

CCA Network Dialogue Series

Facilitated discussions with experts on
critical issues for cervical cancer elimination

A Dialogue on Single-Dose HPV Vaccination: Efficacy, Implementation and Social Mobilization

in partnership with PATH

Hosted on February 27, 2023

Session Summary and Resources

UPCOMING DIALOGUES

- Supporting Healthcare Providers to Increase HPV Vaccine Uptake in Communities
- Affording HPV vaccination programs
- Cervical cancer elimination planning
- Engaging cervical cancer survivors



Single-Dose HPV Vaccination Dialogue

In February 2023, CCAE's inaugural network dialogue brought together partners from around the world to discuss with experts the shift in the WHO's HPV vaccination schedule recommendations, moving from two doses to the off-label option of a single-dose schedule for persons aged 9–20 years.

The following pages comprise a summary of the questions and answers given during the dialogue, and a list of relevant resources for reference. We are grateful to Dr Rebecca M. Casey (US Centers for Disease Control and Prevention) for providing additional input on this summary.

Co-facilitator

Hope Randall, Communications Officer for the for the Single-Dose HPV Consortium at PATH, US

Expert panel and moderators

Dr Cathy Ndiaye, Director of the HPV Vaccine Program at PATH, Senegal

Dr Emmanuel Mugisha, Director of the Typhoid Vaccine Acceleration Consortium and Senior Technical Advisor on Immunizations at PATH, Uganda

Benda Kithaka, Executive Director at KILELE Health, Kenya

George Hayes, Global Partnerships and Advocacy Manager, Cancer Research UK

Updated WHO recommendations

WHO recommends the following schedule:

- A one (off-label) or two-dose schedule for girls and boys aged 9–20 years
- A one (off-label) or two-dose schedule for those aged 15–20
- Two doses for women aged 21 and older
- A minimum of two doses and when feasible three doses remain necessary for those known to be immunocompromised and/or living with HIV

Single-dose HPV vaccine resources

- [PATH's Single-Dose HPV Vaccine Evaluation Consortium](#) resources including a [general summary](#) and an [evidence synthesis review](#) in English, French, Spanish or Chinese (Jul 2022)
- [International Papillomavirus Society's webinar update on WHO recommendations on HPV vaccine schedule optimization and implications](#) (Feb 2023)
- [WHO's human papillomavirus vaccines position paper](#) (Dec 2022)
- [Press release accompanying WHO position paper](#) (Dec 2022)
- [HPV vaccine schedule optimization guide](#) from the HPV vaccine technical support partners to Gavi, the Vaccine Alliance (March 2023)

Single-Dose HPV Vaccination: Efficacy

Q&A highlights



What do the current efficacy studies on single-dose HPV vaccination schedules show, including the effectiveness percentages? How does this compare to two doses?

- Current evidence suggests that a single dose of the HPV vaccine for routine vaccination and multi-age cohort catch-up vaccination in girls has comparable efficacy and duration of protection as two doses and may offer program advantages, be more efficient and affordable, and contribute to improved coverage
- The evidence for this comes from several different studies, including a high-quality randomized control trial which took place in Kenya. This study demonstrated that single-doses of Cervarix (bivalent) and Gardasil-9 (nonavalent) HPV vaccines had very high vaccine efficacy (97.5% efficacy) against persistent HPV16 and 18 infections in girls aged up to 20 years
- Additionally, a follow-up analysis of a trial in India demonstrated vaccine efficacy for a single-dose of Gardasil (quadrivalent) HPV vaccine was comparable in protecting girls aged 10–18 against persistent HPV16 and 18 infections 10 years on from vaccination. In this case, vaccine efficacy was 91.2%/94.5%/94.2% for 3/2/1 doses, respectively
- When evaluating the immune responses induced by single-dose, a randomized trial in Tanzania demonstrated that girls aged 9–14 experienced comparable immune responses against HPV16 and 18 whether they had received 1, 2 or 3 doses 2 years post-vaccination
- There is currently no evidence that the efficacy of single-dose schedules wanes over time

Does the single-dose recommendation apply to all vaccines on the market?

- The WHO advises that regions/countries which are implementing a single-dose schedule should use HPV vaccines with data on single-dose efficacy or immuno-bridging data (Cervarix, Gardasil or Gardasil-9)
- Immuno-bridging refers to evidence when the peak and 24-month plateau antibody levels for an HPV vaccine are comparable to those of HPV vaccines with proven single-dose efficacy.

