

The impact of the human papillomavirus vaccine on women's health: a systematic review

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ABSTRACT. – OBJECTIVE: The World Health Organization (WHO) declared that the human papillomavirus (HPV) is the most widespread infection that affects women's reproductive system. HPV is a serious concern to women's health, as it has a negative impact on women's quality of life. Approximately 70% of all occurrences of cervical cancer globally are caused by HPV strains 16 and 18. A few studies have found that HPV vaccinations play a significant role in protecting women against HPV infections. This study aims to identify the effectiveness of the HPV vaccine and to examine the influence of this vaccine on women's health.

MATERIALS AND METHODS: EBSCO, PubMed, Cochrane, Google Scholar, Science Direct, and ProQuest were selected as electronic databases for systematic research. The inclusion criteria encompassed studies published in English from January 2019 to August 2023, evaluating the effectiveness of the HPV vaccine in women aged 18-76 years globally. This review included different types of studies, including cross-sectional, retrospective cohort, original randomized controlled trials, and prospective studies. Moreover, the included studies were evaluated using the Jonna Briggs Institute (JBI) methodological quality checklist tool. Two reviewers assessed the methodological quality of all studies using JBI guidelines.

RESULTS: The search identified 11,095 articles, 19 of which were included in this review. Significant findings were found regarding the relationship between HPV vaccines and women's health.

CONCLUSIONS: This review highlights the importance of the HPV vaccine and its administration among women to promote their health and prevent future infections.

Key Words:

Human papillomavirus (HPV), Sexually transmitted infections (STIs), Cervical cancer, Women's health, Women's quality of life (QoL).

Abbreviations

HPV: human papillomavirus; ASC-US: atypical squamous cells of undetermined significance; STIs: sexually

transmitted infections; HR-HPV: high-risk human papillomavirus; HSIL: high-grade squamous intraepithelial lesion; ICC: invasive cervical cancer; LR-HPV: low-risk human papillomavirus; LSIL: low-grade squamous intraepithelial lesion; Pap: papanicolaou; SPSS: statistical package for the social scientists; WHO: world health organization; LEEP: loop electrosurgical excision procedure; CIN: cervical intraepithelial neoplasia; QoL: quality of life; PRISMA: preferred reporting item for systematic review and meta-analysis.

Introduction

The human papillomavirus (HPV) is a widespread infection affecting a woman's reproductive system, causing significant health issues, and affecting women's quality of life (QoL). HPV is responsible for various types of cancers, including cervical cancer, which is the fourth deadliest malignancy among women¹. In Saudi Arabia, 358 new cases of cervical cancer are detected annually among women aged 15 to 44 years². HPV is categorized into low-risk (LR-HPVs) and high-risk (HR-HPVs), with LR-HPVs causing cutaneous and anogenital warts and HR-HPVs responsible for penile, cervical, vulvar, vaginal, anogenital, and oropharyngeal cancers. Moreover, HR-HPV types 16 and 18 have been linked to invasive cervical cancer³.

According to Bruni et al² (2023), 70% of all cervical cancer cases globally are caused by HPV strains 16 and 18. HPV vaccinations can help avoid certain health consequences caused by HPV and decrease the prevalence of cervical and other anogenital malignancies. Three forms of prophylactic vaccines have been widely used and have been effective in lowering the incidence of HPV infection and related diseases: the quadrivalent HPV vaccine, the bivalent HPV vaccine, and the nonvalent HPV vaccine. These vaccines specifically target and elicit immunity against LR-HPVs and HR-HPVs, which are responsible

for 70% and 90% of genital and cutaneous warts and malignancies, respectively⁴.

A study in Riyadh City, Saudi Arabia, by Jradi and Bawazir⁵ found that women in Saudi Arabia have limited knowledge regarding HPV infection and vaccination. The researchers suggested implementing a health education campaign to raise awareness of cervical cancer and the benefits of screening and immunization. In India, a study by Shetty et al⁶ revealed that a lack of knowledge regarding HPV vaccines and their prevention is a significant reason for vaccine refusal. The study also highlighted the importance of educating the public about vaccination promotions and including HPV vaccines in the national immunization program for both boys and girls. In eastern Nepal, a study by Bhatta et al⁷ found that raising awareness and knowledge regarding HPV, its involvement in cervical cancer, and prevention methods is crucial for effective prevention. The results revealed that cervical cancer can be prevented with primary, secondary, and tertiary prevention strategies, but low awareness and knowledge of cervical cancer and HPV vaccination pose significant obstacles to effective prevention.

A study⁸ conducted in the US compared the changes in the incidence and mortality due to cervical cancer between 2001 and 2017 using data from the National Center for Health Statistics and the National Program of Cancer Registries. The study found that information on age-based vaccine eligibility can improve public health knowledge by comparing changes in cervical cancer incidence and generating suggestive evidence for vaccine-associated declines in cervical cancer death cases.

