



Evaluation of a single-dose HPV vaccine strategy for promoting vaccine, health, and gender equity

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Although several countries have adopted a single-dose human papillomavirus (HPV) vaccination strategy, many other countries continue to include multiple doses in their vaccination programmes. There are ethical reasons to transition to a single-dose strategy. We discuss how a single-dose HPV vaccination strategy advances equity in three dimensions: vaccine equity, health equity, and gender equity. Adopting a single-dose strategy eases pressure on vaccine supply, lowers programme costs, and is easier to distribute. This change facilitates vaccine procurement and implementation programmes (contributing to vaccine equity) and reaching hard to reach people or populations (contributing to health equity). A lower number of cases of HPV-related diseases that stem from greater vaccine distribution reduces the burden on women, who are at a higher risk of HPV-related disease or who act as caregivers, which prevents them from accessing opportunities that contribute to their empowerment (contributing to gender equity). Thus, pursuing the single-dose HPV vaccination programme strategy is ethically desirable.

Introduction

On December 16, 2022, WHO, on the advice of the Strategic Advisory Group of Experts on Immunization, updated their position on human papillomavirus (HPV) to include an alternative single-dose vaccination schedule as an off-label option for young people aged 9–20 years.¹ The decision was based on several factors, including results from a suite of evidence showing promise for a single dose of the vaccine to achieve an immune response close to that of two doses.^{2–5} A single-dose schedule could replace the two-dose schedule that has been approved in many countries and is part of the routine vaccination strategy.

Several countries, including the UK⁶ and Australia,⁷ have already transitioned to recommending a single-dose HPV vaccination schedule. Likewise, in a report published on May 31, 2023,⁸ the Technical Advisory Group on vaccine-preventable diseases of the Pan American Health Organization (PAHO) recommended a switch to a single-dose HPV vaccination schedule. In November, 2023, the WHO Africa Regional Immunization Technical Advisory Group urged countries in Africa to adopt a single-dose HPV vaccination schedule.⁹ However, the wide adoption of a single-dose HPV vaccination strategy has yet to materialise. As of September, 2023, only ten (21%) of 47 PAHO countries and territories (including some low-income and middle-income countries [LMICs]) had adopted the recommendation.¹⁰ In Africa, national advisory groups from only 16 (59%) of 27 countries that have incorporated HPV vaccine into their routine vaccination programmes have endorsed moving to a single-dose schedule, and few countries (eg, Cameroon and Cabo Verde) have adopted the recommendation.⁹ One reason for the slow adoption is the fact that public health officials might be hesitant to implement a single-dose schedule when some (often high-income) nations continue to use multiple doses of the HPV vaccine, wanting “to avoid having to justify the adoption of what might be perceived in their communities as a lower standard”.¹¹ Practical

considerations, such as fulfilling obligations in existing vaccine purchase contracts might also exist.

There are several compelling reasons to pursue a single-dose HPV vaccination strategy. A single-dose strategy helps to overcome barriers to vaccine procurement and distribution caused by vaccine supply and resource constraints and logistical challenges that come with the need for administration of multiple doses. Equally important, but less discussed, are the ethical reasons for pursuing a single-dose strategy. In this Personal View, we highlight how a single-dose HPV vaccination strategy advances equity on three dimensions—vaccine equity, health equity, and gender equity—and we argue that pursuing such a strategy is ethically desirable.

A single-dose HPV vaccination strategy advances vaccine equity

The UNDP advocates for vaccine equity (ie, “vaccines should be allocated across all countries based on needs and regardless of their economic status”), under the principle that every human should have the right to the “highest attainable standard of health”.¹² The COVID-19 pandemic highlighted both the global inequities in vaccine access and coverage, and the downstream health and economic effects such inequities have on communities struggling to procure and distribute vaccines. For example, a UNDP analysis showed that low-income countries had the lowest access to vaccines for COVID-19, which led to their substantially lower gross domestic product relative to nations with more complete vaccine access. Reduced economic activity pushes more people into poverty and widens wealth gaps both within and between nations, which leads to inequitable health outcomes (due to additional constraints on obtaining and distributing health-related resources). In other words, vaccine inequities exacerbate existing health and economic disparities—programmes that improve access to vaccines can help break that cycle.

