HPV VACCINE SCHEDULE OPTIMIZATION

Key considerations for decision-making, planning, and implementation

Developed by HPV Vaccine Technical Support Partners, including:
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About this document
This document is intended for use by countries in considering and planning for a successful introduction of a single-dose human papillomavirus (HPV) vaccination schedule or a switch from a multi-dose to a single-dose HPV vaccination schedule. The document outlines key considerations and implications for national-level planners, immunization programme managers, and immunization partners involved in providing decision-making and implementation support to countries.

This decision-making and operational guide relating specifically to HPV schedule optimization complements the existing World Health Organization (WHO) documents “Principles and considerations for adding a vaccine to a national immunization programme”¹ and “Guide to introducing HPV vaccine into national immunization programmes”² that cover the important points for consideration when introducing any new vaccine or HPV vaccine into a national immunization programme, respectively, and other widely available resources on HPV vaccination (Appendix 1).

Background
Vaccination to prevent HPV infection, the primary cause of cervical cancer, has been recommended by WHO since 2009. The introduction of HPV vaccines has been slow; while most high-income countries have introduced the HPV vaccine, the proportion of low- and middle-income countries that have successfully introduced it remains low. Global supply shortages over the last years have stalled introductions and left many cohorts of girls unprotected against HPV. In countries that have introduced the HPV vaccine into their routine immunization schedule, coverage with the HPV vaccine in most countries is behind the coverage attained with childhood vaccines. In 2021, 12% of eligible girls were estimated to be protected. Since the adoption of the Global Strategy Toward the Elimination of Cervical Cancer³, countries are urged to introduce the HPV vaccine as part of cervical cancer elimination efforts. The HPV vaccines were originally licensed for a 3-dose schedule. However, not all individuals completed the 3-dose schedule, and post-hoc analyses of the trial data revealed that efficacy against the most high-risk type (HPV 16/18) infection was similar after 1, 2, and 3 doses. These findings have been stable over more than 10 years and have now been confirmed with similar findings from high-quality single-dose trials.

In April 2022, the Strategic Advisory Group of Experts on Immunization (SAGE) reviewed the evidence on the efficacy of a single-dose HPV vaccine schedule, including the first two randomized trials prospectively designed to evaluate the efficacy and immunogenicity of single-dose HPV vaccination versus a comparator. Based on this newly available evidence, in December 2022 WHO position paper for the use of HPV vaccines states that countries may now choose between a one- or 2-dose schedule for the primary target population, 9–14-year-old girls, as well as young adults of both genders up through 20 years of age. This off-label single-dose option for routine and multi-age cohort catch-up vaccination was considered because it provides comparable and high levels of individual

¹ The document “Principles and Considerations for Adding a Vaccine to a National Immunization Programme” can be found at: https://apps.who.int/iris/handle/10665/111548
² The document “Guide to Introducing HPV Vaccine into National Immunization Programmes” can be found at: https://www.who.int/publications/i/item/9789241549769
³ The document “Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem” can be found at: https://www.who.int/publications/i/item/9789240014107

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protection whilst likely to be more efficient from a public health perspective (fewer doses per cervical cancer case prevented), less resource-intensive and easier to implement than a 2-dose schedule. This advice applies to those HPV vaccines for which corresponding single-dose data has been demonstrated or immunobridged against a vaccine with the available single-dose efficacy data. As of December 2022, the licensed pre-qualified vaccines for which such data are available include bivalent (Cervarix®, quadrivalent (Gardasil®), and nonavalent (Gardasil® 9) vaccines. Newer HPV vaccines will require immunobridging studies. As of May 2023, single-dose HPV vaccine immunobridging studies are ongoing for Cecolin® (bivalent, WHO-prequalified) and Cervavac® (quadrivalent, licensed), and have not yet begun for Walrinvax® (bivalent, under WHO prequalification process).

<table>
<thead>
<tr>
<th>Primary target group</th>
<th>Previous WHO position (2017)</th>
<th>Current WHO position (December 2022)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls aged 9–14 years old</td>
<td>Girls aged 9–14 years old</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccination Schedule by age (years)</th>
<th>Previous WHO position (2017)</th>
<th>Current WHO position (December 2022)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9–14</td>
<td>2-dose schedule</td>
<td>Either a 1-dose* or a 2-dose vaccination schedule</td>
</tr>
<tr>
<td>15–20</td>
<td>3-dose schedule</td>
<td>Either a 1-dose* or a 2-dose* vaccination schedule</td>
</tr>
<tr>
<td>≥21</td>
<td>3-dose schedule</td>
<td>2-dose schedule can be used*</td>
</tr>
<tr>
<td>Immunocompromised, including people living with HIV (any age)</td>
<td>3-dose schedule</td>
<td>Should be prioritized and should receive at least 2 doses* but ideally 3 doses, if programmatically feasible.</td>
</tr>
</tbody>
</table>

* off-label recommendation for girls and boys

**HPV vaccine schedule options**

Countries may now choose between a one- or 2-dose schedule for the primary target population, 9–14-year-old girls (Table 1).

Since the single-dose efficacy data come from trials involving females up to age 20 years, either a one-dose or 2-dose schedule can also be used for the vaccination of girls aged 15–20 years old.
For those older than 20 years, a reduced, 2-dose schedule with a minimum interval of 6 months between doses can be used. Data on immunogenicity and efficacy from a post-RCT follow-up study (Appendix 2) give confidence that this reduced-dose schedule will provide protection in older females.

It is uncertain whether immunocompromised individuals, such as people living with HIV, will be protected adequately by reduced dose schedules. Until further evidence is available, immunocompromised persons, irrespective of age, should be prioritized and should receive at least two doses but ideally three doses if programmatically feasible.

For global equity and considering the improving supply situation, WHO recommends that priority should be given to the primary target of girls and that the expansion of HPV programmes to secondary targets should be carefully managed considering supply availability, programme feasibility, and affordability without diverting resources from
vaccination of the primary target population. Countries with a gender-neutral HPV vaccination programme can also choose a single-dose schedule for boys aged 9–20 years based on this WHO position.