Studies⁹ have primarily focused on the efficacy of bivalent and quadrivalent HPV vaccinations among women. A randomized, multicenter, double-blind, parallel, three-arm controlled superiority trial⁹ in Kenya found that both vaccine types were highly effective in preventing incident persistent oncogenic HPV infection, thereby resulting in 97.5% protection against HPV 16/18 infection.

In Mongolia, a single dose of the quadrivalent HPV (4vHPV) vaccine was found¹⁰ to reduce vaccine-targeted HPV genotypes six years after vaccination among young Mongolian women. Both vaccine types were found to be efficient in preventing oncogenic HPV infections.

Extant research¹¹⁻¹³ has revealed that HPV vaccinations have a significant impact on women's health and quality of life. A study¹¹ in Bavaria, Germany, found a decrease in anogenital warts and precancerous lesions among young women

who received HPV vaccinations. To increase the population impact of HPV-related diseases, vaccination rates must be increased. Muñoz-Quiles et al¹² found a 74% reduction in the prevalence of genital warts when all HPV4v vaccines were administered. Schlecht et al¹³ examined the impact of vaccine administration on the prevalence of infections among sexually active adolescent girls and young women in New York City. Their study found that the introduction of vaccines led to a decrease in the detection rates of vaccine-related HPV varieties, but the rates of other nonvaccine-related high-risk HPV forms increased. Thus, the researchers suggest that the prevalence of high-risk HPV should be continuously monitored.

Two studies^{14,15} have evaluated the advantages and drawbacks of HPV vaccines in different regions. In Japan, a literature search¹⁴ found a risk-benefit ratio of 0.0156 for changes in quality-adjusted life years (QALY), but the HPV vaccine had more advantages than disadvantages. In Europe, a systematic review and meta-analysis¹⁵ found that the benefits of vaccination outweigh the dangers, regardless of any causative relationships between HPV vaccines and adverse effects. Both studies found no evidence of increased chronic or autoimmune diseases or negative effects among women but emphasized the need for better-organized collaborations to track uncommon adverse events

Given a lack of research regarding the administration of HPV vaccines, this study aimed to review the effectiveness of the HPV vaccine and determine its influence on the quality of women's lives. The research hypothesis of this study is that the HPV vaccine could improve women's health.

Materials and Methods

Protocol and Registration

This systematic review study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to review the effectiveness of the HPV vaccine and to determine the influence of this vaccine on the quality of women's lives. The period of the search was between August 5, 2023, and August 14, 2023. The methodology of this systematic review was previously registered with the number INPLASY2023120029 on the International Platform of Registered Systematic Reviews and Meta-analysis Protocols (INPLASY).

Eligibility Criteria

The inclusion criteria were studies that included women aged 18-76 years, peer-reviewed, published between 2019 and 2023, studies that describe the effectiveness of the HPV vaccine, studies worldwide, studies in English, quantitative studies (cross-sectional, retrospective cohort study, randomized controlled trial, or prospective study), and those that used placebo for the control group. Studies that did not match the previous criteria were excluded.

Search Strategy Process

The population, intervention, comparison, and outcome (PICO) approach was utilized to develop the search strategy. In this research, P is women; I is the HPV vaccine, C is no vaccine or a placebo; and O is the influence on women's health. The final search terms were generated for the six electronic databases (EBSCO, PubMed, Cochrane, Google Scholar, Science Direct, and ProQuest). The outlines of the search methods that retrieve all articles that are most relevant to the research question are presented in [Supplementary Table I](#). The extracted studies were checked, duplicate studies were deleted, and then the title and abstract were screened. The studies that matched the inclusion criteria were processed for eligibility and quality assessment.

Quality Assessment

The included studies were evaluated by two reviewers who conducted the appraisal process

following the JBI guideline¹⁶ in order to critically assess each study's methodological quality and bias risk. Then, the reviewers extracted the data in the following order: author(s) name, publication year and study region, type of sample, sample size and sampling method, data collection method, data analysis, and the study findings. [Supplementary Table II](#) presents the study characteristics of the included studies, and [Supplementary Table III](#) presents an overview of the key findings and design of the included studies.

Results

Of the 11,095 primary studies analyzed, 19 were included¹⁷⁻³⁵ in this review based on the inclusion and exclusion criteria (Figure 1). These studies were conducted in 13 countries: the United States, Japan, Iran, New Zealand, Malaysia, Bangkok, Germany, South Korea, the Netherlands, Greece, China, Spain, and Canada. Most of the studies originated in Japan (26%), and China and the United States accounted for 10.5% each. The 19 studies for this project were published in the English language in the period 2019-2023. All studies were quantitative studies and employed various study designs, including cross-sectional (seven studies^{17-19,22,23,29,33}: 36.84%), retrospective (six studies^{21,24,28,30-32}: 31.84%), prospective (two studies^{20,27}: 10.53%), and randomized controlled

