# HUMAN PAPILLOMAVIRUS VACCINE

## Lessons Learned from the 2014 Gavi Full Country Evaluations

This brief presents lessons learned from human papillomavirus (HPV) vaccine demonstration in Mozambique and preparation for HPV national introduction in Uganda during the 2014 period of the Gavi Full Country Evaluations (FCE). It was prepared by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington in collaboration with members of the Gavi Full Country Evaluations Team: University of Eduardo Mondlane (UEM), Mozambique; Health Alliance International (HAI), Mozambique; the Infectious Diseases Research Collaboration (IDRC), Uganda; International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b); the University of Zambia (UNZA), Zambia; and Program for Appropriate Technology in Health (PATH), USA. This work is intended to inform evidence-based improvements for HPV vaccine introduction in FCE countries, and more broadly, in all countries seeking Gavi support for HPV introduction. This report is derived from the full 2014 Annual Dissemination Report. The contents of this publication may not be reproduced in whole or in part without permission from the Gavi Full Country Evaluations Team.

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# The Gavi Full Country Evaluations

## Background

The Gavi Full Country Evaluations (FCE) are prospective studies covering the period from 2013 to 2016. They aim to understand and quantify the barriers to and drivers of immunization program improvement, with an emphasis on the contribution of Gavi, the Vaccine Alliance in four countries: Bangladesh, Mozambique, Uganda, and Zambia. The evaluation is funded by Gavi, the Vaccine Alliance.

## Gavi Full Country Evaluation Team

The evaluations are carried out by a team of institutional partners led by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington, in partnership with PATH in the United States; the International Centre for Diarrhoeal Disease Research in Bangladesh (icddr,b); the University of Eduardo Mondlane (UEM) in Mozambique; Health Alliance International (HAI) in Mozambique; the Infectious Diseases Research Collaboration (IDRC) in Uganda; and the University of Zambia (UNZA).

## Method of evaluation

The FCE use a mixed-method approach, covering the full results framework from inputs to impact. The evaluations cover all phases of Gavi support, from the decision to apply, application, and approval, to preparation and implementation, and each of the relevant streams of support in the Gavi FCE countries.

## Gavi support for human papillomavirus vaccine

Two human papillomavirus (HPV) vaccines are licensed in many Gavi-eligible countries: Cervarix and Gardasil. Both vaccines require that at least two doses be given over a six-month period to females between the ages of 9 and 13. Because countries' Expanded Programs for Immunization (EPI) generally target children under the age of 5, they are required to work with a broader set of stakeholders in the areas of education, non-communicable diseases, and women's, adolescent, and child health to target this age group.

To respond to this challenge, Gavi and its partners provide support for HPV vaccine demonstration projects to provide an opportunity for countries to learn and develop an optimal way to deliver the vaccine to girls in the target age cohort. There are two pathways for countries interested in introducing the HPV vaccine to their routine EPI with Gavi support:

- Eligible countries with demonstrated experience in reaching adolescent girls with HPV vaccines can apply for Gavi-supported national introduction.
- Countries lacking experience can apply for support to conduct a smaller-scale demonstration project to gain the experience necessary to apply for national rollout.

## Evaluation of HPV vaccine programs

The FCE are conducting a process evaluation of Gavi's HPV vaccine support by identifying key successes and challenges that affect application for and implementation of Gavi support in the four FCE countries and by positing and investigating root causes. The FCE are evaluating the process of applying for and implementing Gavi HPV support for demonstration projects in Mozambique and Bangladesh and, in Uganda, a national introduction. During the 2014 evaluation period, FCE countries were in varied stages of implementation:

- Mozambique completed the first year of its demonstration project.
- Uganda had previously conducted a demonstration project and was preparing to nationally introduce HPV vaccine in 2015 with Gavi support.
- Bangladesh applied for a demonstration project in September 2014 and selected its demonstration site for 2015 implementation.

