

Improving HPV Vaccination Uptake Among Adolescents in Low Resource Settings: Sociocultural and Socioeconomic Barriers and Facilitators

Mia Ann Xu¹, Jasmin Choi¹, Ariadna Capasso², Ralph J DiClemente¹

¹Department of Social and Behavioral Sciences, School of Global Public Health, New York University, New York, NY, USA; ²Health Resources in Action, Boston, MA, USA

Correspondence: Mia Ann Xu, Email mx489@nyu.edu

Background: Lower- and middle-income countries (LMICs) are disproportionately impacted by human papillomavirus (HPV) and would benefit from implementing the HPV vaccine. In the context of competing health priorities, utilizing scarce domestic infrastructure and human resources for HPV vaccination remains challenging for many LMICs. Given the high benefits of the HPV vaccine, the World Health Organization (WHO) is now encouraging for all countries, particularly LMICs, to introduce HPV vaccines into their routine immunization programs. Understanding the barriers and facilitators to HPV adolescent vaccine programs in LMICs may help strengthen how LMICs implement HPV vaccine programs, in turn, increasing HPV vaccine acceptance, uptake, and coverage.

Objective: To identify and assess barriers and facilitators to implementing adolescent HPV vaccination programs in LMICs.

Methods: This study comprised a review of literature assessing adolescent HPV vaccination in LMICs published after 2020 from a sociocultural perspective.

Results: Overall, the findings showed that LMICs should prioritize increasing HPV vaccine availability and HPV vaccine knowledge, particularly focusing on cancer prevention, as knowledge reduces misinformation and increases vaccine acceptance. Evidence suggests that factors promoting HPV vaccine uptake include fostering low vaccine hesitancy, integrating HPV vaccination as a primary school routine vaccination, and vaccinating both genders. A one-dose HPV vaccine may enable many LMICs to increase vaccine acceptance, uptake, and coverage while controlling financial, infrastructure, and human resource costs.

Conclusion: As HPV is one of the leading causes of death in many LMICs, implementing the HPV vaccine may be highly beneficial. Cohesive national HPV vaccine buy-in and understanding the success and challenges of prior LMIC HPV vaccine implementation is crucial to developing effective, efficient, and sustainable HPV vaccination programs.

Keywords: HPV, LMICs, vaccine hesitancy, HPV cost, vaccine equity

Introduction

People in low- and middle-income countries (LMICs) suffer disproportionately higher incidence and mortality rates from cervical cancer and other human papillomavirus (HPV)-associated cancers, including oropharyngeal and anogenital cancer compared to high income countries.¹ Approximately 84% of new cervical cancer cases and between 80% and 90% of cervical cancer deaths occur in LMICs.^{1,2} Cervical cancer is the second most common cancer among women in LMICs and is the most common cancer in half (23/46) of the countries in sub-Saharan Africa.³ Without utilizing preventative measures to decrease HPV, deaths in LMICs from cervical cancer is projected to increase by 50% by 2040.⁴

The HPV vaccine is one of the most cost-effective primary prevention tools against cervical cancer as it can protect against 70% to 90% of all HPV-attributable cancers.⁵ The HPV vaccine may have a particularly significant impact on the burden of HPV-associated cancers in LMICs where screening is sparse or non-existent, limited in scale, or of poor

quality.⁶ While robust research has supported the HPV vaccine's safety, efficacy, and cost-effectiveness, there has been limited HPV vaccine implementation, particularly in LMICs. Clinical interventions in LMICs have found that vaccinating against HPV can reduce cervical cancer cases by 50% to 75%.⁷ Every five-year delay in HPV vaccine roll-out contributes to 2 million cervical cancer deaths.⁸ The HPV vaccine needs to be given promptly to adolescents as the vaccine is most effective against HPV-related disease outcomes when given at younger ages.⁹ As less than 25% of LMICs have introduced the HPV vaccine into their immunization schedules, the need for timely implementation of the HPV vaccine to adolescents within LMICs is substantial.⁴ Given the benefits of the HPV vaccine, WHO is now encouraging for all countries, particularly LMICs, to introduce HPV vaccines into their routine immunization programs.^{10,11}