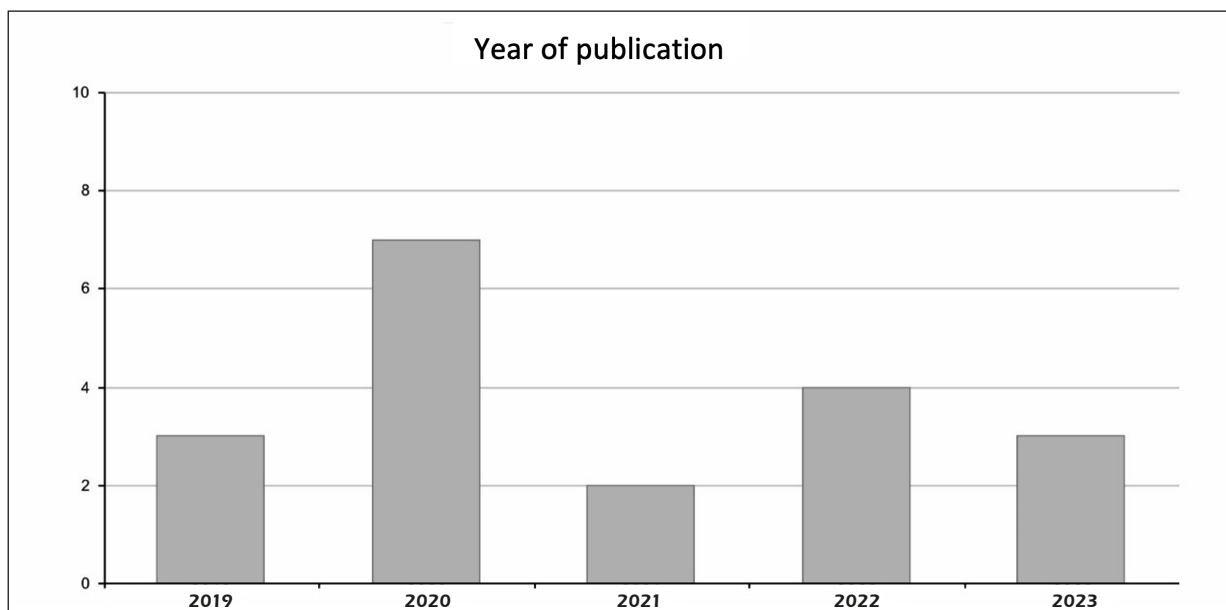


Figure 1. The characteristics of the included studies.

trials (RCTs) (four studies^{25,26,34,35}: 21.05%). Figure 2 displays the number of included studies that were published each year from 2019 to 2023.

Seven studies¹⁷⁻²³ assessed the effectiveness of HPV vaccines for healthy women among a total of 18,854 women. Two studies^{17,18} assessed healthy women with a history of sexual activity. One study¹⁸ provided evidence of reduced HPV 16 and 18. An-

other study¹⁷ revealed no difference in the decrease in HPV infection. Yet another study²⁰ showed no evidence of a reduction in cytological abnormalities. The evidence for the effects of these vaccines was derived from four studies^{19,21-23} on the decreased prevalence of HPV 16 and 18 and cervical cancer.

Four studies²⁴⁻²⁷ were conducted on a total of 1,934 women. One study²⁴ reported on women