# KEY FINDINGS

**There is a lack of clarity about the primary objective and way to implement HPV vaccine demonstration projects as a mechanism for learning and guiding national HPV vaccine introduction. Part of the confusion about the demonstration project's objectives may stem from a degree of misalignment between the demonstration project's learning objective and the requirement for countries to have a demonstrated ability in order to qualify for support for national introduction.**

The HPV vaccine demonstration projects are designed to serve as mechanisms for learning about the coverage, feasibility, acceptability, and cost of vaccine delivery strategies, in order to guide the design of the vaccine delivery strategy eventually implemented in national HPV vaccine introduction (Box 1). Through demonstration projects, countries should adapt and/or develop tools like monitoring systems, training materials, and social mobilization strategies for use in a national introduction. This learning objective suffers from a degree of misalignment with the national HPV vaccine introduction application policy that requires evidence of demonstrated ability to deliver the vaccine to the target cohort (Box 2). Specifically, the incentive to reach the demonstrated ability target may lead to demonstration projects that are designed, both in terms of site selection and implementation process, more to reach the target than to maximize the learning experience for national introduction.

This brief will explore these findings by highlighting data and observations from Mozambique and Uganda.

**Box 1:** Gavi-stated objective of demonstration

> "The primary objective of the HPV vaccination demonstration programme is to allow countries to learn by doing."
>
> ~ HPV demonstration project application guidelines

**Box 2:** Gavi-stated introduction requirement

> "To apply for nationwide introduction of HPV vaccines through Gavi, the country must…have demonstrated ability to deliver a complete multi-dose series of vaccines to at least 50% of a one-year cohort…using strategies similar to those proposed for national HPV vaccine delivery."
>
> ~ National HPV introduction application guidelines

## Mozambique

### An example of this misalignment was the selection of demonstration sites in Mozambique.

The government of Mozambique initially applied for support to implement the demonstration in three districts (Manhiça, Manica, and Mocímboa da Praia) to maximize nationally representative learning for introduction (Figure 1). This proposal was not approved by Gavi. Driven by convenience and all-but-explicit encouragement from Gavi Secretariat,