Formative research has identified three major barriers to the HPV vaccine's introduction into LMICs: sociocultural, health system, and political.¹² Studies or reviews focusing primarily on understanding the socio barriers and facilitators holistically in LMICs are scarce.^{13,14} By synthesizing findings from the literature review on HPV vaccine implementation in LMICs, this paper considers barriers and facilitators that could improve HPV vaccination uptake among adolescents from a sociocultural and socioeconomic perspective. A socio perspective is influenced by individuals' beliefs, expectations, subjective norms, and attitudes towards health and the healthcare service, which determines their utilization of services.¹⁵

This review examined steps to enhancing HPV vaccine uptake among adolescents in LMICs using a sociocultural and socioeconomic lens. The review considered HPV knowledge and misconceptions, societal values and stigma, and cost-benefit perception and attitude. Models such as HBM, social norms, and social determinants were used to focus on the social aspect of addressing HPV vaccine uptake.

Materials and Methods

The authors conducted a rapid review of the empirical evidence on HPV vaccination programs in LMICs from a sociocultural and socioeconomic perspective. A literature review of relevant articles identified through a search of electronic databases on PubMed, and Scopus using the following title search terms: "Human papillomavirus" OR "HPV" AND "vaccine" OR "vaccination" AND "low- and middle-income country" OR "low resource setting" OR "Gardasil" OR "Cervarix". The search was restricted to English language items published since 2020, the year the United Nations started actively promoting that all countries should have 90% of girls fully vaccinated with the HPV vaccine by 15 years of age and created consistent HPV vaccination guidelines.^{10,16} Figure 1 provides a flowchart of the search strategy.

Articles focusing solely on high income countries were excluded; however, items that included a mix of high- and low-income countries were included for thematic analysis. The World Bank classification system was used to define country income groups.¹⁷ The articles were restricted to include only children and adolescents, defined as those under 18 years of age. We included literature that reported HPV vaccine implementation, including pilot projects in LMICs. The authors reviewed the 50 most relevant peer-reviewed qualitative and quantitative scientific literature on sociocultural and socioeconomic barriers and facilitators that could improve HPV vaccination uptake among adolescents in low-resource settings.

Through a theory-driven approach, several psychosocial models have been understood to enhance sociocultural behavior change for vaccine uptake. For this review, we employed the Health Belief Model (HBM), which focuses on beliefs regarding the presence of a threat and the potential actions to address that threat.^{18,19} Also critical in HBM is considering the perceived susceptibility of the adverse health outcomes compared to the perceived barriers.^{20,21} HBM can be supplemented with the social norm's framework and the WHO social determinants of health model to influence HPV vaccine uptake.^{21–23}

Results

Low HPV and HPV Vaccine Knowledge and Misconceptions

Despite the WHO recommending that all countries should have 90% of girls fully vaccinated with the HPV vaccine by 15 years of age, low knowledge of HPV remains a challenge in enhancing vaccine uptake.^{24–26} Many individuals may not know that HPV is associated with the prevention of cervical and other cancers.¹⁴ In Uganda, there is low HPV vaccine uptake despite it being free of charge because of the lack of education materials on HPV vaccination available to