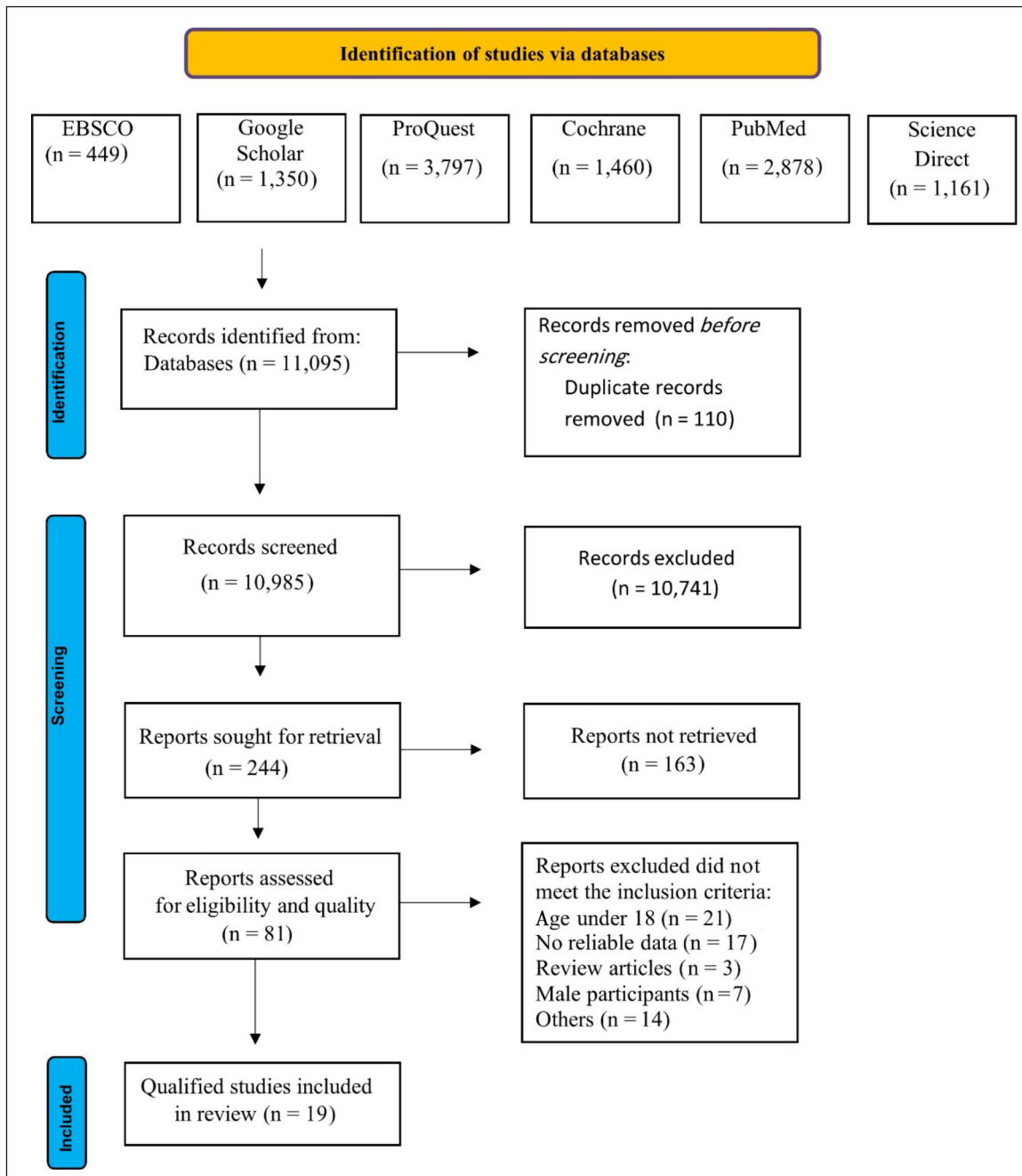


Figure 2. Systematic Review Flow Diagram (PRISMA) including all relevant studies.

with high-grade cervical intraepithelial lesions (HSILs) or cervical intraepithelial neoplasia (CIN) 2-3 who received bivalent or quadrivalent vaccines after treatment and provided significant evidence that there was a decrease in the rate of persistence and reoccurrence of HPV infections after treatment for these women. Two RCT studies^{25,26} administered prophylactic vaccines after treatment; they also found that there is strong evidence that the percentage of recurrent CIN 1-3 was decreased compared to those who did not receive vaccines. Another study²⁷ reported on women with low-grade (LG) cytology and provided significant evidence that the prevalence of LG cytology was reduced.

Four studies²⁸⁻³¹ reported data on women who participated in national vaccine programs in different countries. One study²⁸ revealed no evidence that HPV vaccines could improve women's health. However, the researchers affirmed that HPV vaccine programs could lead to a decrease in cervical cancer. The other three studies²⁹⁻³¹ reported data indicating a significant reduction in HPV infections among vaccinated women.

In one study³², one dose of the HPV vaccine was administered, and it was found that a single dose in patients aged below 18 years lowered high-grade cytology. Three studies³³⁻³⁵ administered (bivalent or quadrivalent) vaccinations against HPV in three-spaced doses. They provided evidence for the reduction of HPV 6, 11, 16, and 18 and the prevention of cervical cytological abnormalities. Of these three studies, two RCT studies^{34,35} found findings compared to those who did not receive vaccines.

Discussion

Effectiveness Of HPV Vaccines for Healthy Women

Our findings relate to the role of prophylactic vaccines against HPV infections. In Bavaria¹¹, a decline in anogenital warts and precancerous lesions was found among young women who received HPV vaccinations. A previous study¹² discovered substantial evidence that the average prevalence of genital warts decreased by 74% when all HPV4v vaccinations were given to female patients between the ages of 14 and 65 years. This outcome aligns with the findings of another study by Loenenbach et al²². The researchers investigated the effectiveness of HPV vaccines

(bivalent or quadrivalent) among women aged 20-25 years. The results of this study revealed that the quadrivalent HPV vaccine protected against at least one HPV genotype. Furthermore, Lee et al²¹ analyzed the effectiveness of the HPV vaccine. They found that the HPV vaccine was 84.6% effective in lowering HPV 16/18 positivity and 88.0% effective in reducing atypical squamous cells of undetermined significance (ASC-US+) associated with HPV 16/18. According to Kudo et al¹⁹ the bivalent HPV vaccine is highly effective against HPV 16 and 18. The results validate what Taniguchi et al²³ observed. Vaccinated women tended to be better protected against all forms of possible cervical cancer. These four studies^{19,21-23} concluded that HPV vaccines are important in improving women's health and QoL and in preventing numerous types of cancer.