**Off-label vaccine recommendations**

An off-label vaccine recommendation generally refers to a difference between the labelled instructions on how to use the vaccine as approved by the regulatory authorities (or “label”) and the recommendations for use issued by public health advisory bodies at national (e.g., National Immunization Technical Advisory Groups) and/or international levels (e.g., SAGE). For example, the label may recommend a specific vaccine schedule or dose based on data from controlled trials at the time of initial licensure of the vaccine, while public health authorities may provide different recommendations based on additional post-marketing data and benefit-risk analyses or other factors. After an initial label is approved, additional post-marketing data may support or require an eventual change in the label, but this is not always done.

Examples of off-label vaccine use include:

- Use of heptavalent pneumococcal conjugate vaccine (PCV7) in a 2+1 schedule (public health recommendation for off-label use) instead of a 3+1 schedule (per label) based on new evidence from immunogenicity studies (Canada, Belgium, and the United Kingdom).
- Use of fractionated doses of yellow fever or inactivated poliomyelitis vaccines as recommended by SAGE in the context of vaccine supply challenges (multiple countries).
- Administration of rotavirus vaccines to children >24 months is not recommended and this WHO-recommended upper age limit constitutes an off-label recommendation.
- Use of influenza vaccines among pregnant women after a SAGE recommendation despite the label of these vaccines at the time not recommending use during pregnancy in most countries (multiple countries, including 27 European Union countries in 2015).

Vaccine labels may also differ between countries because of the variation among independent regulatory authority assessments, policies, and other criteria used in the vaccine assessment. For example, in 2013, the European Medicines Agency (EMA) approved the change from a three-dose HPV vaccine schedule to a 2-dose schedule for children between 9 and 14 years, whereas the HPV vaccines in the U.S. were recommended in a three-dose schedule in this age group at that time.

Countries are encouraged to inform their national regulatory authority (or equivalent) of the evidence-based programmatic decision to use the single-dose off-label HPV vaccination schedule. The differences between public health recommendations and the product label regarding vaccine use may lead to confusion for vaccinators and vaccinees, which may result in lower compliance with national vaccination schedules. Therefore, good communication among regulatory bodies, public health authorities, companies, and health care providers or vaccinators is critical.
Summary of evidence supporting single-dose HPV vaccination

The option to use a single-dose HPV vaccination schedule is based on randomized controlled efficacy trials against incident persistent infections, immunobridging trials, post hoc analyses of efficacy trials (Appendix 2), and post-licensure observational studies demonstrating that a single-dose of HPV vaccine elicits a protective immune response against the incident and persistent HPV infection—the necessary prerequisites to further development of cervical lesions and, in the longer term, cervical cancer. Additional clinical trials (Appendix 3) and observational study data are expected to provide more information on the duration of the protection and relative efficacy and effectiveness of single-dose versus multidose schedules. However, the existing data support the conclusion that a single-dose HPV vaccination for immunocompetent girls provides equivalent or near-equivalent protection to 2-dose vaccination and should be considered for those HPV vaccine products with data on efficacy or immunobridging to vaccines with proven single-dose efficacy. As of May 2023, the products for which efficacy and immunogenicity data support use in a single-dose schedule are bivalent (2vHPV, Cervarix®), quadrivalent (4vHPV, Gardasil®), and nonavalent (9vHPV, Gardasil® 9) vaccines.

Immunogenicity and efficacy trials

These data include a high-quality randomized controlled trial (RCT) in Kenya (KEN SHE45) in which sexually active 15–20 year-old females (N=2,250) were randomized to three arms: single-dose 2vHPV, 9vHPV, or delayed vaccination. Single-dose HPV vaccination was highly efficacious (>95%) against incident persistent HPV infection over three years: 9vHPV vaccine efficacy (VE) was 98.8% (95% CI [91.3–99.8], p=<0.0001); bivalent VE was 97.5% (95% CI [90.0–99.4], p=<0.0001).

In a post hoc analysis of an RCT (India IARC67) comparing dose regimens of 4vHPV (Gardasil) in females 10–18 years of age, VE against HPV-16/18 infections was similarly high (>90%) up to at least 10 years post-vaccination across different schedules (single-dose, 2-doses at 0,6 months, and 3-doses at 0, 1, 6 months), including among ~5000 subjects who only received a single-dose of the vaccine. Ten years after vaccination, the antibody levels were at least two times higher in single-dose recipients compared to those following natural infection. No HPV16/18-related CIN2/3 was detected in vaccinated women.

Similarly, in a post hoc analysis of a randomized clinical trial (Costa Rica HPV Vaccine Trial, CVT8,9) comparing a 3-dose regimen of 2vHPV (Cervarix) to active control (Hepatitis A vaccine) among females aged 18–25 years, VE estimates against prevalent HPV 16/18 infections were similar after single-dose vaccination to a multi-dose...
regimen. Sixteen years after HPV vaccination, HPV16 and 18 seropositivity was almost 100% among HPV-vaccinated women and they remained seropositive irrespective of the number of HPV vaccine doses received. A minimal decline in the antibody concentration was observed over time, especially for the single-dose HPV vaccine group.

Among females (N=930) aged 9–14-years-old randomized to 1, 2, or 3 doses of 2vHPV or 9vHPV in a randomized open-label trial (DoRIS10) in Tanzania, seropositivity was >97.5% for all dose groups for 2vHPV and 9vHPV vaccines at 24 months post-vaccination. Immunobridging11 showed that single-dose HPV 16/18 antibody responses (geometric mean titers, GMTs) were non-inferior in DoRIS compared with those in studies where single-dose efficacy has been observed (CVT, India IARC, KEN SHE).

**Observational Studies**

Data on the immunogenicity of a single HPV vaccine dose compared to multi-dose schedules (and compared to natural HPV infection) are available from observational studies of partially vaccinated populations.12 Although these observational study findings are subject to bias (mainly information bias and confounding) and considered to be lower quality, most studies found very high rates of seropositivity for HPV genotypes protected against by the vaccine type administered, regardless of the number of doses received. Few found a difference in seropositivity rates among participants who received one, two, or three vaccine doses. Most studies found that antibody levels were lower in the single-dose arms compared to the multi-dose arms. However, a minimal antibody titer sufficient for protection has not been identified, so the clinical relevance of these differences is unclear. Similarly, in a systematic review13 of post-licensure effectiveness studies of HPV vaccination by number of doses among women aged 18 years or younger at the first vaccine dose, the adjusted HPV infection prevalence ratios were similar for three doses (0.08; 95% CI [0.04–0.15]), two doses (0.07; 95% CI [0.01–0.47]), and one dose (0.08; 95% CI [0.01–0.54]).