How would the shift to single-dose affect at-risk groups (such as people living with HIV), older age cohorts and boys? Should girls aged 9–14 still be the priority?

- The WHO recommends that as an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years, but the primary target for the HPV vaccine remains girls aged 9–14 years
- This is the primary target group because research shows that younger people have a better immune response to the vaccine than those in their late teens and early 20s. In addition, the vaccines will prevent the target strains of HPV only if it has been given before exposure to the virus, which is less likely to be the case in older individuals
- Vaccination of secondary target populations (e.g. females aged ≥ 15 years, boys, older males or men who have sex with men) is recommended only if this is feasible and affordable, and does not divert resources from vaccination of the primary target population or effective cervical cancer screening programs
- For women aged 21 and over, the WHO recommends they receive two doses
- The WHO recommends that immuno-compromised individuals receive a minimum of two doses and, where possible, three doses. This is because no published data are available on the immunogenicity or effectiveness of 1- or 2-dose schedules among people living with HIV

Single-Dose HPV Vaccination: Implementation

Q&A highlights



What are the factors that a government needs to consider in terms of making the switch from two doses to one?

- Governments may wish to consider current levels of HPV vaccination coverage and strategies for ensuring there are sufficient opportunities to vaccinate all age-eligible girls against HPV, in consideration of the reduced schedule; resources available for updating guidelines and materials, and re-training healthcare workers; public and provider sensitization, including clear and confident messaging that does not damage the trust that parents/teachers/healthcare workers have in the vaccination program, or instill confusion for groups still requiring multiple HPV vaccination doses

How would the shift to single-dose affect risk groups, multi-age cohorts and boys?

- The WHO acknowledged that as an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years, but the primary target for the HPV vaccine remains girls aged 9–14 years
- For women aged 21 and over, WHO recommends they receive two doses
- The WHO recommends that immunocompromised individuals receive a minimum of two doses and, where possible, three doses

Which countries are switching to single-dose and which will stay with two doses?

- As of March 2023, Cabo Verde, Solomon Islands, Mexico, the UK, Ireland, the Netherlands, Sweden, and Australia are all switching to single-dose for girls aged 9–14
- Tonga and Albania have introduced HPV vaccination into their national immunization program for the first time with a single dose schedule
- the national technical advisory groups on immunization in Nigeria, India, and Bangladesh have all advised introducing the vaccine into the respective national immunization schedules with a single dose schedule

What policy changes are needed to proceed with the shift to single-dose?

- Each country should have the move to single-dose approved by their national immunization advisory committee. For countries that have yet to include HPV within their national immunization schedule, the introduction be approved by the national immunization advisory committee, regardless of whether they are launching with single-dose or two-dose schedules

What do you foresee are the key risks or challenges in the implementation of single-dose HPV vaccines?

- If we find out later that a booster is needed, it will be challenging to track girls when they are older
- Communication materials will need to be revised and new guidelines and health worker training will need to be delivered to a standard that ensures there is no loss in confidence and no confusion around dosing for at-risk groups

What strategies can be implemented to ensure the target population is still reached?

- Any resources saved from moving to single-dose need to be invested in reaching hard-to-reach girls (i.e. those out of school or in rural areas). Reaching girls early in school – ideally primary school – remains the most effective strategy but girls outside of school must not be forgotten. This can be achieved by integrating HPV vaccination into other services and working with community health workers
- More implementation research is needed

Single-Dose HPV Vaccination: Social Mobilization

Q&A highlights



What campaign messages should be developed and deployed – for both the public and providers – to mobilize around the shift to single-dose?

- It has been shown that 1 dose is enough. Also, there's no danger in having more than 1 dose if it's later considered to be required
- Reassuring messaging about effectiveness
- The decision to reduce doses is driven and guided by research and science
- Ministries of Health, Education, and others need to collaborate on coordinated messaging and dissemination

How would single-dose schedules impact groups that are immunocompromised?

- Immunocompromised individuals and those living with HIV will require at least 2 doses
- Communications will need to be developed for groups that still require more than 1 dose

Are there best practice examples from other LMIC vaccination campaigns which could be drawn upon to support the shift to single-dose?

- HPV dosing schedules have already shifted from 3 doses to 2; lessons can be learned from this
- Cabo Verde, Solomon Islands, and Mexico are all shifting to single-dose

How do you respond to the question "after my daughter receives the vaccine, does she still need to screen for cervical cancer? What is the point of the vaccine if she still has to screen?"