Another aspect to be considered in this study is sexual activity. Previous studies^{13,36} conducted by various authors examined sexually active girls and women and observed a reduction in the detection rates of vaccine-associated HPV types; the incidence of HPV genotypes related to the vaccine was abnormally low. One recommendation made by the researchers was to regularly track the prevalence of high-risk HPV. Positive correlations between an early sexual debut or having several sexual partners and HPV highlighted the importance of immunizing at the recommended age of 12-13 years for optimal vaccine impact. The results corroborate the notion that HPV vaccination is critical in enhancing women's quality of life. The analysis aligns with the argument of Kitamura et al¹⁸. The results of their study concluded that women who had received the HPV vaccine, regardless of the vaccine type or immunization dose, had a significantly lower risk of contracting the HPV 16/18 infection. The authors highlighted that unvaccinated, sexually active females must receive at least one dose of the HPV vaccine to be protected.

Effectiveness of HPV Vaccines for Women with High-Grade Cervical Intraepithelial Lesions (HSIL), Cervical Intraepithelial Neoplasia (CIN), and Low-Grade (LG) Cytology

The findings of this review highlight the importance of prevention of HPV infections and of administering HPV vaccinations for women who have HPV infections, including LG cytology, HSIL, and CIN grades 1-3 after treatment. Karimi-Zarchi et al²⁵ studied the effects of prophylactic

quadrivalent HPV vaccination on women with CIN 1-3. The study revealed the effectiveness of HPV vaccination in preventing residual or recurring cervical dysplasia and reducing the need for repeated surgery when combined with treatment. The outcomes reflect the observation of Van de Laar et al²⁶ that indicated that the efficacy of the HPV vaccination, in addition to loop electrosurgical excision procedure (LEEP), might be advantageous in preventing residual or recurring cervical dysplasia and reducing the likelihood of requiring repeated surgical treatments. The data are in accordance with the findings of previous studies in the literature in which the vaccine was more effective for cervical cancer among vaccinated women. In addition, it was found⁸ a reduction in the incidence of cervical cancer and death caused by cervical cancer in girls and women between the ages of 15 and 24 following the introduction of the HPV vaccine.

Casajuana-Pérez et al²⁴ suggest that when women with HSIL/CIN 2-3 received vaccination, the prevalence of persistent/recurrent HSIL/CIN 2-3 declined. Valasoulis et al²⁷ found that giving HPV16, HPV18, HPV31, and HPV33 VLP vaccinations appeared to guarantee a statistically significant earlier clearance of HPV infection in patients with LG cytological abnormalities compared to patients in the non-vaccinated cohort.

Effectiveness of Administration of One Dose or Three Doses of HPV Vaccines for Women

In 2020, Innes et al³² performed a retrospective population-based cohort study in New Zealand, examining 104,313 women born between 1990 and 1994 whose cervical cytology or histology was recorded between January 1, 2010, and December 31, 2015. The women were divided into three groups – unvaccinated, vaccinated before turning 18, and recently immunized (those who received HPV vaccinations at the age of 18 years or older). Receiving the quadrivalent HPV vaccine at least once before turning 18 years of age was found to be associated with a decrease in high-grade cytology by 25% and a decrease in the incidence of high-grade histology by 31%. On the other hand, Barnabas et al⁹ analyzed the efficacy of single-dose nonvalent and bivalent vaccinations among young women between 15 and 20 years of age. Similar to multidose regimens, both vaccination types were found to be highly effective at preventing incidents of persistent oncogenic HPV infection, yielding 97.5% protection against HPV

16/18 infection. The results reported by Batmunkh et al¹⁰ are representative of young females aged 11-17 years in Mongolia. The researchers studied the potential impact of a single dose of the quadrivalent HPV (4vHPV) vaccine on the incidence of HPV detection in young Mongolian women. They found that there was a significant decline in HPV genotypes targeted after vaccination with a single dose of the 4vHPV vaccine.

Other studies^{33,35} have also confirmed the value of administering three doses of HPV vaccines. Zhu et al³⁵ measured the efficacy of the AS04-HPV 16/18 vaccine in women 72 months after the initial immunization. The results revealed that infection, abnormal cytology, and CIN lesions linked to HPV 16/18 were all prevented by the AS04 HPV-16/18 vaccine in young Chinese women. In Accra and Kumasi cities of Ghana, a study³³ indicated the distribution, prevalence, and risk factors associated with HPV genotypes among women presenting for reproductive health services, with a total of 317 women aged 21 to 76 years. The study found a high prevalence of HR-HPV among women, which suggests that multivalent vaccinations were effective in reducing the HPV burden among women in the general population. Furthermore, the nonvalent vaccination provided protection against HPV 16 and 18, as well as seven other HPV types among women in Ghana.

Other findings from Zhao et al³⁴ determined the long-term efficacy of the HPV4v vaccination in preventing HPV-related illnesses. Chinese women aged 20-25 years received the HPV4v vaccine³⁴. The analysis of the results of a follow-up (at a median of 94 months) reported sustained protection against HPV-16/18-related genital precancerous and cancer cases, with a tendency of continuous protection for up to 11 years. Additionally, the vaccine may help the health system by lowering abnormalities in cervical cytology.