**Modeling and health economics data**

Based on modeling studies (Appendix 1), single-dose HPV vaccination yields substantial health benefits and is good value for money. The current approach (routine vaccination with a 2-dose regimen and without multi-age cohort catch-up) prevents fewer cases and is less efficient than a single-dose multi-age cohort approach. Immediate implementation of a single-dose HPV vaccination programme leads to greater health benefits than delaying implementation until more conclusive information on vaccine efficacy is available from ongoing clinical trials. The impact and cost-effectiveness of adding a second dose are driven by the duration of single-dose HPV vaccine protection and possibly, the ability to achieve higher coverage with single-dose versus multiple doses. Even if contradictory to existing evidence, a lower vaccine efficacy level of 80% is assumed or a shorter duration of protection of ten years, single-dose HPV vaccination yields substantial health benefits and is good value for money compared to no vaccination.14

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Country decision-making process for HPV schedule optimization

The decision-making process around choosing a single-dose HPV vaccination schedule should be country-led, systematic, and evidence-based. Each country’s public health advisory bodies (e.g., NITAG) and decision-making bodies (e.g., the Ministry of Health/Expanded Programme for Immunization (EPI)) must decide whether additional data may be needed for decision-making (e.g., knowledge, attitudes, and perceptions of key stakeholders). The decision-making should be coordinated with other components of the health system and be comprehensive. Some factors may outweigh others in importance, depending on the specific circumstances (e.g., disease burden, product characteristics, estimated budget, cost-effectiveness). These programme considerations are context-specific and depend on available information at any given moment; so countries that choose not to introduce or switch to a single-dose HPV vaccination schedule at this juncture may decide to revisit the issue later as more evidence becomes available or when other conditions change.

Reasons to choose a single-dose HPV vaccination schedule

The focus of this section is on the use of a single-dose compared to a multi-dose schedule for the primary target group, girls aged 9–14 years, either as a new vaccine introduction or as a change in schedule (“schedule switch”) for an existing programme.

There are several potential programmatic and economic benefits of a single-dose HPV vaccination schedule (Figure 1). A single-dose HPV vaccination schedule could simplify delivery for key stakeholders (Figure 2), provide new integration opportunities, lower costs, and/or create new programme opportunities with the resources saved. These opportunities could include building an adolescent or school health platform, conducting multi-age cohort catch-up strategies, or investing in cervical cancer screening and treatment. Furthermore, a single-dose schedule may allow for better integration. It may be possible to co-deliver using the existing platforms for single-visit interventions for which there is already high community demand or existing platforms for intensified vaccination efforts at a specific time (e.g., child health days). Countries should also consider the ability of the HPV programme to reach specific population subgroups, such as immunocompromised persons who are currently recommended to receive a multi-dose schedule based on the existing data.

Figure 1. An illustrative example of potential programme and economic benefits of switching to a single-dose HPV vaccination schedule

Source: PATH
Countries may decide to introduce HPV vaccination in a single-dose schedule or switch from a multi-dose to a single-dose HPV vaccination schedule for a range of reasons, especially when the current programme is already experiencing challenges. Examples include:

- **Limited domestic resources for introducing and/or sustaining a successful HPV programme**
  - Financial costs (e.g., cost of the vaccine, community outreach, school outreach, catch-up activities, defaulter tracking)
  - Human resources (e.g., health worker workload and staffing challenges exacerbated by the COVID-19 pandemic)
  - Challenges with the limited logistics, cold chain, storage, and/or stock management capacity

- **Sub-optimal performance of existing multi-dose HPV programme**
  - Challenges with subnational HPV vaccine supply and delivery
  - Challenges with achieving successful sustainable school outreach activities for a multi-dose schedule
  - High drop-out for the second dose of a multi-dose schedule

- **Sub-optimal resource allocation within the HPV vaccination programme or broader cervical cancer elimination strategy**
  - For example, within a limited resource setting, second-dose vaccine and programme costs could be more effectively allocated to other HPV programme areas, such as risk communication and community engagement.

- **Sub-optimal HPV vaccination access and/or community demand**
  - Challenges with reaching under-immunized communities (e.g., out-of-school girls) with two doses
  - Caregiver’s/girls’ negative perception/implications of multi-dose schedule (risk, convenience, pain, resources, cost)

Single-dose schedule options may also offer benefits to all programmes, including those that are performing well. Some of these include the following:

- **Cost savings through reduced vaccine procurement requirements, and reduced strain on the supply chain**
- **Identified opportunities to improve HPV vaccination coverage with a single-dose strategy by:**
  - Harnessing new HPV vaccine delivery options to reach all target girls, including populations that are not being reached currently (e.g., with new preferred locations for one-time HPV vaccination in the community or during child-health weeks)
  - Incorporating lessons learnt from programmes that have successfully achieved and sustained high-coverage with other single-dose schedule antigens or single-visit health interventions
  - Integrating single-dose HPV vaccine within a new platform for adolescent health

- **Reduction in the programmatic need for HPV vaccination catch-up strategies for multiple missed or under-vaccinated cohorts** (e.g., using single-dose multi-age cohort campaigns for an extended age range target population of girls aged 9–18 years)
- **Possible increase in acceptability because of the need for fewer vaccinations**
- **Provide increased programmatic resilience against a change in country context** (e.g., weakened health and immunization systems in fragile and conflict settings).
Figure 2: Potential programme benefits: Simplified vaccine delivery for key stakeholders

Potential programme benefits: simplified delivery

More convenient for caregiver/girl
Less perceived or actual expenditures or adverse events relating to immunization

Reduced time burden for healthcare worker
Fewer outreach visits to schools
Reduced catch-up activities
Less time commitment for other key stakeholders (e.g., teachers)