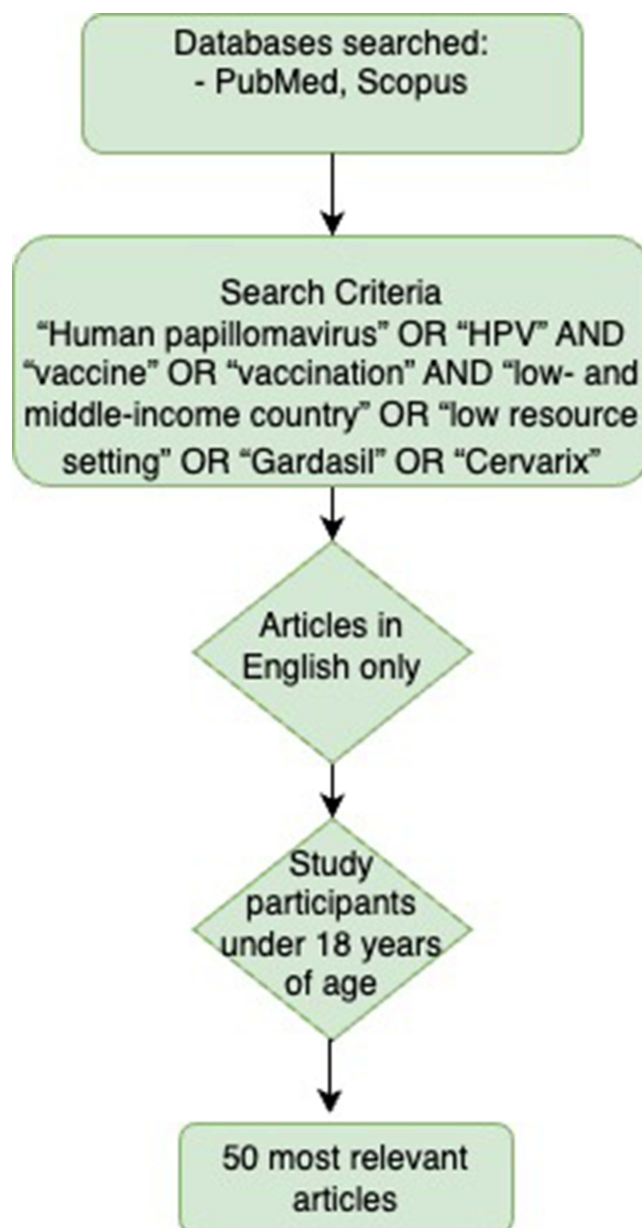


Figure 1 Search Strategy.

adolescents and parents such as education about cervical cancer, prevention, and HPV vaccination benefits.²⁵ Health stakeholders should ensure HPV vaccine information is accessible to those with higher socio-economic status and those with less opportunities to access health knowledge and support resources. In Tanzania and Senegal, HPV health literacy is associated with reduced understanding of the need to vaccinate, increased risk of vaccine misinformation, and negative HPV vaccine attitude.¹⁴

Without clear, consistent, transparent communication about vaccine risks and benefits, misinformation about the vaccine is shared among community members, creating poor HPV vaccine attitude and uptake. HPV vaccine hesitancy stemming from misinformation is often the primary reason parents and adolescents decline vaccination.²⁷ Common parental and adolescent concerns of side effects stem from misinformation such as the HPV vaccine being a birth control method, potentially leading to fertility issues and sterilization of adolescents, and it can even cause cervical cancer.^{28–30} There is also the misconception that cervical cancer is caused by witchcraft and prevention by witch doctors and traditional medicine could substitute for the HPV vaccine.³¹ Health stakeholders should prioritize addressing vaccine

hesitancy and misconceptions through increasing vaccine knowledge. Parent and adolescent knowledge about the HPV vaccine, particularly its cancer prevention benefits and its effectiveness in adolescents' early years, were associated with enhancing positive vaccine attitude, trust, uptake, and coverage.^{26,29,31–34} To address the low HPV knowledge and awareness, culturally sensitive education and community vaccine promotion is critical.