Effectiveness of an HPV Vaccination Program for Women

After the World Health Organization (WHO) approved HPV vaccines, several studies²⁸⁻³¹ in different countries were conducted to confirm the efficacy of HPV programs among women. Previous studies³⁷ have revealed the importance of implementing an information campaign regarding different aspects of these vaccines. Amponsah-Dacosta et al³⁷ agreed with several authors, including Shetty et al⁶ and Bhatta et al⁷, that to promote initiatives to provide HPV vaccines for women, the level

of public awareness and knowledge in this regard must be raised. These results align with studies by Khoo et al²⁹, Clark et al³⁰, Li et al²⁸ and Seong et al³¹, which concluded that vaccinated women who received vaccines in HPV programs had a higher level of education. These results emphasize the value of awareness and education campaigns prior to activating these programs intended to contribute to reducing the rate of HPV infections and other types of cervical cancers.

Addressing the Research Question and Aim: How Effective Is the HPV Vaccine in Improving Women's Health Compared to Not Taking It?

The findings of this study confirm that HPV vaccinations in different doses in women are related to improving women's health by reducing the spread of HPV infections and the incidence of recurrent infections and cervical cancer compared to women who did not receive these vaccinations. In addition, the findings of all included studies are in line with the hypothesis that the benefits of prophylactic vaccines are positively correlated with reducing HPV infections and other types of cervical cancer.

Limitations

This study has potential limitations. The first is that the review was restricted to studies written in the English language only, which implies that further relevant studies published in non-anglophone countries may have been excluded. The second limitation is that a few studies had small sample sizes, which implies that the sample may not be representative of the general population. The third limitation is that the keywords that were used in the search strategy might be insufficient; this may affect the results as certain relevant articles may have been excluded.

Conclusions

The correlation between the efficacy of the HPV vaccine and women's health was verified. The strong evidence collected supports the benefits of HPV vaccinations to women's health, which may lead to improving women's QoL, preventing disease, and reducing the high risk of HPV infection. Further findings from 19 studies identified several aspects of HPV vaccines. These vaccines have a significant impact on reducing or treating recurrent and persistent HPV infections, such as CIN

grades 1-3 and HSIL. Raising awareness of the importance of vaccines in improving women's health and preventing high-risk infections is an essential part of vaccination programs because vaccinations administered at an early age have greater benefits than those received later in life. However, despite this, receiving the vaccine at any age still decreases the risks of HPV infection among females.

Conflict of Interest

The authors declare that they have no conflict of interest.

Authors' Contributions

AJ and AA extracted and reviewed the data, AJ drafted and edited the manuscript, and AA reviewed and edited the manuscript.

Ethics Approval and Informed Consent

This study did not require an ethical review or informed consent since it does not fall under the institutional review board's definition of human subject research, as it utilizes deidentified, publicly available data.

Funding

None.

Data Availability

The study's data are contained in the article and its Supplementary Tables.

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References

- 1) Kombe Kombe AJ, Li B, Zahid A, Mengist HM, Bounda GA, Zhou Y, Jin T. Epidemiology and burden of human papillomavirus and related diseases, molecular pathogenesis, and vaccine evaluation. *Front Public Health* 2021; 8: 552028.
- 2) Bruni L, Albero G, Serrano B, Mena M, Collado JJ, Gómez D, Muñoz J, Bosch FX & de Sanjosé S ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World Summary Report 22 October 2021. 2023. Available at: <https://hpvcentre.net/statistics/reports/SAU.pdf>.