Key decision-making considerations for HPV vaccine schedule optimization

As discussed, the off-label single-dose HPV vaccination option might be considered because it provides comparable and high levels of individual protection whilst likely to be more efficient from a public health perspective (fewer doses per cervical cancer case prevented), less resource-intensive, and easier to implement than a multi-dose schedule. However, there are also other key programmatic aspects and risks to consider (Figure 3). These include consideration of risks and benefits to the existing HPV or broader immunization programme (e.g., how the introduction of or switch to a single-dose schedule will be perceived by the key stakeholders and how trust in the immunization programme might change). Another consideration is the impact on equity (e.g., how a single-dose strategy could impact the programme’s potential to vaccinate hard-to-reach populations, and whether the HPV programme will have the capacity to reach immunocompromised girls with a multi-dose schedule). Importantly, the EPI programme should work with other national decision-making and regulatory authorities to consider what the implications are for off-label HPV vaccine usage, including lessons learned from previous off-label vaccine use in the country (if any).
Figure 3: Decision-making considerations for HPV schedule optimization

Many of these discussions will be context-specific, and even countries with similar programmes or data could choose to switch or introduce a single-dose or continue with a multi-dose schedule for a multitude of reasons. For example, a country with an existing high 2-dose HPV vaccination coverage could choose to switch to a single-dose schedule to save resources and, based on country capacity, to conduct a catch-up campaign for a second dose if the data suggests that a booster dose is needed in the future. Similarly, a programme with existing high 2-dose HPV vaccination coverage could choose not to switch to a single-dose schedule because the country resources are not constrained and the switch is perceived as an unnecessary risk to the programme, or because HPV vaccine touchpoints are used to deliver other adolescent interventions (Table 2).
Table 2: Context specific examples of programme considerations for HPV vaccine schedule optimization based on the HPV programme characteristics (HPV1 coverage, HPV2 coverage, high risk communities)

<table>
<thead>
<tr>
<th>Existing HPV programme characteristics (HPV1 and HPV2 coverage, high-risk communities)</th>
<th>Programme decision</th>
</tr>
</thead>
</table>
| High HPV1 
High HPV2 | Need to save and repurpose resources (e.g., for other programmes) 
High programme capacity for catch-up if later needed |
| High HPV1 
Low HPV2 | Need to save and repurpose resources (e.g., to sustain high HPV1 coverage, catch-up missed girls, and reach multi age cohorts) |
| Low HPV 1 
Low HPV2 | Need to save and repurpose resources to increase HPV1 coverage |
| High risk geographies or groups | Need to save and repurpose resources for HPV1 demand creation and delivery for hard-to-reach geographies or groups |

Examples of programme considerations

- High barriers to successfully communicating schedule change
- High perceived barriers if catch-up campaign later needed e.g., poor vaccination documentation or hard to reach older women
- Maintaining high trust in the programme is critical to maintain high HPV1 coverage — country prefers to collect local data on acceptability before switching. In the interim country can reduce HPV2 delivery and catch-up efforts with no official schedule change
- Maintaining a multi-dose schedule ensures that the target groups have multiple opportunities for vaccination
- In countries with high proportions of undiagnosed persons living with HIV, a schedule switch can equate to more risk for vulnerable individuals. Ensuring multi-dose schedule for high-risk groups may be more challenging in context of a national single dose schedule

Schedule switch to single dose

No schedule switch (or later switch)
Key planning and implementation considerations for HPV vaccine schedule optimization

Countries should develop a comprehensive implementation plan with timelines to ensure that all aspects and implications of a single-dose introduction or schedule change are accounted for (Figure 4). Several considerations in planning, such as how trust in the programme will be maintained, the way stakeholders will be engaged, and how high coverage with a single-dose strategy will be achieved are critical for the sustained success of the HPV programme (Box 1).

Box 1: Key planning questions for countries considering HPV vaccine schedule optimization

- How might trust in your existing HPV programme change (e.g., among providers and clients)?
- How can confidence and programme resiliency be maintained?
- How can you ensure that important stakeholders (e.g., professional gynecologists and oncologist associations) support the change and understand the scientific basis?
- How will you engage key stakeholders, such as teachers, parents, and girls to successfully communicate the programme change?
- Additional outreach visits to administer the second dose may also represent an opportunity to catch girls who missed the first HPV vaccine dose (e.g., with a 6-month outreach schedule). How will high coverage be achieved and maintained with a single-dose strategy? What additional strategies and mechanisms to catch up those who did not receive the single-dose at the routine age should be created?
- What is the national and subnational HIV prevalence among girls aged 9 to 14 years? How can high coverage with a multi-dose schedule continue to be ensured for certain high-risk groups (e.g., HIV-infected girls)?
- What will be the initial cost of change to the programme? Consider expenses for training and sensitization of healthcare workers, updates to policy and schedule, guidance documents and advocacy materials, logistics management systems, and vaccination recording and reporting tools. How will these costs be funded? If relevant, how could Gavi funding (e.g., a switch grant) be used to cover such costs?
- What will be the country’s contingency plan in the case that future evidence would suggest the 2-dose schedule would offer better protection?
The country should consider the budgetary impact of the schedule switch or the choice of a single-dose schedule on the national budget and affordability in relation to any short- or long-term complementary funding that might be available from donors. This should include the operational costs—both the short-term costs of the introduction and longer-term recurrent costs. An HPV vaccine schedule switch to a single-dose schedule will have cost-savings for supplies, outreach and catch-up for the second dose, distribution systems, and waste management. However, there will be additional costs associated with the switch or introduction of a single-dose schedule (e.g., re-training activities for health care workers and possibly teachers, re-training materials, the redesign, print, and dissemination of new guidelines, paper and electronic recording and reporting forms and tools, conducting readiness assessments, supportive supervision, data quality monitoring and/or post-switch evaluation activities). Additionally, there may be other increases in costs, such as catch-up for the first dose and supplementary activities for social mobilization, community education, and communications. An example of the budget impact considerations is provided in Table 3.
Table 3: Budget impact considerations for switching to a single-dose HPV vaccine schedule