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Vaccine inequities are not unique to COVID-19. There are wide disparities in coverage of several routine vaccines,¹³ especially between high-income and low-income countries.¹⁴ Uptake of the HPV vaccine in some LMICs is estimated to be as low as 5% among eligible girls, compared with approximately 90% in many high-income countries.¹⁵ Unsurprisingly, a disproportionate number of cervical cancer cases (primarily caused by HPV infection) and deaths occur in settings with less access to HPV vaccines.¹⁶ Thus, cervical cancer has been described as a “disease of inequity of access to healthcare”.¹⁷

Inequities in vaccine coverage often stem from several barriers to access and distribution, such as local resource constraints and logistical challenges. For example, material (eg, vaccine, syringes, needles, etc) and human resource costs (eg, someone to safely inject the vaccine, keep records, etc) associated with each administered vaccine dose can make a multiple-dose HPV vaccination strategy cost-prohibitive as part of a public health programme in some communities. A single-dose strategy requires fewer vaccines and only one interaction with individuals or communities receiving the vaccine, and thus, it is typically cheaper to implement.¹⁸ Shortages in the global supply¹⁹ also create barriers that lead to inequities, as shortages raise competition for procuring vaccines that can leave LMICs or marginalised communities at a disadvantage in obtaining enough doses to ensure sufficient coverage.²⁰ A 2022 WHO Global Market Study on HPV¹⁹ suggests that adoption of a single-dose strategy would improve the supply–demand balance and allow for a wider expansion of current HPV vaccination programmes (eg, to older cohorts).

The recommendation of a single-dose HPV vaccination schedule should not be considered only for countries that cannot afford multiple doses. Unless a single-dose schedule is adopted by communities that currently use multiple-dose schedules, particularly high-income countries, bringing new communities on board will only add to the demand for HPV vaccines. Furthermore, a decision to maintain a multiple-dose schedule considering the WHO recommendation might be interpreted as a double standard, especially for low-income nations. Vaccines are essential to optimising the health of populations, both locally and globally, and should be treated as a public good rather than a market commodity. Katz and colleagues²¹ note that “the commodification of global public goods reinforces widespread inequities in access and exacerbates vast disparities in health and economic wellbeing”. A single-dose strategy promotes vaccine equity, as fewer doses are needed to complete vaccination; eases pressures on scarce supply so that it is available to those most in need; lowers the overall cost of implementing a vaccine programme, so that such programmes are more accessible to the LMICs that have the greatest burden of

HPV related disease; and facilitates distribution of vaccine in populations where multiple contacts with individuals is challenging or not feasible.

A single-dose HPV vaccine strategy advances health equity

WHO defines equity as “the absence of unfair, avoidable or remediable differences among groups of people”.²² In many cases, these differences result from the conditions under which people among those groups live. When these differences bear on health outcomes, the result might be inequities in health. WHO maintains that “health equity is achieved when everyone can attain their full potential for health and wellbeing”.²² Health equity can be promoted by minimising or eliminating the conditions that lead to differences in access to care and health.

There are substantial geographical and demographical disparities in HPV infection and related disease that are primarily due to uneven and incomplete access to and distribution of HPV vaccines. In addition to overcoming economic barriers and supply scarcity, a single-dose strategy can facilitate reaching the unreachable (ie, segments of a community whose context makes it difficult to deliver health care and maintain continuity in care even when vaccine supply and related resources are sufficient). These groups include itinerant and transient populations, such as refugees, people living in politically unstable regions, remote rural populations, and urban populations at high risk (eg, the unhoused), among others. Likewise, HPV vaccine programmes in many communities operate through schools, and so children who are not attending school might be missed.²⁰

Maintaining continuity of care is especially important for completing a two-dose vaccine schedule, as a single-dose schedule does not require multiple interactions with individuals. A shift to a single-dose strategy opens ways to service communities where continuity of care is challenging or not feasible with current strategies. For example, pop-up clinics or door-to-door programmes that can offer vaccines to a community in a single effort are amenable to a single-dose strategy.²³ A vaccine schedule that provides health officials with more tools to service their communities can help ensure wider vaccine coverage. Where these programmes can be effectively implemented, inequities in access that underlie cervical cancer and other HPV-related diseases will be inevitably reduced. Furthermore, by requiring fewer resources compared with a multiple-dose schedule, a single-dose schedule might free up scarce resources that can be directed to promote health in other contexts. Achieving health equity is a clear goal of both public health and global health efforts, and as health equity is a key component of ethics frameworks for both, there is an ethical imperative to pursue programmes in service of that goal.