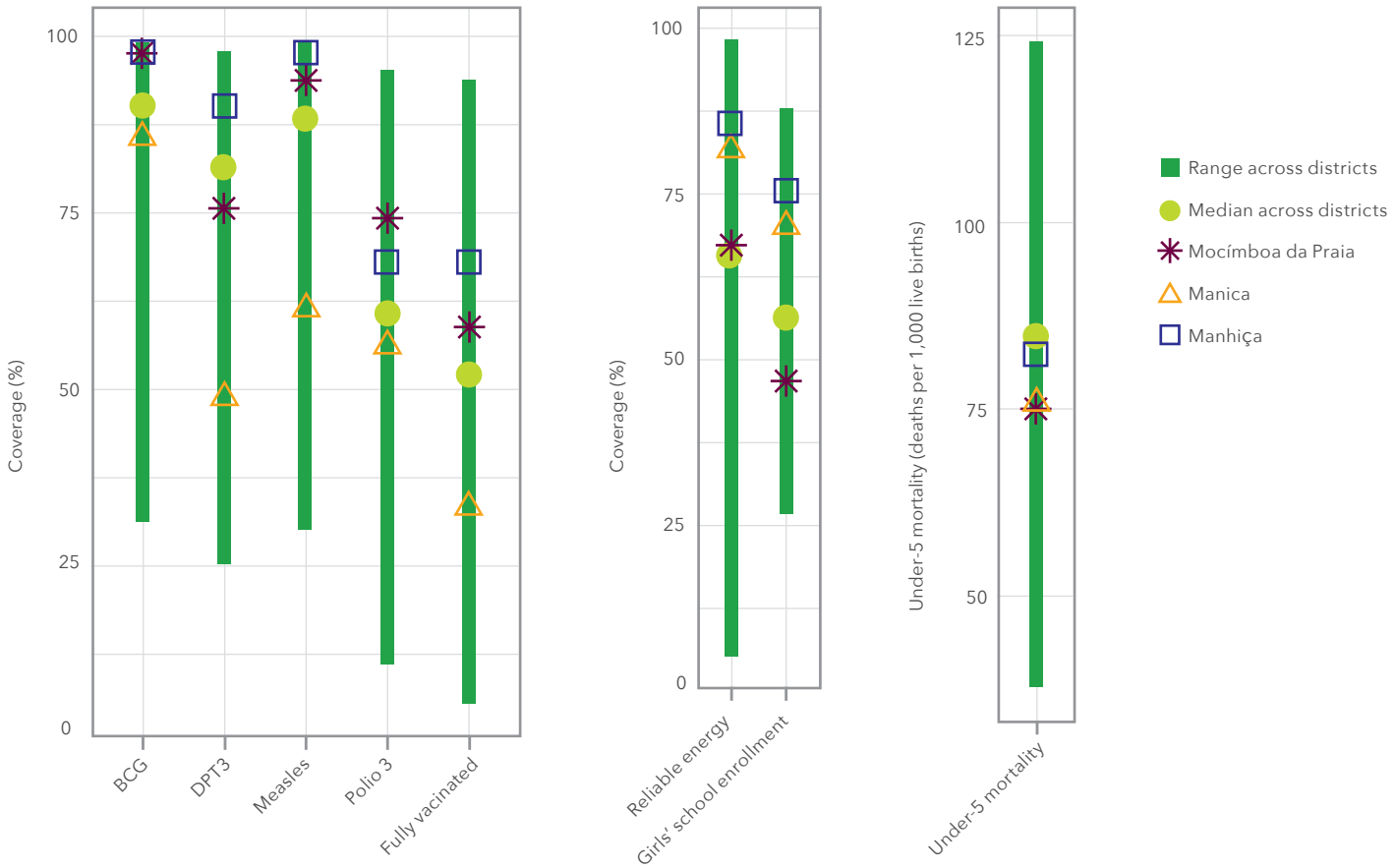
> "The government wanted to expand to various districts but Gavi was concerned that if they didn't run a good quality demo project it would affect their ability to apply for a national program."
>
> ~ Global-level key informant

Manhiça was selected as the sole demonstration district in Mozambique's second application for HPV vaccine demonstration support.

Manhiça is an atypical district socioeconomically and in terms of partner support (Figure 1). This district is located near the capital city, has access to high-quality technical assistance from Manhiça Health Research Centre (CISM), and has a population familiar with participation in health research as part of a Demographic Surveillance Site (DSS).

Ultimately, the government decided to fund additional demonstration sites in Manica and Mocímboa da Praia to broaden the learning opportunities beyond the Gavi-funded Manhiça district. The government of Mozambique's later decision to include and independently fund two additional HPV vaccine demonstration districts will likely lead to a broader set of lessons learned which will be more applicable and which will result in tools and plans that are better adapted for national introduction. This decision is better aligned with the stated learning objective of Gavi's HPV vaccine demonstration support.