- 3) Cheng W, Xu F, Gao L, Liu J. The correlation between the determination of vaginal micro-ecological composition and the outcome of HPV infection by High-Throughput Metagenome Sequencing Information Technology on the Illumina Platform. *J Infect Public Health* 2020; 13: 1961-1966.
- 4) Wang R, Pan W, Jin L, Huang W, Li Y, Wu D, Liao S. Human papillomavirus vaccine against cervical cancer: Opportunity and challenge. *Cancer Lett* 2020; 471: 88-102.
- 5) Jradi H, Bawazir A. Knowledge, attitudes, and practices among Saudi women regarding cervical cancer, human papillomavirus (HPV) and corresponding vaccine. *Vaccine* 2019; 37: 530-537.
- 6) Shetty S, Shetty V, Badiger S, Shetty AK. An exploratory study of undergraduate healthcare student perspectives regarding human papillomavirus and vaccine intent in India. *Women's Health* 2021; 17: 17455065211055304.
- 7) Bhatta MP, Johnson DC, Lama M, Maharjan B, Lhaki P, Shrestha S. Cervical cancer and human papillomavirus vaccine awareness among married Bhutanese refugee and Nepali women in Eastern Nepal. *J Community Health* 2020; 45: 516-525.
- 8) Tabibi T, Barnes JM, Shah A, Osazuwa-Peters N, Johnson KJ, Brown DS. Human papillomavirus vaccination and trends in cervical cancer incidence and mortality in the US. *JAMA Pediatr* 2022; 176: 313-316.
- 9) Barnabas RV, Brown ER, Onono MA, Bukusi EA, Njoroge B, Winer RL, Galloway DA, Pinder LF, Donnell D, Wakhungu I, Congo O, Biwott C, Kimanathi S, Oluoch L, Heller KB, Leingang H, Morrison S, Rechkina E, Cherne S, Schaafsma TT, McClelland RS, Celum C, Baeten JM, Mugo N. Efficacy of single-dose human papillomavirus vaccination among young African women. *NEJM evidence* 2022; 1: EVIDoa2100056.
- 10) Batmunkh T, Dalmau MT, Munkhsaikhan ME, Khorolsuren T, Namjil N, Surenjav U, Toh ZQ, Licciardi PV, Russell FM, Garland SM, Mulholland K, von Mollendorf C. A single dose of quadrivalent human papillomavirus (HPV) vaccine is immunogenic and reduces HPV detection rates in young women in Mongolia, six years after vaccination. *Vaccine* 2020; 38: 4316-4324.
- 11) Osmani V, Fett S, Tauscher M, Donnachie E, Schneider A, Klug SJ. HPV vaccination leads to decrease of anogenital warts and precancerous lesions of the cervix uteri in young women with low vaccination rates: a retrospective cohort analysis. *BMC Cancer* 2022; 22: 1293.
- 12) Muñoz-Quiles C, López-Lacort M, Díez-Domingo J, Rodrigo-Casares V, Orrico-Sánchez A. Human papillomavirus vaccines effectiveness to prevent genital warts: a population-based study using health system integrated databases, 2009-2017. *Vaccine* 2022; 40: 316-324.
- 13) Schlecht NF, Diaz A, Nucci-Sack A, Shyhalla K, Shankar V, Guillot M, Hollman D, Strickler HD, Burk RD. Incidence and types of human papillomavirus infections in adolescent girls and young women immunized with the human papillomavirus vaccine. *JAMA Netw Open* 2021; 4: e2121893-e2121893.
- 14) Kitano T. Stopping the HPV vaccine crisis in Japan: quantifying the benefits and risks of HPV vaccination in quality-adjusted life-years for appropriate decision-making. *J Infect Chemother* 2020; 26: 225-230.
- 15) Willame C, Gadroen K, Bramer W, Weibel D, Sturkenboom M. Systematic review and meta-analysis of Postlicensure Observational Studies on human papillomavirus vaccination and autoimmune and other rare adverse events. *Pediatr Infect Dis J* 2020; 39: 287-293.
- 16) JBI Manual for Evidence Synthesis. JBI; 2020. Available at: https://jbi.global/sites/default/files/2019-05/JBI_Critical_Appraisal-Checklist_for_Systematic_Reviews2017_0.pdf.
- 17) Closson K, Karim ME, Sadarangani M, Naus M, Ogilvie GS, Donken R. Association between human papillomavirus vaccine status and sexually transmitted infection outcomes among females aged 18-35 with a history of sexual activity in the United States: A population survey-based cross-sectional analysis. *Vaccine* 2020; 38: 8396-8404.
- 18) Kitamura T, Suzuki M, Shigehara K, Fukuda K, Matsuyama T, Kume H. Prevalence of Human Papillomavirus Types 16/18 and Effect of Vaccination among Japanese Female General Citizens in the Vaccine Crisis Era. *Viruses* 2023; 15: 159.
- 19) Kudo R, Yamaguchi M, Sekine M, Adachi S, Ueda Y, Miyagi E, Hara M, Hanley SJB, Enomoto T. Bivalent human papillomavirus vaccine effectiveness in a Japanese population: High vaccine-type-specific effectiveness and evidence of cross-protection. *J Infect Dis* 2019; 219: 382-390.
- 20) Kurokawa T, Yamamoto M, Onuma T, Tsuyoshi H, Shinagawa A, Chino Y, Yoshida, Y. The study protocol of the evaluation for the preventive efficacy of the HPV vaccine for persistent HPV16/18 infection in Japanese adult women: the HAKUOH study. *BMC Cancer* 2020; 20: 1-5.
- 21) Lee GY, Inthasorn P, Laowahutanont P, Lawpolsri S, Kamolratanakul S, Lungchukiet P, Oh J, Termrungruanglert W, Taechakraichana N, Pitisuttithum P. Long-term effectiveness of human papillomavirus vaccines among adult women: A real-world scenario. *Vaccine* 2022; 40: 1968-1976.
- 22) Loenenbach A, Schönfeld V, Takla A, Wiese-Poselt M, Marquis A, Thies S, Sand M, Kaufmann A, Wichmann O, Harder T. Human papillomavirus prevalence and vaccine effectiveness in young women in Germany, 2017/2018: results from a nationwide study. *Front Public Health* 2023; 11: 1204101.
- 23) Taniguchi M, Ueda Y, Yagi A, Ikeda S, Endo M, Tomimatsu T, Nakayama T, Sekiguchi M, Enomoto T, Kimura T. Cervical cancer screening rate differs by HPV vaccination status: An interim analysis. *Vaccine* 2019; 37: 4424-4426.
- 24) Casajuana-Pérez A, Ramírez-Mena M, RUIPÉREZ-PACHECO E, Gil-Prados I, García-Santos J, Bellón-Del Amo M, Hernández-Aguado JJ, de