A single-dose HPV vaccine strategy advances gender equity

Gender equity is about fairness. To achieve fairness, “strategies and measures must often be available to compensate for women’s historical and social disadvantages that prevent women and men from otherwise operating on a level playing field”.²⁴ The burden of HPV infection disadvantages women in several ways. HPV infections can lead to several diseases, including cervical cancer, genital cancers, and genital warts. Although these conditions affect both men and women, HPV-related morbidity and mortality overwhelmingly affects women. The National Cancer Institute estimates a ten-fold higher number of HPV-related cancers in women compared with men.²⁵ Currently, HPV vaccine programmes have limited scope due to cost constraints and barriers to vaccine distribution. Therefore, many people who can benefit from vaccines are left out. Barriers to accessing HPV vaccines are especially concerning for women, as they carry a higher burden of HPV-related diseases, and thus, would benefit the most from infection prevention efforts.

The cutoff for HPV vaccine programme eligibility is often determined by considering the relative benefit given resource requirements—most HPV infections occur in younger cohorts, and thus, there is a diminishing return on the benefit of the vaccine when directed at comparatively older cohorts. Where resources for vaccine programmes are less constrained, programmes can recommend HPV vaccination for all genders and set higher age cutoffs for eligibility (eg, up to age 26 years and even up to age 45 years for some individuals in the USA).²⁶ In contrast, in many LMICs, where the burden of HPV-related disease is highest, programmes must limit their scope to girls aged 9–14 years.

As discussed, a single-dose strategy improves access to vaccines by overcoming barriers to procurement, affordability, and distribution. Thus, such a strategy might create an opportunity to expand vaccination programmes to those who can also benefit but are not prioritised due to resource constraints. That group might include older cohorts of girls and women, such as individuals who are currently not eligible due to resource rationing or those who were unable to acquire the vaccine when they were in the defined age range (and are now over that cutoff), but might still benefit. A single-dose strategy could also allow for programmes that are currently restricted to girls and women to be expanded to include boys and men. HPV is a sexually transmitted infection, and thus, vaccinating boys and men contributes to reduction in overall disease transmission while also reducing (albeit a lesser) burden of HPV-related disease in boys and men. By solely focusing on women because of the higher burden of HPV-related disease, we risk framing HPV infection as a women-specific disease, where women are seen as being responsible for its

prevention.²⁷ Likewise, programmes that must prioritise girls because of resource constraints put an undue responsibility of disease mitigation on girls and women.²⁸ Gender equity is advanced through fair distribution of the responsibility of disease mitigation,²⁸ which might be more achievable through the adoption of a single-dose HPV vaccination schedule.

Increased risk of HPV-related disease due to lack of access to vaccination is not the only way women are disadvantaged in the context of HPV infection. In many communities, women are the primary caregivers in the household²⁹ and “spend disproportionately more time on unpaid care work than men”.³⁰ Additional caregiver responsibility for women due to a greater burden of disease in their communities “potentially limits them from work, financial security, and education, and thus perpetuates existing social inequalities”,³¹ which contributes to disempowering women. This disempowerment negatively affects economic development. Where development is diminished, obtaining resources for health in those communities is further constrained. A single-dose strategy improves access to vaccines. More complete uptake of HPV vaccines translates to fewer infections and fewer cases of disease, which means a lesser burden on women to provide care. Thus, a single-dose HPV vaccine strategy advances gender equity by reducing the burden on women that prevents them from accessing opportunities that contribute to their empowerment, which is integral to achieving several of the UN Sustainable Development Goals (SDGs).

Conclusions

Morbidity and mortality due to HPV-related cancers, especially cervical cancer, is now primarily affecting women living in regions with inequity of access to health-care technologies and services. If we are to take seriously our commitment to equity that underwrites public and global health and if we are committed to achieving the UN SDGs, especially those around good health and wellbeing, we have an ethical obligation to promote strategies that can prevent HPV-related cancer deaths moving forward. Modelling presented by Canfell and colleagues suggests that millions of premature deaths from cervical cancer can be avoided through greater uptake of HPV vaccines³² and indicate their potential to eradicate HPV infection and virtually eliminate cervical cancer.