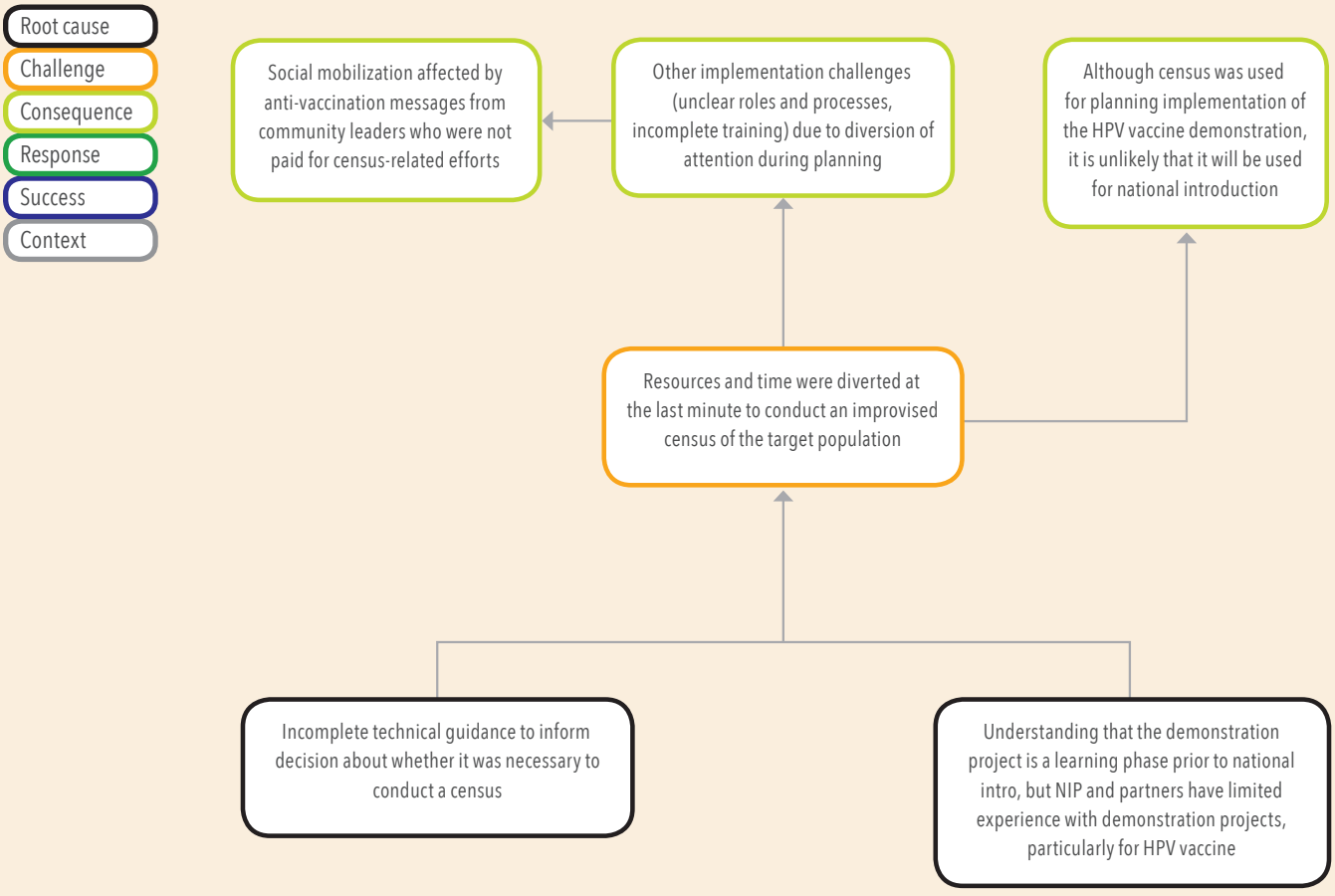
**Figure 1:** Comparison of various characteristics among HPV demonstration districts in Mozambique



**Mozambique's implementation of an improvised census of the target cohort for the demonstration project illustrates insufficient technical guidance and underutilized technical assistance for HPV vaccine demonstration projects.**

As part of the demonstration project, the country decided to conduct a census of the target cohort to have a more accurate estimate of the number of girls to be immunized. However, as it was not included in the original implementation plan and was largely unfunded, the methods to do so were improvised. After a substantial amount of effort, the improvised census was abandoned because the quality of data was low and the implementation of a census for national introduction was infeasible. The resources required to conduct the census diverted critical attention from other preparatory activities, affecting the quality of the HPV demonstration project. The decision to conduct the census stemmed partly from insufficient technical guidance and underutilized technical assistance in conjunction with the NIP and country-level partners' limited knowledge of implementing HPV vaccine demonstration projects. Figure 2 depicts the root causes contributing to the implementation of the improvised census and the ensuing consequences that emerged.