<table>
<thead>
<tr>
<th>Cost domain</th>
<th>Switch cost savings</th>
<th>Switch cost incurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Supplies</td>
<td>Vaccines, syringes, safety boxes</td>
<td>Vaccine wastage rate (e.g., if vials discarded due to expiry)</td>
</tr>
<tr>
<td></td>
<td>Vaccine wastage rate (e.g., increased size of vaccination sessions)</td>
<td></td>
</tr>
<tr>
<td>2. Personnel and vaccine delivery</td>
<td>Monitoring for 2nd dose</td>
<td>Re-training activities</td>
</tr>
<tr>
<td></td>
<td>Outreach for 2nd dose</td>
<td>Re-training materials</td>
</tr>
<tr>
<td></td>
<td>Catch-up for 2nd dose</td>
<td>Increased catch-up for first dose</td>
</tr>
<tr>
<td></td>
<td>Different delivery strategy</td>
<td>Different delivery strategy</td>
</tr>
<tr>
<td>3. Distribution system</td>
<td>Transportation of vaccines, cold storage,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>storage and transportation of supplies</td>
<td></td>
</tr>
<tr>
<td>4. Waste management</td>
<td>Incinerator fuel, salaries of staff, transport</td>
<td></td>
</tr>
<tr>
<td></td>
<td>if incinerator not at vaccination site</td>
<td></td>
</tr>
<tr>
<td>5. Guidance, data and monitoring</td>
<td>Redesign, print and disseminate new guidelines, recording and reporting forms and tools (paper and electronic)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Readiness assessment, supportive supervision,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>data monitoring and post-switch evaluation</td>
<td></td>
</tr>
<tr>
<td>6. Other costs</td>
<td>Social mobilization for 2nd dose</td>
<td>Community education and communications</td>
</tr>
<tr>
<td></td>
<td>Revised crisis communication plan</td>
<td>Revised crisis communication plan</td>
</tr>
<tr>
<td></td>
<td>Programme assessments and strengthening</td>
<td></td>
</tr>
</tbody>
</table>

Many of the activities carried out to prepare, implement, and monitor a single-dose HPV vaccine introduction or schedule switch may also present opportunities to improve the immunization programme as a whole and the overall health system. A country could choose to conduct a situation analysis of the immunization programme to identify weaker areas that could be strengthened before/during the introduction/switch. These could include strengthening the monitoring and evaluation of immunization and HPV programme performance, including recording practices for vaccination data, immunization coverage data quality, the use of a disease surveillance/registry, or improving communication strategies and the crisis communication plan. If the country is also planning the introduction or switch of another vaccine, combining the preparatory activities and budgets for both activities is recommended. A comprehensive example of planning and implementation considerations of a 2-dose compared to a single-dose schedule is provided in Appendix 4.

Once the introduction or switch is implemented, regular monitoring of the progress or barriers to reaching the HPV programme objectives, targets, and goals by EPI should continue; as well as documentation of lessons learned.
Appendix 1: Resources available to support evidence-based decision-making for HPV vaccine schedule optimization

Epidemiology, burden, and coverage

- WHO HPV vaccine introduction and coverage monitoring dashboard

Compiled scientific evidence on single-dose immunogenicity and efficacy

- PATH Single-Dose HPV Vaccine Evaluation Consortium. Current state of evidence on single-dose HPV vaccination and its implications for policy April 6, 2022 SingleDoseHPV_Statement_April2022_final.pdf (path.org)

Policy documents

- SAGE April 2022 recommendations on HPV vaccines
- World Health Organization Human papillomavirus vaccines:
  - WHO position paper (December 2022) Human papillomavirus (HPV) (who.int)
  - Table: GRADE evidence profile for single-dose HPV vaccine compared with no vaccine for HPV infection
  - Table: Effectiveness and immunogenicity of 1-dose of HPV vaccine compared with 2-doses
  - Powerpoint: HPV vaccine session introduction and key questions, April 2022
  - Cochrane review report: Efficacy, effectiveness, and immunogenicity of one dose of HPV vaccine

Introduction guidance

- World Health Organization Guide to introducing HPV vaccine into national immunization programmes (who.int)

HPV vaccine product information

- World Health Organization Prequalified vaccines Prequalified vaccines | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)
- Product information for vaccines and cold chain equipment Gavi detailed product profiles

Off-label vaccine use

**Information leaflets about off-label vaccine use for parents and healthcare professionals**

**Evidence from modeling studies for decision-making**


### Appendix 2: Summary of trials with data on single-dose vaccination

<table>
<thead>
<tr>
<th>Trial/Country</th>
<th>Vaccine</th>
<th>Sex</th>
<th>Age Group (yrs)</th>
<th>Description</th>
<th>Evidence</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVT&lt;sup&gt;2&lt;/sup&gt; Costa Rica</td>
<td>2vHPV</td>
<td>Females 18–25</td>
<td>Post hoc analyses: participants randomized to 3 doses or control, but analyzed as 1-, 2-, 3-dose groups.</td>
<td>Efficacy/Immunogenicity</td>
<td>• Protection after 2, 2, or 3 doses of 2vHPV through 11 years - persistent HPV 16/18 infection among single-dose recipients was 1.8% (95% confidence interval (CI) [0.3–5.8], n=212) compared to 1.6% (95% CI [0.1–7.7], n=62) among 2-dose recipients and 2% (95% CI [1.3–2.8], n=1,365) among 3-dose recipients. Vaccine efficacy (VE) was 82.1%, 83.8%, and 80% among recipients of 1, 2, and 3 doses, respectively.</td>
<td></td>
</tr>
<tr>
<td>India IARC&lt;sup&gt;3,4&lt;/sup&gt; India</td>
<td>4vHPV</td>
<td>Females 10–18</td>
<td>Post hoc analyses: Participants were randomized to 2 or 3 doses, but randomization was lost and data was analyzed as 1-, 2-, 3-dose groups</td>
<td>Efficacy/Immunogenicity</td>
<td>• Protection after 2, 2, or 3 doses of 4vHPV through 10 years - persistent HPV 16/18 infection among single-dose recipients was 0% (95% CI [0–0.3]; n=2454) compared to 0.1% (95% CI [0–0.4]; n=1,685) among 2-dose recipients and 0.1% (0–0.4; n=) among 3-dose recipients. Vaccine efficacy was 94, 74%, and 92% among recipients of 1, 2, and 3 doses, respectively as compared to the control group.</td>
<td></td>
</tr>
<tr>
<td>KEN SHE&lt;sup&gt;5,6&lt;/sup&gt; Kenya</td>
<td>2vHPV</td>
<td>Females 15–20</td>
<td>RCT: 1 dose of 2vHPV, and gP pepV, vs 0 dose (Meningococcal A vaccine group)</td>
<td>Efficacy</td>
<td>• Single-dose HPV vaccination was highly efficacious (&gt;95%) over three years; 9vHPV vaccine efficacy (VE) was 98.8% (95% CI [91.3–99.8], p=&lt;0.0001); bivalent VE was 97.5% (95% CI [90.0–99.4], p=&lt;0.0001).</td>
<td></td>
</tr>
<tr>
<td>DoRIS&lt;sup&gt;7&lt;/sup&gt; Tanzania</td>
<td>2vHPV</td>
<td>Females 9–14</td>
<td>RCT: 1-, 2-, 3-dose groups (Bridging --&gt; KEN SHE --&gt; CVT --&gt; India IARC)</td>
<td>Immunogenicity</td>
<td>• Immunogenicity: Seropositivity &gt;97.5% for all dose groups for both vaccines • Antibody levels by dose, vaccine, and kinetics over time were similar to those in other HPV vaccine studies.</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- Unvaccinated women had no HPV16/18 infections.
- Ten years after vaccination, the antibody levels were at least two times higher in single-dose group.
- Protection after 1, 2, or 3 doses of 9vHPV (VE) was 98.8% (95% CI 91.3–99.8, p=<0.0001).
- Protection after 1, 2, or 3 doses of 2vHPV (VE) was 94.1%, 74%, and 92% among recipients of 1, 2, and 3 doses, respectively.
- Ten years after vaccination, the antibody levels were at least two times higher in single-dose recipients compared to those following natural infection.
- No HPV16/18-related CIN2/3 was detected in vaccinated women.
- Two Kenyan women aged 15–20 years; 15 lifetime partners; HIV-negative; HPV 16/18 HPV DNA-negative (external genital and cervical swabs) at enrollment and month 3 (self-collected vaginal swab), and HPV antibody negative at enrollment.