A single-dose HPV vaccine schedule is not a panacea. Even though a single-dose schedule might help overcome barriers to vaccine procurement and distribution, some people might not be reached by the implemented programmes and access might be restricted for others due to barriers that cannot be overcome by a single-dose schedule.^{33,34} Furthermore, many people are already living with HPV infection and related diseases. Improving vaccine coverage is only one part of the global strategy to eliminate cervical cancer, adopted by the World Health

Assembly in 2020.³⁵ The strategy also calls for 70% coverage in screening for cervical disease in individuals by age 30 years and again by age 45 years, and 90% coverage in treatment for cervical disease. Neither of these goals can be reached through a shift to a single-dose HPV vaccination schedule. Advancing equity also demands that people living with HPV infection or HPV-related diseases are not left behind. Thus, building and maintaining capacity for access to screening and treatment should continue to be part of any HPV general strategy.

Equity is a core consideration in global health ethics. A single-dose strategy will advance three dimensions of equity—vaccine, health, and gender—by making it more feasible to implement vaccine programmes in communities that suffer the highest burden of HPV-related disease. Not coincidentally, these are the same communities for which multiple-dose strategies are currently insufficient due to several resource and logistical barriers. Widespread adoption of a single-dose vaccination strategy creates opportunity to direct scarce resources towards individuals most in need, and eases the burden on women who too often are forced to compromise their own education and economic opportunities, while living with disease or caring for others. Easing that burden helps avoid further entrenchment of existing inequities.

Contributors

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References

- WHO. Human papillomavirus vaccines: WHO position paper (2022 update). *Wkly Epidemiol Rec* 2022; **97**: 645–72.
- Markowitz LE, Drolet M, Perez N, Jit M, Brisson M. Human papillomavirus vaccine effectiveness by number of doses: systematic review of data from national immunization programs. *Vaccine* 2018; **36**: 4806–15.
- Brotherton JML, Budd A, Rompotis C, et al. Is one dose of human papillomavirus vaccine as effective as three? A national cohort analysis. *Papillomavirus Res* 2019; **8**: 100177.
- Barnabas RV, Brown ER, Onono MA, et al. Efficacy of a single-dose human papillomavirus vaccination among young African women. *NEJM Evid* 2022; **1**: 1–12.
- Watson-Jones D, Chagalucha J, Whitworth H, et al. Immunogenicity and safety of one-dose human papillomavirus vaccine compared with two or three doses in Tanzanian girls (DoRIS): an open-label, randomised, non-inferiority trial. *Lancet Glob Health* 2022; **10**: e1473–84.
- UK GOV. JCVI statement on a one-dose schedule for the routine HPV immunisation programme. 2022. <https://www.gov.uk/government/publications/single-dose-of-hpv-vaccine-jcvi-concluding-advice/jcvi-statement-on-a-one-dose-schedule-for-the-routine-hpv-immunisation-programme> (accessed March 11, 2024).
- Department of Health and Aged Care. Change to a single dose HPV vaccine. 2023. <https://www.health.gov.au/ministers/the-hon-mark-butler-mp/media/change-to-single-dose-hpv-vaccine> (accessed March 11, 2024).
- Pan American Health Organization. X ad hoc meeting of the PAHO Technical Advisory Group (TAG) on vaccine-preventable diseases. 2023. https://iris.paho.org/bitstream/handle/10665-2/57896/PAHOCIM230013_eng.pdf?sequence=5&isAllowed=y (accessed March 11, 2024).
- WHO Africa. Africa immunization advisory group urges single-dose HPV vaccine adoption to advance vaccination efforts. 2024. <https://www.afro.who.int/news/africa-immunization-advisory-group-urges-single-dose-hpv-vaccine-adoption-advance-vaccination> (accessed March 11, 2024).
- Pan American Health Organization. PAHO Technical Advisory Group recommends countries of the Americas to use single-dose HPV vaccine schedule. 2023. <https://www.paho.org/en/news/5-9-2023-paho-technical-advisory-group-recommends-countries-americas-use-single-dose-hpv> (accessed March 11, 2024).
- Shadab R, Lavery JV, McFadden SM, Elharake JA, Malik F, Omer SB. Key ethical considerations to guide the adjudication of a single-dose HPV vaccine schedule. *Hum Vaccin Immunother* 2022; **18**: 1917231.
- UNDP. Global dashboard for vaccine equity. <https://data.undp.org/vaccine-equity/> (accessed March 11, 2024).
- WHO. Immunization coverage. 2023. <https://www.who.int/news-room/fact-sheets/detail/immunization-coverage> (accessed March 11, 2024).
- Casey RM, Dumolard L, Danovaro-Holliday MC, et al. Global routine vaccination coverage, 2015. *MMWR Morb Mortal Wkly Rep* 2016; **65**: 1270–73.
- Dorji T, Nopsopon T, Tamang ST, Pongpirul K. Human papillomavirus vaccination uptake in low-and middle-income countries: a meta-analysis. *EClinicalMedicine* 2021; **34**: 100836.
- Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; **71**: 209–49.
- Denny L. Cervical cancer is a disease of inequity: here's how to save 60 million lives. *The Conversation*. 2022. [https://theconversation.com/cervical-cancer-is-a-disease-of-inequity-heres-how-to-save-60-million-lives-176041#:-:text=Cancer%20of%20the%20cervix%20is,of%20human%20papillomavirus%20\(HPV\)](https://theconversation.com/cervical-cancer-is-a-disease-of-inequity-heres-how-to-save-60-million-lives-176041#:-:text=Cancer%20of%20the%20cervix%20is,of%20human%20papillomavirus%20(HPV)) (accessed March 11, 2024).
- Prem K, Choi YH, Bénard É, et al. Global impact and cost-effectiveness of one-dose versus two-dose human papillomavirus vaccination schedules: a comparative modelling analysis. *BMC Med* 2023; **21**: 313.
- WHO. Global Market Study: HPV. Market information for access to vaccines. 2022. https://cdn.who.int/media/docs/default-source/immunization/mi4a/who-mi4a-global-market-study-hpv.pdf?sfvrsn=649561b3_1&download=true (accessed March 11, 2024).
- Tsu VD, LaMontagne DS, Atuhebe P, Bloem PN, Ndiaye C. National implementation of HPV vaccination programs in low-resource countries: lessons, challenges, and future prospects. *Prev Med* 2021; **144**: 106335.
- Katz IT, Weintraub R, Bekker L-G, Brandt AM. From vaccine nationalism to vaccine equity—finding a path forward. *N Engl J Med* 2021; **384**: 1281–83.
- WHO. Health equity. https://www.who.int/health-topics/health-equity#tab=tab_1 (accessed March 11, 2024).
- Gibson E, Zameer M, Alban R, Kouwanou LM. Community health workers as vaccinators: a rapid review of the global landscape, 2000–21. *Glob Health Sci Pract* 2023; **11**: e2200397.
- UN Population Fund. Frequently asked questions about gender equality. 2005. <https://www.unfpa.org/resources/frequently-asked-questions-about-gender-equality> (accessed March 11, 2024).
- National Cancer Institute. HPV and cancer. 2023. <https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-and-cancer> (accessed March 11, 2024).
- Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human papillomavirus vaccination for adults: updated recommendations of the advisory committee on immunization practices. *MMWR Morb Mortal Wkly Rep* 2019; **68**: 698–702.
- Daley EM, Vamos CA, Thompson EL, et al. The feminization of HPV: how science, politics, economics and gender norms shaped US HPV vaccine implementation. *Papillomavirus Res* 2017; **3**: 142–48.
- Dykens JA, Peterson CE, Holt HK, Harper DM. Gender neutral HPV vaccination programs: reconsidering policies to expand cancer prevention globally. *Front Public Health* 2023; **11**: 1067299.