**Figure 2:** Root cause analysis for the affected quality of the HPV vaccine demonstration implementation



## Uganda

**The importance of carefully and comprehensively assessing financial sustainability throughout the process of designing the vaccine-delivery strategy (including at the demonstration phase) is highlighted by the late realization of the ongoing costs of the proposed HPV vaccine delivery model for national HPV vaccine introduction in Uganda.**

The demonstration project in Uganda, which was not Gavi-funded, established that the proposed vaccine delivery model for national introduction would be a hybrid model combining a school-based model with a model integrated with a Child Days Plus (CDP) program (Table 1).

In the wake of a reduction in Child Days Plus (CDP) funds for districts, concerns regarding the financial sustainability of the proposed delivery model led to the present decision to modify the delivery model to one more incorporated with routine EPI.

**Table 1:** HPV vaccine-delivery models used in Uganda

| | HPV demonstration project (2008-2009) | | Scale-up model (2010 to date) | National rollout: current proposed model |
|---|---|---|---|---|
| **Location** | **Ibanda district** | **Nakasongola district** | **12 new districts in addition to Ibanda and Nakasongola** | **All districts** |
| **HPV delivery model** | School-based approach (selection by grade) | Child Days Plus-based approach (selection by age) | Hybrid approach (selection by grade) | Routine immunization-based approach (selection by grade) |
| **Description** | Health workers visited all schools within the catchment area to deliver three doses of HPV vaccine. Girls were identified based on school grade. Alternatively, out-of-school girls aged 10 years were eligible. Out-of-school girls were vaccinated either through community outreaches or at health facilities. Out-of-school girls were identified and mobilized by village health teams to come to outreach posts. | HPV vaccine doses one and three were delivered in schools during the biannual Child Days Plus (CDP). The second dose was delivered through a standalone outreach in schools and outreach posts outside of CDP months. Girls were identified by age.<br><br>Out-of-school girls who were 10 years old were eligible. Out-of-school girls were vaccinated either through community outreaches or at health facilities. Out-of-school girls were identified and mobilized by village health teams to come to outreach posts. | A combination of the two piloted delivery models is used. HPV vaccine doses one and three were delivered in schools during the biannual CDP. The second dose was delivered as a standalone school visit program. All girls in relevant grades were targeted.<br><br>Out-of-school girls aged 10 years were eligible. Out-of-school girls were vaccinated either through community outreaches or at health facilities. | HPV vaccine will be integrated into routine immunization. This approach maps all schools within the catchment area of each health facility. Schools close to facilities take the eligible girls to the health facility during static immunization days while remote schools visit the nearest outreach posts. Health facilities will draw up a program/schedule for all schools within their catchment area. Health workers will only visit schools that serve as venues for outreach sessions. All girls in primary four, regardless of age, will be targeted.<br><br>The out-of-school girls aged 10 years are eligible and will attend static clinics or outreaches depending on their convenience. |

**At key points throughout the HPV vaccine introduction application process, several opportunities were missed to account for the feasibility and sustainability of the chosen and tested HPV vaccine delivery model:**

- There was a lack of participation of key partners (Ministry of Finance, Ministry of Education, costing analyst) in the application development process; these partners may have provided critical financial perspective.
- After 12 districts were added and funding for delivery through the demonstration program ended, the program struggled to deliver the vaccine to schools.
- Applications for national introduction should be accompanied by an explicit and in-depth costing and sustainability analysis for HPV vaccine, given the different target population and delivery modes that delivery of this vaccine entails. Although this is a stated requirement of past and present HPV vaccine guidelines, our evaluation in Uganda suggests that this requirement was not afforded the necessary level of attention and review that it deserved both at country and Secretariat levels.

This highlights the need for careful consideration of financial sustainability, including the sustainability of other platforms to be leveraged (such as CDP), when selecting delivery models to test in the demonstration phase. It also highlights the need to ensure that different delivery models of varying feasibility are tested. An assessment of financial sustainability prior to implementing the HPV demonstration project would help to guide the appropriate delivery model(s) to be tested.