Word of mouth communication about the HPV vaccine was most effective at reaching caregivers and adolescents, and increasing HPV vaccine uptake.³⁵ HPV health literacy and vaccine information should be provided by multiple trustworthy sources and integrated into other health communications for the greatest accessibility and reach.³⁶ Initially, HPV vaccine education support should prioritize health workers, such as providers, nurses, and community health workers, as they are the most preferred source of vaccine information and markedly influence vaccine uptake decisions. Health workers should receive training on optimizing their presentation of HPV vaccine information.^{25,37} Greater health worker knowledge and education on the importance of the HPV vaccine may also encourage clinician reminders about the vaccine and improve patient-provider vaccine communication. As communication needs to be tailored to the community's concerns, local community mobilized social support and advocates such as parents, village, and religious leaders may serve to increase knowledge and decrease misinformation.³⁸ Training teachers from schools on basic health topics to become school health vaccine coordinators greatly supported HPV vaccination campaigns.³⁵ For long-term HPV health literacy sustainability, peer influence is key to vaccine uptake as many adolescents who had completed the HPV vaccine on time were encouraged to do so by their peers.²⁹ Empowering women within the community as HPV vaccine leaders may ensure continuous HPV communication with less misinformation within the community, increasing the likelihood of sustained vaccine uptake and completion.¹⁴

Societal Values and Stigma

There are many societal values and stigmas that challenge HPV vaccine uptake.

As HPV is a sexual infection, the conversation surrounding HPV often evokes negative moral connotations in many communities, decreasing HPV vaccine discussion and uptake. Sexually conservative countries that have sensitivities regarding the dissemination of sex-related information often face barriers to enabling the wide reach of vital sexual health practices for families and communities. Cultural taboos may view premarital sexual intercourse as deviant behavior and uphold the norms of sexual abstinence before marriage, particularly for girls. As a result, the widespread prioritization and discourse on providing HPV vaccine for girls and decreasing cervical cancer may detrimentally affect the perception and uptake of the vaccine. Even seeking the HPV vaccine may be stigmatized as it may connote that the adolescent is already sexually active or desiring to engage in premarital sex.¹³ Gender-specific immunization has been historically challenging and has resulted in many stigmatizing HPV rumors targeted toward girls.^{39,40} It may not be best for HPV vaccine campaigns to focus solely on vaccinating girls and prioritizing reducing cervical cancer as the main goal of the vaccine. Focusing on communicating the HPV vaccine's cervical cancer benefits increases the stigma that HPV is a female disease and places the blame and burden of the issue on females when both genders could benefit.

Boys are rarely considered for HPV vaccination despite many male-related HPV cancers, creating a large HPV vaccination gap. The lack of encouraging male HPV vaccine participation may further stigmatize HPV as a female disease. As there are no significant gender differences in the safety and effectiveness of HPV vaccines and with the high likelihood of cross-infection of HPV to females, vaccinating only girls unfairly shifts the responsibility for preventing HPV predominantly onto women.^{41,42} When vaccination rates among women are high, men receive secondary protection and receive the benefits of the vaccine without participation; however, this places unnecessary vaccine burden and stigmatization on women. Adolescent boys are willing to vaccinate once they obtain knowledge of the HPV vaccine's effectiveness in preventing penile, anal, mouth, and throat cancers.²⁶ Many communities have skepticism and hesitancy on why the vaccine is only for girls and not boys.⁴³ Targeting HPV vaccine to both genders before sexual exposure also increases the likelihood of reducing HPV hesitancy and increasing vaccine uptake within the community and there is support for this approach among health workers.^{43–45} In settings where the coverage of female vaccination is less than 75%, gender neutral vaccination strategies prove cost-effective by rapidly building herd immunity for boys and indirectly protecting those who are unvaccinated.³⁸

Providing gender-neutral HPV vaccination knowledge including its cancer-reducing benefits for both genders may reduce HPV stigma and help desensitize the sexual aspect of the vaccine. HPV and HPV vaccine information is often not disseminated among males. Male partners and fathers often reported low HPV knowledge; however, they considered the vaccine more acceptable once they were well informed.⁴⁶ Empowering both genders to understand HPV and the importance of the HPV vaccine is vital to vaccine acceptance and uptake.⁴⁷ Gender-neutral HPV vaccine awareness and implementation provides gender equity, enabling women to obtain the HPV vaccine, particularly in countries where women's health issues are largely ignored.⁴⁸