- 29 Menéndez C, Lucas A, Munguambe K, Langer A. Ebola crisis: the unequal impact on women and children's health. *Lancet Glob Health* 2015; **3**: e130.
- 30 Ferrant G, Pesando LM, Nowacka K. Unpaid care work: the missing link in the analysis of gender gaps in labour outcomes. 2014. https://www.oecd.org/dev/development-gender/Unpaid_care_work.pdf (accessed March 11, 2024).
- 31 WHO. Guidance framework for testing genetically modified mosquitoes, second edition. 2021. <https://iris.who.int/bitstream/handle/10665/341370/9789240025233-eng.pdf?sequence=1> (accessed March 11, 2024).
- 32 Canfell K, Kim JJ, Brisson M, et al. Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries. *Lancet* 2020; **395**: 591–603.
- 33 Aggarwal S, Agarwal P, Gupta N. A comprehensive narrative review of challenges and facilitators in the implementation of various HPV vaccination program worldwide. *Cancer Med* 2024; **13**: e6862.
- 34 Ebrahimi N, Yousefi Z, Khosravi G, et al. Human papillomavirus vaccination in low- and middle-income countries: progression, barriers, and future prospective. *Front Immunol* 2023; **14**: 1150238.
- 35 WHO. Global strategy to accelerate the elimination of cervical cancer as a public health problem. 2020. <https://iris.who.int/bitstream/handle/10665/336583/9789240014107-eng.pdf?sequence=1> (accessed March 11, 2024).

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