**There is a lack of clarity about the potential pathways from the initial HPV vaccine demonstration project to national introduction.**

Our evaluation found that there appears to be a lack of clarity about the use of demonstration projects and the potential pathways leading to application for national introduction. For example, one option for countries may be to focus on the demonstrated ability criteria in a more favorable site before expanding to more representative sites for broader learning and then applying for support for national introduction. In its review of Mozambique's application, the Independent Review Committee (IRC) picked up on a related suggestion by the Mozambique Interagency Coordinating Committee (ICC):

> "The ICC notes that...further demo projects may be needed in other geopolitical sections of the country to gain needed experience prior to national application."
>
> ~ Mozambique Interagency Coordinating Committee

The HPV application guidelines do not outline this multi-phase rollout approach as a potential pathway to national introduction. Further clarification of the guidelines is needed regarding the option of a staged approach of multiple demonstration sites leading to national introduction and the degree to which this is supported by Gavi.

# CONCLUSION

Gavi may wish to revisit the implicit and explicit goals of the HPV vaccine demonstration policy to more clearly align the design and implementation of the HPV program with those goals. Potential responses include the following:

- Gavi can offer more clarity for countries on potential pathways between demonstration projects and national introduction. One option for countries may be to focus on the demonstrated ability criteria in a more favorable site before expanding demonstration activities to more representative sites for broader learning. This staged approach to national rollout may be valuable.

- The inclusion of a rough costing analysis in an application for a demonstration project may ensure that delivery modes tested in demonstration projects are feasible and sustainable. Additionally, assessment of financial sustainability should be carefully reviewed in applications for national introduction.

- Gavi should emphasize the learning objectives of the demonstration project to inform national introduction through guidelines, tools, and technical assistance. Relatedly, Gavi should support countries to select demonstration sites that maximize potential for representative experience to inform national introduction.

Table 2 summarizes all relevant HPV vaccine findings and recommendations presented in the full 2014 Annual Dissemination Report.

**Table 2:** Summary of findings and recommendations

| Finding | Recommendation(s) | Audience | Generalizability |
|---|---|---|---|
| **MOZAMBIQUE** | | | |
| The district ultimately chosen as the Gavi-supported site for the HPV vaccine demonstration in Mozambique represents a district with relatively favorable implementation conditions that include strong partner support and comparatively higher socioeconomic conditions. The government of Mozambique (GOM)'s later decision to include and independently fund two additional HPV vaccine demonstration districts will likely lead to lessons learned which will be more applicable and result in tools and plans that are better adapted for national introduction. | Gavi and country governments should continue to ensure that selection of demonstration sites maximizes the potential for a representative experience that may contribute to lessons learned for national introduction. This may include supporting multiple demonstration sites in a simultaneous or phased manner and/or encouraging co-financing of additional demonstrations sites by country governments or other donors. | Country governments and Gavi Secretariat | Medium. While site selection was a finding specific to Mozambique, our interviews at the global level suggest that this may be occurring in other countries. A review of site selection in other countries is warranted. |
| Insufficient technical guidance and underutilized technical assistance, coupled with the National Immunization Programme (NIP) and country-level partners' limited knowledge of implementing HPV vaccine demonstration projects led to the unsuccessful implementation of a target population census in the HPV vaccine demonstration sites, which was ultimately abandoned. The resources required to conduct the census resulted in a lack of attention being paid to other preparatory activities that affected the quality of the HPV demonstration project. | 1. The Gavi Secretariat and partners should provide technical guidelines for HPV vaccine demonstration project implementation that includes guidance on how demonstration activities relate to national rollout of the HPV vaccine. Relatedly, in guidelines, the demonstrated ability criterion should be revised to more clearly emphasize demonstrated ability based on an average or representative site and conditional on development of a feasible delivery model for national introduction.<br><br>2. Partners and Gavi should ensure that sufficient technical guidance (guidelines, tools, and technical assistance) specific to HPV vaccine demonstration projects is available and accessible and encourage uptake. | Gavi Secretariat, WHO, and UNICEF | High. As the HPV vaccine involves a target population in other countries that is very different from those for routine EPI, there is likely to be limited technical expertise in country to design delivery models to reach the target population on a routine basis. The absence of demonstration project guidelines that address these specific issues will affect all countries. A review of technical capacity and assistance needs for HPV vaccine demonstration programs is warranted. |
| Funds were disbursed early from Gavi, in response to lessons from Mozambique's experience with PCV. The disbursement entity, roles, and responsibilities of the NIP and partners, however, changed from what was stated in the approved application for HPV vaccine demonstration project support in Mozambique. Even though these changes were positive because they better aligned with the purpose of the demonstration project, the changes were poorly communicated across all stakeholders and were not well planned. As a result there was confusion in roles and responsibilities and delayed in-country disbursement of funds to implementing agencies. | 1. The Gavi Secretariat should establish a formalized process for changes to implementation plans that occur after approval, including changes in designated roles and funding recipients. Country governments, country-level partners, and the Gavi Secretariat should ensure that changes in these roles are communicated to all relevant parties.<br><br>2. Gavi should continue to ensure that the leading implementer for demonstration is the MOH if it will be the main implementer for national introduction. | Gavi Secretariat, country partners, and country governments | Medium. Our finding suggests that the process for changing roles and responsibilities from the initial application is not formalized, which may lead to similar issues in other countries. |