**Version 2.1, June 2023**
Immunobridging showed that 1-dose responses were non-inferior in DoRIS compared with those in studies where 1-dose efficacy was observed (CVT, India IARC).


5. Burrin A, Raimondo A, Siemiatycki J, et al. Immunobridging showed that 1-dose responses were non-inferior in DoRIS compared with those in studies where 1-dose efficacy was observed (CVT, India IARC).

Appendix 3: Additional evidence on single-dose HPV vaccination and timeline to expected results (year)

<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>Study / site</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact of 1 dose in HIV+ girls</td>
<td>HOPE, South Africa, (Impact study, n=small)</td>
<td>2023</td>
</tr>
<tr>
<td>1-dose immunogenicity &amp; efficacy</td>
<td>CVT, Costa Rica, (Post RCT)</td>
<td>2023, 2026</td>
</tr>
<tr>
<td>14, 16 and 20-year data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-dose VE against CIN (&gt; 10 year)</td>
<td>INDIA – IARC (Post RCT)</td>
<td>2024</td>
</tr>
<tr>
<td>1 vs 2 dose non-inferiority VE against</td>
<td>ESCUDO (RCT)</td>
<td>2024/2025</td>
</tr>
<tr>
<td>HPV infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-dose data in younger children (4-8yr)</td>
<td>HANDS, Gambia (RCT)</td>
<td>2025</td>
</tr>
</tbody>
</table>

VERSION 2.1., JUNE 2023
Appendix 4. Comparison table of planning and implementation considerations for a 2-dose schedule compared to a single-dose routine HPV vaccination schedule

<table>
<thead>
<tr>
<th>Programme area</th>
<th>2-dose routine schedule</th>
<th>Considerations</th>
<th>Single-dose routine schedule</th>
</tr>
</thead>
</table>
| Vaccine supply and procurement, logistics management information system (LMIS) | Advantages:  
- Country could choose from a wider selection of HPV vaccines.  
- Forecasting the supply needs for a 2-dose schedule has been done before.  
- Countries may still choose to implement a multi-age cohort (MAC) approach or campaign for catch-up of missed cohorts without significant new changes to the routine programme and planning.  

Challenges:  
- If the country would like to implement additional catch-up activities (e.g., MAC) the HPV vaccine supply forecast, costing, and request will need to be updated.  | Advantages:  
- Countries will need to purchase fewer doses for routine delivery (cost-saving)  
- Other programme savings might include reduced supplies (e.g., injection materials, safety boxes, cold chain requirements), and reduced logistics and logistics management costs.  
- May help to alleviate vaccine supply and delivery challenges at the subnational levels.  
- May help to reduce risk and negate disruption to the national HPV programme when the global vaccine supply is challenged.  

Challenges:  
- The country will need to create new estimates for the required vaccine doses, but this could be combined with calculations and planning for catch-up activities of recent unimmunized or under-immunized cohorts.  
- The country should choose a vaccine for which evidence to support the single-dose schedule is available; alas, there will be fewer vaccines with this data initially. |
| Target population and catch-up of un- or under-immunized girls or cohorts | Advantages:  
- The country could choose to maintain a 2-dose routine schedule for the target population if the existing programme is trusted and successful. Resources could still be saved by reducing catch-up activities for the second dose. Single-dose MAC could still be an option for catch-up as it is done with other antigens. This could simplify the change in messaging.  

Challenges:  
- At an additional cost, the country could still choose to do a catch-up MAC for the target population +/- extended age range for missed cohorts. However, resources may be more limited for successfully reaching girls outside of the routine 2-dose delivery.  | Advantages:  
- Countries could choose to offer single-dose HPV vaccination at routine age (e.g., 10-year-old girls) in combination with vaccination opportunities for girls up to 14 years of age who previously missed vaccination.  
- Cost-savings resulting from a single-dose vaccine schedule for the target population could be used to fund a single-dose MAC campaign for girls in an extended age range (e.g., girls aged 9–18 years. This may be supported by Gavi if the country was eligible for MAC at the time of the previous introduction.  
- If the single-dose HPV vaccine schedule option is used globally, the HPV vaccine supply challenges are likely to improve, and the vaccine is likely to reach more of the primary and secondary target populations.  