- HPV comes in many different strains. HPV bivalent vaccine directly protects against 2 strains that cause cancer and the nonavalent directly protects against 9 strains. The reason that we advise that screening is still needed is because these vaccines do not cover all the strains that cause cancer. Approximately 15% of the strains that can cause cervical cancer are not covered by vaccines. Screening can protect against cancerous changes caused by that 15% of strains

How could messaging address the concern that shifting to single-dose reduces vaccination effectiveness?

- Unified messaging to address this concern should be clearly communicated to the public and providers through diverse channels
- This messaging should reflect the evidence overviewed on page 3 of this summary in a clear and accessible way
- Healthcare workers should be trained in delivering this unified messaging

How should messaging address concerns that shifting to single-dose is driven only by cost-savings, in order to avoid distrust?

- There is a cost saving that comes from only needing to provide a single dose of HPV vaccine for the majority of vaccine recipients, but initial financial input will likely be required to facilitate the shift (see page 6)
- It is also recommended that the cost-savings from the shift are reinvested into improving coverage of HPV vaccination programs, in order to achieve 90% coverage of girls and vaccinate hard-to-reach groups
- This information should be communicated clearly to the public and providers

How can we mobilize vaccine producers to register their HPV vaccine labels for single-dose?

- Engage pharmaceutical companies' social responsibility arm
- While producers may experience some loss in earnings from countries going from 2 doses to 1, there are gains to be made in countries that may now be able to include HPV vaccination in their national schedules for the first time. Emphasizing this to producers could benefit conversations

Single-Dose HPV Vaccination:

Pros and cons of different dosing schedules

Coverage	High first HPV dose coverage	High first HPV dose coverage	Low first HPV dose coverage	High risk geographies or groups
Program Choice	High second HPV dose coverage	Low second HPV dose coverage	Low second HPV dose coverage	
Switch to single dose	<p>Pro: The saved resources from reducing the dosing schedule can be repurposed towards multi-age cohorts and additional catch-up programs</p> <p>Pro: If a second dose catch-up is needed in the future, there is existing capacity for catch-up programs to achieve high second dose coverage</p>	<p>Pro: The saved resources from reducing the dosing schedule can be repurposed towards improving first dose coverage</p> <p>Con: It would be more difficult to implement a second dose catch-up in the future if needed because older females are hard to reach and vaccination documentation can be poor</p>	<p>Pro: The saved resources from reducing the dosing schedule can be repurposed towards improving first dose coverage</p>	<p>Pro: The saved resources from reducing the dosing schedule can be repurposed towards improving first dose coverage for hard-to-reach geographies or groups</p>
No switch or later switch	<p>Pro: Switching may compromise public trust in the HPV immunization program or broader essential immunization program, so not switching would minimise this risk</p>	<p>Pro: No official policy change would be required to reduce the HPV vaccine dosing schedule</p>	<p>Pro: There are more opportunities to provide the first HPV dose with a multi-dose schedule</p>	<p>Pro: There are more opportunities to reach high-risks groups (such as populations with a greater % of girls living with HIV) with a multi-dose schedule</p>

Table and content kindly contributed by Dr Rebecca M. Casey, Global Immunization Division, US Centers for Disease Control and Prevention

Single-Dose HPV Vaccination:

Budget impact considerations for switching to single-dose schedules

Cost area	Switch cost savings	Switch cost incurred
Supplies	<p>Vaccines, syringes, safety boxes</p> <p>Vaccine wastage e.g., fewer vaccination sessions so potentially fewer opportunities for wastage</p>	Vaccine wastage e.g., if expired vials have to be discarded
Personnel and vaccine delivery	<p>Outreach for second dose</p> <p>Catch-up for second dose</p>	<p>Re-training inc new training materials</p> <p>Catch-up for first dose</p> <p>Developing different delivery strategy</p>
Distribution system	Transportation of second dose vaccines, cold storage, and storage and transportation of supplies	
Waste management	Costs associated with wastage incineration	
Surveillance and monitoring		<p>Redesign, print and disseminate new guidelines, recording and reporting forms and tools (paper and electronic)</p> <p>Readiness assessment, supportive supervision, data quality monitoring and post-switch evaluation, and strengthening where required</p>
Other costs		Social sensitization

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