- la Fuente-Valero J, Zapardiel I, Coronado-Martín PJ. Effectiveness of prophylactic human papillomavirus vaccine in the prevention of recurrence in women conized for HSIL/CIN 2-3: The VENUS study. *Vaccines (Basel)* 2022; 10: 288.
- 25) Karimi-Zarchi M, Allahqoli L, Nehmati A, Kashi AM, Taghipour-Zahir S, Alkatout I. Can the prophylactic quadrivalent HPV vaccine be used as a therapeutic agent in women with CIN? A randomized trial. *BMC Public Health* 2020; 20: 1-7.
- 26) van de Laar RLO, Hofhuis W, Duijnhoven RG, Polinder S, Melchers WJG, van Kemenade FJ, Bekkers RLM, Van Beekhuizen HJ. Adjuvant VACCination against HPV in surgical treatment of Cervical Intra-epithelial Neoplasia (VACCIN study) a study protocol for a randomized controlled trial. *BMC Cancer* 2020; 20: 1-7.
- 27) Valasoulis G, Pouliakis A, Michail G, Kottaridi C, Spathis A, Kyrgiou M, Paraskevaidis E, Daponte A. Alterations of HPV-related biomarkers after prophylactic HPV vaccination. A prospective pilot observational study in greek women. *Cancers (Basel)* 2020; 12: 1164.
- 28) Li C, Hall TG, Hall JJ, He WQ. Effectiveness of quadrivalent HPV vaccination in reducing vaccine-type and nonvaccine-type high risk HPV infection. *Epidemiol Infect* 2023; 151: e37.
- 29) Khoo SP, Muhammad Ridzuan Tan NA, Rajasuriar R, Nasir NH, Gravitt P, Ng CW, Woo YL. Changes in genital Human Papillomavirus (HPV) prevalence among urban females a decade after the Malaysian HPV vaccination program. *PLoS One* 2022; 17: e0278477.
- 30) Clark M, Jembere N, Kupets R. The impact of a universal human papilloma virus (HPV) vaccination program on lower genital tract dysplasia and genital warts. *Prev Med (Baltim)* 2021; 150: 106641.
- 31) Seong J, Ryou S, Yoo M, Lee J, Kim K, Jee Y, Cho CH, Kim SM, Hong SR, Jeong DH, Lee WC, Park JS, Kim TJ, Kee MK. Status of HPV vaccination among HPV-infected women aged 20-60 years with abnormal cervical cytology in South Korea: a multicenter, retrospective study. *J Gynecol Oncol* 2020; 31: e4.
- 32) Innes CR, Williman JA, Simcock BJ, Hider P, Sage M, Dempster-Rivett K, Lawton BA, Sykes PH. Impact of human papillomavirus vaccination on rates of abnormal cervical cytology and histology in young New Zealand women. *N Z Med J* 2020; 133: 72-76.
- 33) Debrah O, Agyemang-Yeboah F, Donkoh ET, Asmah RH. Prevalence of vaccine and non-vaccine human papillomavirus types among women in Accra and Kumasi, Ghana: a cross-sectional study. *BMC Womens Health* 2021; 21: 1-12.
- 34) Zhao C, Zhao Y, Li J, Li M, Su Y, Mi X, La Tu SY, Shen D, Ren L, Li Y, Wang L, Wei L. The eight-year long-term follow-up on the effectiveness of the quadrivalent human papillomavirus vaccine in Chinese women 20-45 years of age. *Hum Vaccin Immunother* 2022; 18: 2052700.
- 35) Zhu FC, Hu SY, Hong Y, Hu YM, Zhang X, Zhang YJ, Pan QJ, Zhang WH, Zhao FH, Zhang CF, Yang X, Yu JX, Zhu J, Zhu Y, Chen F, Zhang Q, Wang H, Wang C, Bi J, Xue S, Shen L, Zhang YS, He Y, Tang H, Karkada N, Suryakiran P, Bi D, Struyf F. Efficacy, immunogenicity and safety of the AS04-HPV-16/18 vaccine in Chinese women aged 18-25 years: End-of-study results from a phase II/III, randomised, controlled trial. *Cancer Med* 2019; 8: 6195-6211.
- 36) Subasinghe AK, Wark JD, Phillips S, Cornall A, Brotherton JML, Garland SM. Quadrivalent human papillomavirus vaccination successfully reduces the prevalence of vaccine-targeted genotypes in a young, vaccine-eligible-age sample of Australian females. *Sex Health* 2020; 17: 510-516.
- 37) Amponsah-Dacosta E, Blose N, Nkwinika VV, Chepkurui V. Human papillomavirus vaccination in South Africa: programmatic challenges and opportunities for integration with other adolescent health services? *Front Public Health* 2022; 10: 799984.