HPV vaccination willingness across categories of trust in HPV vaccine effectiveness and safety.** High willingness was defined as reporting being somewhat willing or very willing to receive HPV vaccination. Percentages were calculated within each trust category. Overall chi-square tests were significant for trust in HPV vaccine effectiveness ($p$ <0.001), domestic bivalent vaccine safety ($p$ <0.001), and imported vaccine safety ($p$ <0.001).

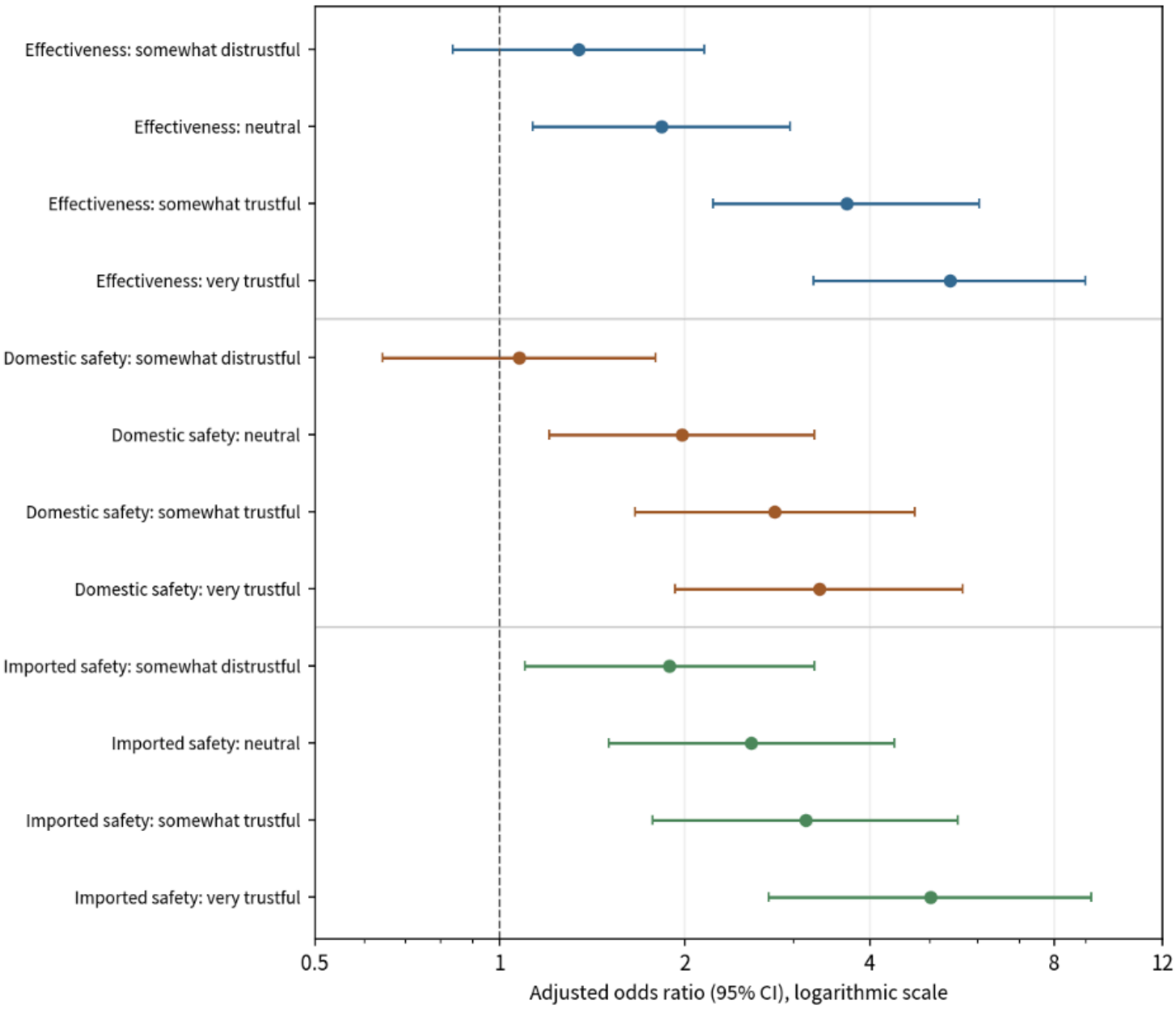



**Figure 3**

**Adjusted odds ratios and 95% confidence intervals for high HPV vaccination willingness according to categories of trust in HPV vaccine effectiveness, the safety of domestically produced bivalent HPV vaccines, and the safety of imported HPV vaccines among unvaccinated female college students.** Points represent Model 3 adjusted odds ratios and horizontal bars represent 95% confidence intervals on a logarithmic scale. All three trust measures were entered simultaneously. The reference category for each trust measure was “very distrustful.” Model 3 adjusted for the covariates listed in **Table 3**. This figure presents the complete category-specific gradient, whereas **Table 3** presents the evolution of the extreme-category comparison across the three sequential models.

# Supplementary Files

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- SupplementaryMaterial1.docx
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