Challenges:  
- Ensuring that all key stakeholders, including the caregiver and target populations, accept programme change and demand HPV vaccination.  |
| Guidelines, materials, and tools* | Advantages:  
- If no schedule change, no change may be needed in guidelines and tools.  | Advantages:  
- Represents an opportunity to update and improve guidance documents and tools if needed—perhaps, with partner support on request. |
- Any potential changes to these tools and forms could result in more data errors. Vaccinators should be aware of the existing data recording/reporting tools to capture the first dose (HPV1) and second dose (HPV2) coverage.
- There is also the option to revise tools and materials to remove the second dose catch-up activities/recording/reporting, even if the country has a 2-dose routine schedule (e.g., the text could read that each girl requires “at least 1 dose”).

Challenges:
- Ongoing difficulties with correct recording, reporting, and monitoring HPV1/HPV2 doses
- Guidelines would need to be updated in any case to reflect, for example, the change to:
  - eligible age group in case of extended age catch-up activities; or,
  - an optional second dose in the routine schedule

Advantages:
- Less risk to the HPV vaccination programme: Established programmes may choose to continue with the existing 2-dose schedules and strategies that have already been shown to be effective in their context. Countries using a 6-month interval between HPV1 and HPV2 could first consider a change to annual vaccination to prepare for a future change to a single-dose schedule, rather than choosing to switch at the earliest opportunity.
- HPV2 activities may continue to serve as an additional vaccination opportunity for girls who missed HPV1 (compared to a single-dose programme with a reduced number of HPV vaccination sessions).
- Outreach activities and mop-up will likely be required regardless of schedule, even for a single-dose schedule.

Challenges:
- Continuing with more complicated and costly vaccine delivery and catch-up strategies compared to the single-dose schedule option.
- Diverts potentially limited resources from HPV1 to HPV2.

Advantages:
- Single-dose HPV programmes are likely to be simpler to deliver and could accomplish a higher coverage as compared to multi-dose strategies.
- The programme can have more opportunities for reaching high HPV1 coverage if the same number of vaccination sessions is maintained.
- There will be less complicated organization and logistics planning between the health and education sectors.
- Some other established health intervention delivery strategies can now fully meet HPV vaccine schedule needs (e.g., child health days/weeks).
- Campaign-style delivery could be used with new vaccination sites in the community.
- The country could leverage the HPV vaccine introduction or schedule switch to a single-dose to provide catch-up opportunities for an extended age range, do vaccine co-introductions, or initiate other adolescent health interventions.
- School outreach and mop-up might be done with less frequency for a single-dose schedule (likely cost-saving).
- Cost-savings could lead to increase resource investment in other programme areas, such as creating demand and attaining high coverage in unimmunized and under-immunized groups (e.g., out-of-school girls).
- Country has an opportunity to incorporate lessons learnt from other programmes that have successfully achieved and sustained high coverage with other single-dose schedule antigens or single-visit health interventions.
- The need to track individual girls for both doses will be decreased.

*National immunization policy; Immunization Handbook, home-based records, recording and reporting tools; Guidebook and job aids for health workers; Data recording and programme monitoring forms (tally sheets, monthly reporting forms, vaccination cards, stock registers); Health information systems (DHIS2)
### Integration

**Advantages:**
- The multi-dose regimen is already established and accepted in many countries globally. If the HPV delivery platform is deemed reliable and trusted, it could already be successfully used for other adolescent health interventions or vaccinations.

**Challenges:**
- Integration or co-administration of HPV with other interventions carries risk if the second intervention is poorly perceived (or becomes poorly perceived) by the target population.

**Advantages:**
- When the HPV vaccine is given as a single-dose vaccination, there will be new opportunities to integrate better or more easily with other “one time” adolescent immunizations (e.g., tetanus/diphtheria vaccine booster doses, vaccination screening, and catch-up doses with other antigens), or health interventions (e.g., deworming, distribution of hygiene kits, distribution of long-lasting insecticidal nets, family planning services, HIV screenings, health education, and counselling).
- Single-dose schedule for HPV vaccination may also be a more appealing integration option for other programmes because of fewer follow-up and monitoring requirements.
- There will be opportunities to establish or strengthen the platform for adolescent health for integrated interventions.
- Merging training, planning, or monitoring activities for HPV vaccine introduction or schedule switch with other interventions will be possible, especially if the country could introduce or switch multiple antigens at the same time.

**Challenges:**
- Introductions or changes to an existing program may need to be successfully established before integration opportunities can be fully leveraged and maximized.
- Integration or co-administration of HPV with other interventions carries risk if the second intervention is poorly perceived (or becomes poorly perceived) by the target population.

### Training for health workers

**Advantages:**
- Training of appropriate staff at all levels of the health and education sectors can be an expensive and time-consuming activity; if there are no or minor changes to the programme, these changes could be communicated without any comprehensive retraining.

**Challenges:**
- Missed opportunity for retraining and strengthening staff engaged with HPV vaccine service delivery.

**Advantages:**
- Training and content of training materials for single-dose vaccination schedules are simpler than those required by multi-dose vaccinations.
- If a country is eligible, Gavi switch grants can provide the opportunity to refresh training on HPV.

**Challenges:**
- Programme change may be difficult to communicate and manage.
- Refresher training would be needed for any schedule change. However, brief +/- inexpensive modalities to conduct these refreshers could be explored (e.g., 1–2 hour briefing during an existing EPI meeting). Experience with the use of online platforms during the pandemic could be one model to consider for reducing refresher training costs.
| Sensitization for school leaders and teachers | **Advantages:** |
| - If the programme achieves high coverage and the changes to the programme are none or only minor, there will be no need for major change to messages, materials, or activities for sensitization. |
| **Challenges:** |
| - Missed opportunity for retraining and strengthening staff engaged in communication about HPV with other key stakeholders (e.g., parents, caregivers, adolescents). |
| Sensitization for other leaders at national, provincial, and community levels | **Advantages:** |
| - If the programme achieves high coverage and the changes to the programme are none or only minor, no major change to the messages, materials, or activities for sensitization will be necessary. |
| **Challenges:** |
| - Missed opportunity for retraining and strengthening the knowledge of leaders engaged in communication about HPV with key stakeholders. |

- **Advantages:** |
- Training would need to include new operational considerations, cold chain requirements, storage space calculations, micro-planning review, reporting, identifying missed children, etc.
- **Advantages:** |
- Training and the content of sensitization activities and materials for single-dose vaccination schedules is simpler than those for multi-dose vaccinations.
- The message of “just a single-dose at any time between the ages of 9 and 14 years” could be an easier one to both understand and reinforce within the school system and for adolescents.
- The country will still need to sensitize again in the future, but it is likely that the energy required to do this then will be to a lesser extent if suitable network of sensitized staff is developed and the supporting resources are available.
- If a country is eligible, Gavi switch grants can provide the opportunity to refresh sensitization activities on HPV.