Caregivers' Acceptance and Attitude Towards Vaccination

Caregiver consent is a crucial factor in enabling adolescent HPV vaccination. As the adolescent's caregivers are the primary decision-makers for adolescent healthcare choices, health stakeholders need to consider caregivers' HPV vaccine knowledge, beliefs, and attitudes. Health stakeholders need to consider the caregiver's education, social status, income, and cultural and religious preferences when explaining why their child needs an HPV vaccine.⁴⁹ Comprehensive HPV vaccine communication and education campaigns tailored to the caregivers' perspectives must be implemented prior and during HPV vaccination campaigns to reduce vaccine misinformation.⁵⁰ The lack of HPV vaccination awareness campaigns preceding and during the vaccination program may cause for caregivers, particularly those with low general vaccine knowledge, to be heavily influenced by negative vaccine information on social media and distrust the HPV vaccine.⁵¹ HPV vaccine education campaigns prior to vaccine rollout must target both caregivers and health providers as it is difficult for caregivers to trust the vaccine if health providers have difficulties explaining it.⁴⁹ Health provider vaccine recommendation also significantly increases caregiver's likelihood to provide vaccine consent.⁵²

Cost-Benefit Perception and Attitudes

National buy-in is essential to ensuring sustainable HPV vaccination.^{53,54} In the context of competing health priorities, utilizing scarce domestic infrastructure and human resources for HPV vaccination remains challenging for many LMICs.⁴³ Policymakers debating the implementation of the HPV vaccine will need to consider the HPV disease burden within the country, the country's health system, and its capacity to sustain the vaccination program.⁵⁵ Many LMICs do not have sufficient data on vaccine impact such as the disease burden and cost saving, which poses barriers to advocating for national HPV vaccination plans.⁴³ However, the high perceived HPV vaccine cost and logistical challenges may not be as insurmountable with current changes in HPV vaccine implementation. New HPV vaccine implementation methods may enable a shift in attitude that the benefit of the HPV vaccine outweighs the barriers and other competing health priorities.

A key method to reduce infrastructure, human resource and vaccine cost challenges is to consider a one-dose HPV vaccine schedule. Many LMICs have yet to implement HPV vaccination programs, and those who do, often have lower vaccine completion rates compared to higher-income countries because of multi-HPV vaccine dosage schedules.^{56,57} A one-dose HPV schedule has been shown to deliver comparable HPV protection to a 2 or 3-dose schedule for those ages 9 to 20.^{58,59} In LMICs, low HPV vaccine coverage is often due to barriers in the cost and logistics of providing a multi-dose vaccine schedule; hence, a one-dose schedule increases vaccine supply and reduces associated resources and costs.^{57,59-61} Boosting the feasibility of the HPV vaccine may enhance positive attitudes towards the benefits and ease in implementation of the HPV vaccine, encouraging health stakeholders to implement widespread vaccination across various age groups and for both genders.^{43,62} Lower overall HPV vaccine costs per person may also enable the vaccine to be available for free or at low cost, which has been shown to be a key issue in vaccine acceptance and uptake.^{63,64} With evidence of the effectiveness of a one-dose schedule, many LMICs are starting to implement the HPV vaccine. Nigeria, for example, introduced a routine immunization program with a single-dose schedule in 2023 and plans to vaccinate 7.7 million girls.¹⁶ With increasing HPV vaccination in LMICs, vaccine costs may be further reduced with time. Over the last five years, prices for the HPV vaccine have consistently decreased across all sourcing and income categories; should there be a substantial demand for the vaccine, prices will drop further due to increased competition from new market entrants.^{65,66}

