EVIDENCE AND POTENTIAL IMPACT FOR SINGLE-DOSE HPV VACCINATION

OVERVIEW

Cervical cancer is a leading cause of cancer death among women in low- and lower-middle-income countries and almost all cases can be attributed to human papillomavirus (HPV). HPV vaccines have been licensed for over 15 years and are the primary prevention tool to accelerate cervical cancer elimination. They are highly effective and have significantly reduced HPV infections and precancerous cervical lesions since introduction.

Based on current evidence that shows a single-dose of HPV vaccine provides similar protection against HPV infection as a multi-dose regimen, the World Health Organization's (WHO) Strategic Advisory Group of Experts (SAGE) on Immunization endorsed the optimization of HPV vaccine schedules.

The Potential for Single-Dose HPV Vaccination
With greatly reduced costs and simplified implementation, health and economic impact analyses show that single-dose HPV vaccination could be a high-value public health intervention. Specifically, single-dose HPV vaccination will likely:

- Accelerate introduction for countries that have yet to introduce the vaccine.
- Facilitate new options for current national programs by simplifying delivery, lowering program costs, and potentially increasing coverage.
- Reduce the potential for supply shortages and delivery challenges, such as those faced during the COVID-19 pandemic.
- Accelerate achieving the vaccination target of WHO's cervical cancer elimination initiative.

WHO SAGE Reccomendation (June 2022)

- One or two-dose HPV vaccine for the primary target of girls aged 9-14 years old (yo).
- One or two-dose schedule for young women aged 15-20 yo.
- Two doses with a 6-month interval for women over 21 yo.
- Immunocompromised individuals, including those with HIV, should receive three doses if feasible, and if not, at least two doses.

SAGE urged countries to introduce HPV vaccine for the primary target group of girls aged 9–14 yo and, where feasible and affordable, prioritize catch-up in older cohorts and missed girls through multi-age cohort vaccination up to the age of 18 yo.

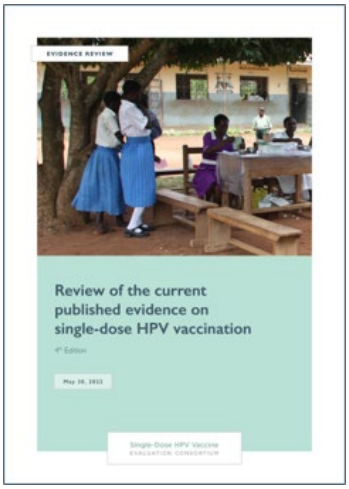
Read the Weekly Epidemiological Record: https://apps.who.int/iris/bitstream/handle/10665/356579/WER9724-eng-fre.pdf

KEY TAKEAWAYS ON EXISTING EVIDENCE

Data accumulated to date from clinical trials and high-quality observational clinical studies provide strong evidence that single-dose HPV vaccination could substantially reduce the incidence of HPV-attributable cervical precancer and cancer. Evidence shows comparable efficacy and effectiveness between single and multidose schedules in preventing HPV infections, lasting up to 10 years following vaccination.

Clinical Trials

- A randomized controlled trial in Kenya with girls and women aged 15-20 showed single-dose vaccination with Gardasil®9 or Cervarix™ **was about 98% effective in preventing HPV 16/18 persistent infections.**[1]
- The immune response 24 months post-vaccination of a single dose in girls aged 9-14 in Tanzania was **non-inferior to a single dose in historical cohorts for which single-dose efficacy was shown**.[2]
- **A single dose was shown to elicit a similar level of protection compared to multidose schedules** in high-quality observational clinical studies in India and Costa Rica to at least ten years post-vaccination.[3,4]



Modelling Studies[5]

- Compared to no vaccination, single-dose HPV vaccination yields substantial health benefits and is good value for money.
- Reaching more girls with a single dose will avert much more cervical cancer cases than vaccinating fewer girls with a second dose.
- Immediate implementation of a single-dose HPV program leads to greater health benefits than delaying implementation.

THE SINGLE-DOSE HPV VACCINE EVALUATION CONSORTIUM

The Single-Dose HPV Vaccine Evaluation Consortium was formed to collate and synthesize existing evidence and evaluate new data on the potential for single-dose HPV vaccination. Since 2018, the Consortium, composed of eminent experts on HPV, has compiled an Evidence Review of the current, published evidence on single-dose HPV vaccination, including data from efficacy trials, immunogenicity studies, other observational studies, and mathematical impact modeling. The Consortium also provides commentary on the strength of that evidence and remaining gaps remain. Its goal is to evaluate this evidence to inform global policy discussions and program guidance, as well as to raise awareness and understanding of its implications.

For additional information and resources, please visit: www.path.org/singledosehpv.

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[1]Barnabas R, Brown E, Onono M, et al. Efficacy of Single-Dose HPV Vaccination Among Young African. *NEJM Evidence*. 2022. doi: 10.1056/EVIDoa2100056.

[2]Watson-Jones D, Changalucha J, Whitworth H, et al. Immunogenicity and Safety Results Comparing Single Dose Human Papillomavirus Vaccine with Two or Three Doses in Tanzanian girls - the DoRIS Randomised Trial. *Lancet*. Preprint posted online March 11, 2022. https://dx.doi.org/10.2139/ssrn.4055429.

[3]Basu P, Malvi SG, Joshi S, et al. Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study [published correction appears in Lancet Oncol. 2022 Jan;23(1):e16]. *Lancet Oncology*. 2021;22(11):1518-1529. doi:10.1016/S1470-2045(21)00453-8.

[4] Kreimer AR, Sampson JN, Porras C, et al. Evaluation of Durability of a Single Dose of the Bivalent HPV Vaccine: The CVT Trial. *Journal of the National Cancer Institute*. 2020;112(10):1038-1046. doi:10.1093/jnci/djaa011.

[5] Takeaways from model-based analyses assume lower vaccine effectiveness for single dose.

The consortium, coordinated by PATH, includes Harvard University, London School of Hygiene & Tropical Medicine, Université Laval, University of British Columbia, US Centers for Disease Control and Prevention, US National Cancer Institute, Wits Reproductive Health and HIV Institute, and the Kirby Institute at University of New South Wales.

In addition to the consortium members, representatives from the following institutions serve as advisors: the British Columbia Provincial Health Authority; International Agency for Research on Cancer; Medical Research Council Unit, The Gambia; Instituto Nacional de Salud Pública de Mexico; and Quebec Institut National de Santé Publique.