**Challenges:** |
- Programme change may be difficult to communicate and manage.
- It is likely that IEC materials may need to be re-developed, re-printed, and re-distributed, resulting in additional financial costs (printing, supplies, distribution), as well as human resources (time, opportunity cost). Existing stock may go to waste.
| Communicating with parents, caregivers, and girls | Advantages: | - Easier to continue with current messaging and re-enforce existing programme. | Advantages: | - Single-dose schedule may be innately more appealing to caregivers/target population, because of convenience, less time, discomfort, and perceived risk of vaccination. |
| | Challenges: | - If other communities, such as neighboring countries switch to a single-dose schedule, parents or caregivers may be concerned about the need for a multi-dose schedule. | Challenges: | - Change to the existing schedule has the potential to create mistrust in the vaccination programme, including the generation of rumors, conspiracy theories, etc. - Changes in the parent/caregiver attitude towards HPV vaccination may also impact vaccination with other antigens. - Single-dose schedule may be perceived to be less effective. - If a country is eligible, Gavi switch grants can provide the opportunity to refresh communication activities on HPV. |

| Vaccine storage (cold chain), logistics (stock management), and distribution | Advantages: | - Existing competent systems for cold chain and ongoing monitoring of vaccine supply and distribution between levels in the health system could be maintained without an increased investment of resources. | Advantages: | - Theoretically, the vaccine cold chain storage needs for a single-dose strategy will be reduced by 50% (for the target population only). - There could be potentially easier vaccine distribution logistics from the national/regional/district level to facilities when fewer doses are delivered less frequently. - It may also be easier to coordinate the distribution of the HPV vaccine together with other vaccine supplies. - It may help to reduce risk and negate disruption to the HPV programme when subnational supply is challenged. |
| | Challenges: | - Regardless of the number of doses in the routine schedule, countries may need a time-limited increase in cold chain and logistics requirements, if they choose to do MAC. | Challenges: | - Retraining may be required. - Changes to existing systems may lead to an initial period with higher errors in vaccine management and reporting. |

| Human resources | Advantages: | - Communicating schedule change may be complex and time-consuming—especially if a significant emphasis on the importance of the second dose has historically been communicated to key stakeholders, caregivers, and the target population. | Advantages: | - Single-dose strategy could help reduce health worker workload and staffing challenges exacerbated by the COVID-19 pandemic, especially for outreach activities. |
| | Challenges: | - Asking staff to continue delivering more complicated and costly vaccine delivery and catch-up strategies compared to the single-dose schedule option might be challenging. - Staff may still need to communicate other changes to the HPV programme, such as extended target age range only. | Challenges: | - There would be increased initial demand on health workers for training, comprehension, and proper utilization of new materials and tools. This would need to be timed carefully in consideration of other competing priorities within the EPI programme. |
### Funding and financing

**Advantages:**
- Costs to maintain the existing HPV programme are already understood; there will be no change to the routine HPV delivery cost.

**Challenges:**
- Missed opportunity to reduce programme costs
- Opportunity cost—savings on resources could be re-purposed.
- Difficulty in achieving high HPV vaccination coverage with a sustainable affordable delivery model
- Additional costs of MAC must be considered.
- Some funding models may incentivize introduction or switch to a single-dose schedule; hence, there may be missed funding opportunities.

**Advantages:**
- There is an opportunity for cost-savings (e.g., cost of the vaccine, community outreach, school outreach, and catch-up activities).
- Better resource allocation within the HPV vaccination programme or broader cervical cancer elimination strategy could be possible, such as a second-dose vaccine. Programme costs could be more effectively allocated to other HPV programme areas, such as risk communication and community engagement, or strategies to reach unreached groups.
- Currently, there is an opportunity for Gavi-eligible countries to receive funding for the schedule switch.

**Challenges:**
- Ensuring high sustained HPV1 vaccination coverage with a new delivery model.

### Monitoring and evaluation:

**Advantages:**
- No anticipated routine change is required.

**Challenges:**
- MAC might need additional monitoring in line with any other intensified routine vaccination or campaign activities.
- Monitoring and reporting needs for HPV2.

**Advantages:**
- Easier monitoring and evaluation using a single-dose approach.
- Opportunity to invest resources in monitoring and evaluation.

**Challenges:**
- Increased initial cost for adequate supervision, monitoring, and evaluation after programme change.

### Timeline:

**Advantages:**
- If the multidose schedule is maintained, then the timeline for programme improvement activities could be paced as planned.

**Challenges:**
- Less opportunity to leverage and move forward with the current renewed focus and energy being invested by global partners and institutions in HPV.

**Advantages:**
- Opportunity to leverage and move forward with the current renewed focus and energy being invested by global partners and institutions in HPV and cervical cancer elimination efforts.

**Challenges:**
- Timeline needs to be carefully planned and adhered to ensure a successful introduction or switch.
- Shifting to a single-dose schedule would require additional planning and time to ensure all the programme areas above are adequately prepared for this change. This is especially true for health worker materials and tools, communication messages or materials, and vaccine stocks that need to be estimated and made available at the community level.

### Ethical:

**Advantages:**
- The programme has offered a 2-dose schedule, and a country may feel that this agreement with key stakeholders should not be rescinded, especially for those who have already received HPV1.

**Challenges:**

**Advantages:**
- Single-dose strategies can reach all girls, including the most vulnerable groups, more successfully than multi-dose strategies.
- Single-dose vaccination could enable girls to continue getting vaccinated if there is a change in the country context (e.g., weakened health and immunization systems in fragile and conflict settings).
| - There are fewer studies supporting the use of a single-dose schedule compared to a multi-dose schedule. However, given the existing evidence, the use of a 2-dose schedule may be a less equitable option if fewer girls have access to it. |
| Challenges: |
| - Resistance to consider new schedules or innovations. |
| - The evidence to support long-term protection after single-dose HPV vaccination is for a shorter follow-up period than that of a multi-dose schedule. |