Encouraging the HPV vaccine to be readily available in the community without requiring a specific HPV vaccine health appointment enhances accessibility and promotes greater opportunities for HPV vaccination.⁶⁷ Adolescents use health services minimally in most LMICs and most tend not to have a primary care doctor or nurse.^{26,56} Many LMICs have implemented school-based HPV vaccination programs, which have seen relatively high HPV vaccination rates with great potential for sustainability and scalability particularly in primary schools.^{7,13,68–71} School-based delivery strategies on average had higher coverage and performed better than facility-based programs and the majority (90%) of LMIC vaccination campaigns utilized school-based or a mix of school and facility-based programs.⁵⁶ Integrating the HPV vaccine into other school-based health services and other community outreach services for adolescents not enrolled in school may further decrease delivery cost and increase vaccine coverage.^{38,60,68} To further promote HPV vaccination in schools, it is necessary to develop a detailed school-based vaccine communication and education plan so that school educators and health workers can provide sound HPV vaccine recommendations, thereby positively influencing vaccine acceptance and uptake.⁷² The plan should include training programs with frequent refreshers for educators and health workers, customized school messages, and parental vaccine information materials.³⁹ Health stakeholders must ensure that consistent scheduling and coordination are employed between the education sector and those providing the HPV vaccine so that all stakeholders can provide persistent and holistic vaccine messaging and timely vaccination.^{73,74}

Discussion

This study reviews current literature on the sociocultural and socioeconomic barriers and facilitators that could improve HPV vaccination uptake among adolescents in low-resource settings. The study summarizes the current experiences of implementing the HPV vaccine in LMICs to enable countries considering introducing or improving their national HPV vaccine programs to build upon these lessons and establish best practices. Key factors enhancing HPV vaccine uptake are summarized in **Box 1**. Many LMICs have overstretched and under-resourced public health systems.⁴³ A one-dose, gender-neutral, primary school routine HPV knowledge and vaccination program may be an efficient and cost-effective HPV vaccination strategy.

Increasing positive vaccine attitudes and decreasing vaccine hesitancy is crucial to successful vaccine uptake. Having a one-dose vaccine increases the affordability of the HPV vaccine with lower human resource and infrastructure costs decreasing vaccine implementation constraints. A lower-cost HPV vaccine schedule is a good initial step to increasing vaccine uptake likelihood; however, only considering economics is insufficient. If the parental and adolescent social norms in the country stigmatize and discriminate against the HPV vaccine, there will be low vaccine acceptance. Overall, community knowledge of the high disease burden associated with HPV infection and the high cancer prevention benefits of the HPV vaccine is paramount to LMIC vaccine initiation, coverage, and sustainability. Regardless of whether the HPV vaccine is delivered through a school, facility, or community platform, the acceptability of the vaccine and the engagement of adolescents and communities are essential to enhancing HPV uptake.²⁴

To increase community HPV cancer and vaccine knowledge, responsible sexuality should be taught to both adolescents in schools and adults in the community. Gender-neutral HPV health literacy decreases vaccine stigma.

Box 1 Key Factors Enhancing HPV Vaccine Uptake

Factors Enhancing HPV Vaccine Uptake

- Provide accessible education materials on the vaccine
- Discussion on HPV's cervical cancer prevention benefits
- Clear communication on HPV vaccine's side effects
- Increasing health provider's HPV vaccine knowledge
- Training schoolteachers as school health vaccine coordinators
- Mobilize and train local community members as vaccine educators
- Vaccinating both adolescent boys and girls
- Providing a one-dose HPV vaccine schedule
- Widespread HPV vaccination awareness campaigns to increase caregivers' understanding of the vaccine

Desensitizing the community to perceive discussions on sexual health as a taboo would ease the dissemination of sexual health knowledge, enabling more parents and adolescents to accept the vaccine. Having broader, open community HPV discussions would encourage early preparedness to manage HPV rumors and misconceptions. In many LMICs, being female with low education and income decreased the individuals' vaccine intention potentially because they received vaccine information from non-health sources, eg, relatives, leading to misconceptions and fears about vaccine safety.⁷⁵ Consistent, broad, vaccine communication within the community by trained health workers, school personnel, and community leaders would enhance vaccine uptake as misconceptions and rumors are the main reason for vaccine hesitancy.^{27,74,76} A broader HPV vaccine discussion may also enable those who are not enrolled in school to learn about HPV and seek opportunities to vaccinate when they seek health facility services or other community outreach services.