| Finding | Recommendation(s) | Audience | Generalizability |
|---|---|---|---|
| **UGANDA** | | | |
| Key steps in the application process failed to account for the feasibility, sustainability, and ongoing financial resources required for the chosen and tested HPV vaccine delivery model (a combination of school-based and campaign-based delivery) for national introduction. These failures include lack of participation in the application development process on the part of key partners who could have provided this financial perspective, and failure of the Independent Review Committee (IRC) review process to ensure that this information was provided prior to approval of the application. This led to a switch to a delivery model based on routine EPI that was not one of the primary models tested as part of the HPV vaccine demonstration project in Uganda. | 1. Acknowledging that HPV vaccine targets a different age group than other routine vaccines, country governments, partners, and Gavi should more comprehensively consider the costs and plan for sustainability of the chosen national delivery strategy. As this is a specific criterion of Gavi's previous and new application guidelines, it is essential that this be included in the application materials and could be ensured by incorporating a section in the application template dedicated to the costing and planning for ongoing vaccine delivery. This information should be carefully reviewed by the IRC and Gavi Secretariat.<br>2. MOHs, partners, and Gavi should increase efforts to integrate the Ministry of Finance into all immunization-related partnerships and the Ministry of Education for HPV-specific partnerships.<br>3. Country governments and partners when designing HPV vaccine demonstration projects should, where feasible, consider including different delivery models that vary in the resources required to implement them. For example, demonstration projects could test whether a lower-cost option of integrating HPV vaccination as part of the routine EPI delivery system is effective. | Country governments and Gavi Secretariat | Medium. Part of this finding stems from the need for a more careful review of financial sustainability by the IRC and Gavi Secretariat, suggesting that this may be occurring in other settings. We suggest follow-up investigation on the issue of financial sustainability of national HPV vaccine introduction in other countries. |
| Lessons learned from the introduction of PCV led to the Uganda National Expanded Programme on Immunisation (UNEPI) and partners initiating the preparatory phase for the national HPV vaccine introduction earlier than past vaccine introductions. However, there was uncertainty among in-country stakeholders as to when the Vaccine Introduction Grant (VIG) funds would arrive in country to cover the costs of the preparatory activities. This is the result of a mismatch in understanding of the procedures and timeline for disbursement of the HPV vaccine introduction grant between the Gavi Secretariat, UNEPI, and partners. | The Gavi Secretariat should establish a formal process for requesting vaccine introduction grants which should include details on the timing of disbursement. | Gavi Secretariat | High. This finding is similar to what was reported as part of the 2013 Gavi FCE report and reflects the need for a more formalized process for requesting vaccine introduction grants. |

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