Encouraging vaccination among both boys and girls encourages HPV discussions to reach the entire community and reduces community hesitancy on why the vaccine is only available to girls.⁴³ Countries with male dominance in the household may benefit from gender-neutral HPV vaccine discussions as males who understand the risk of HPV cancers gain more sympathy and support towards addressing HPV for women.⁴⁶⁻⁴⁸ Having gender-neutral vaccine communication may make HPV vaccination easier to develop into a standard policy and operating procedure, so there is not much of a discussion on the need to vaccinate as it is a norm to vaccinate within the community. Normalizing HPV vaccination for both genders before sexual intercourse may promote more timely and wider vaccine coverage, increasing the chances of herd immunity and eventually HPV eradication.⁷⁷ Creating sustainable HPV vaccine routines may be cost-beneficial and increase health equity for many LMICs. For every \$1 US invested into reducing HPV through 2050, an estimated \$26 US is gained in societal and economic benefits.⁷⁸ Cohesive national HPV buy-in should be a health priority for LMICs.

In addition to cervical cancer, the HPV vaccine may reduce adverse outcomes of pre-cancerous lesions. Surgical treatment for cervical carcinoma from HPV increases birth risks among young women who are seeking pregnancy and being immunized for HPV reduces the occurrence of precancerous lesions and cervical carcinoma, helping reduce the significant pregnancy risks.⁷⁹ Future research may consider providing the HPV vaccine to adult women as research shows that women who had treatment for HPV-related diseases still benefited from the HPV vaccine.⁸⁰

In sum, there is an urgent need for government ownership and support in HPV vaccine implementation. Health stakeholders should recognize that, given today's current global society, eliminating the disease burden of HPV is not feasible without addressing the disproportionate rates of HPV morbidity and mortality in LMICs.

Limitations and Future Directions

Several of the studies reviewed had methodological limitations. For example, some studies used data collection methods with a high risk of self-report bias. There is inadequate financial support for cancer surveillance in many LMICs, making it difficult to understand the burden on HPV and the effectiveness of HPV vaccination in those countries.³ The review was restricted to only literature in English, potentially missing literature published in other languages. We have limited knowledge of the efficacy of single dose-HPV vaccine after ten years.⁵⁷ However, decreasing cost and resource constraints through a single dose schedule may encourage greater vaccine implementation and coverage which may increase herd immunity even with somewhat lower vaccine efficacy. With the greater implementation, vaccine costs may decrease further, making it easier to implement a second dose to the populations needing a booster later in life.

In the future, further cost-effectiveness value analysis for a gender-neutral one-dose HPV vaccine schedule is needed. Future studies should consider how to allocate critical resources to primary school-based vaccine delivery while maintaining cost-effectiveness and ensuring sustainability and scaling-up potential.

Conclusion

HPV vaccination remains crucial to decreasing many HPV-related cancers among males and females. The literature found that limited HPV health literacy is associated with reduced understanding of the need to vaccinate, increased risk of vaccine misinformation, and negative HPV vaccine attitude. To accelerate progress to reach the 90-70-90 goals, LMICs should prioritize increasing HPV vaccine knowledge particularly on its cancer prevention benefits, as knowledge

reduces misinformation and increases vaccine acceptance. To ensure timely vaccination before adolescent sexual intercourse, it may be effective to integrate the HPV vaccination as a primary school routine vaccine for both boys and girls. A one-dose HPV vaccination may enable many LMICs to increase vaccine acceptance, uptake, and coverage while reducing financial and human resource costs.

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