Title:

HPV vaccine introduction in Rwanda: Impacts on the broader health system

Authors:

Sergio TORRES-RUEDA MSc^a, Stephen RULISA MD, Mmed^b, Helen E.D. BURCHETT PhD^a, N. Victor MIVUMBI Mmed^c, Sandra MOUNIER-JACK MSc^a

^aLondon School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH, UK

^bUniversity of Rwanda, School of Medicine, Department of Obstetrics & Gynaecology, and University Teaching Hospital of Kigali, Department of Clinical Research, Kigali, Rwanda

^cMaternal and Child Health Department, Ministry of Health, Kigali, Rwanda

Email addresses:

Sergio TORRES-RUEDA: sergio.torresrueda@lshtm.ac.uk

Stephen RULISA: s.rulisa@gmail.com

Helen E.D. BURCHETT: helen.burchett@lshtm.ac.uk

N. Victor MIVUMBI: mivumbi.victor@gmail.com

Sandra MOUNIER-JACK: sandra.mounier-jack@lshtm.ac.uk

Corresponding author:

Sergio Torres-Rueda; Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH, UK. Telephone: +44 (0)207 958 8310, Fax: +44 (0)207 927 2701, email: sergio.torresrueda@lshtm.ac.uk

ABSTRACT

Objectives: Rwanda was the first country in Africa to introduce the human papillomavirus (HPV) vaccine. This was achieved through multi-year school-based campaigns. Our study evaluated the impact of the HPV vaccine introduction on the country's immunisation programme and health system.

Methods: Thirty key informants were interviewed at national and district levels, and in participating schools. Twenty-seven health facilities completed a questionnaire exploring the effects of the new vaccine introduction on six health systems building blocks, as defined by the World Health Organization. Routine service activity data were collected during a 90-day period around the introduction.

Results: Routine vaccination activities were not disrupted during the delivery, likely due to a strong Expanded Program on Immunization, appropriate planning and a well-resourced operation. Opportunities were seized to co-deliver other interventions targeted at children and adolescents, such as health promotion. Collaboration with the Ministry of Education was strengthened at national level. Although there were some temporary increases in staff workload, no major negative effects were reported.

Conclusion: Despite its delivery through school-based campaigns, the HPV vaccine integrated well into the immunisation programme and health system. The introduction had no major negative effects. Some opportunities were seized to expand services and collaborations.

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Keywords: Health systems, HPV, vaccination, adolescent health, Rwanda

INTRODUCTION

An estimated 528,000 new cases of cervical cancer and 266,000 related deaths were reported worldwide in 2012. The burden of cervical cancer is particularly high in less developed regions, where approximately 84% of new cases and 87% of deaths occur. East Africa has the highest mortality rates for cervical cancer of any region in the world. In Rwanda incidence rates are higher than for any other type of cancer among both women and men (1).

The human papillomavirus (HPV) is the principle cause of cervical cancer (2). HPV types 16 and 18 in particular are responsible for approximately 70% of cases (3).

Two vaccines, Gardasil® and Cervarix®, offer protection against HPV types 16 and 18 and have been approved by the World Health Organization (WHO) (4, 5).

Gardasil® also offers protection against types 6 and 11, which are responsible for the majority of cases of anogenital warts (6). It is recommended that pre-adolescent and adolescent girls be vaccinated with three doses of the vaccine prior to the onset of sexual activity, which is a very different target group to those receiving traditional infant vaccinations, or accessing one-off campaigns (e.g. meningitis A).

In April 2011, the Ministry of Health of Rwanda introduced the HPV vaccination nationwide for the first time, using the vaccine Gardasil®. This introduction was the first introduction of HPV vaccination in Africa and was made possible by a three-year donation from Merck totalling 2 million doses (7). The Government of Rwanda covered the delivery costs. In 2013, Gavi, the Vaccine Alliance (Gavi) committed to finance the costs of the vaccine from 2014 to 2017, totalling nearly USD 8.9 million (8).

The Ministry of Health, along with international partners, conducted a situational analysis on stakeholders' knowledge, attitudes and beliefs in order to inform introduction decisions (9). At the time, Rwanda had had some previous experience carrying out other vaccination campaigns (defined as vaccination taking place outside the health facility for a limited period of time), against namely measles and polio, but none targeted specifically at adolescents and pre-adolescents (10). Given the country's high school enrolment rates, it was decided that the HPV vaccine would be delivered to girls mainly on school premises, through two-day campaigns conducted three times a year. The vaccination would be organised and delivered by nearby health facility staff. Due to difficulties in ascertaining people's exact ages in rural settings, a decision was also made to pursue a grade-based strategy of distribution, initially targeting Grade 6 of primary school. The introduction of HPV vaccination is therefore an expansion of the immunisation programme to a new age group and, largely, through a new delivery strategy (school-based).

The vaccine was also made available at health facilities for a limited period of time, targeting 12-year old girls who were out of school or who were absent during vaccination days (9). Catch-up activities, aiming to vaccinate those who did not receive the vaccine during previous campaigns but who still fell within an eligible age/grade range, were carried out in 2012 and 2013 for girls in third year of secondary school (9). Reported coverage of the vaccine has been high with 92,107 girls vaccinated with all three doses in 2011, corresponding to a 92% coverage rate (9).

Despite the success of the vaccine introduction in obtaining high coverage, questions remain about the wider effects of the introduction on the immunisation programme and the broader health system (11). The introduction of HPV vaccination

not only expanded the traditional vaccination programme by delivering a new vaccine, it also expanded the programme to a new age group and involved a completely new delivery mechanism, i.e. school-based campaigns. Vertical interventions (defined as targeted interventions that are not fully integrated into a system) such as vaccination campaigns have been shown to have both positive and negative effects on health systems (12-14). There has been little research exploring the impact of vaccine introductions, particularly in low-income countries where health systems tend to be weaker (14, 15). As far as the authors are aware, no study has as of yet focused on the effects of an HPV vaccine introduction that targets a new population group through a dedicated school-based delivery model. The aim of this study was to evaluate the impact of the HPV vaccine introduction on the Expanded Program on Immunization (EPI) and on the broader health system in Rwanda. It was part of a larger study, exploring the impact of seven vaccine introductions in six low- and middle-income countries (16).

METHODS

A mixed methods approach was used, incorporating three data collection methods: (1) semi-structured interviews with key informants, (2) questionnaires at the health facility level and (3) facility-level routine health service use data (see Table 1).

Study site

Three regions were selected for inclusion in this study to reflect a range of routine vaccination coverage (Northern, Eastern and Kigali). Within each region, three

districts were chosen to reflect different profiles of urbanisation and rurality. Three health facilities were selected in each district based on increasing distance from the main urban centre; 27 facilities in total. Both public and faith-based health facilities were included in the study.

<< Insert Table 1>>

Data collection methods

The framework used to structure the data collection tools and subsequent analysis was adapted from the WHO Health Systems Framework (17) and from the WHO ad hoc working group on new vaccines and health systems in 2010 (see Table 2) (18).

<< Insert Table 2>>

(1) Key informant interviews:

A total of thirty semi-structured interviews were carried out with key informants. Twenty-three were done at the national and district levels in order to understand the perceived effects of the introduction on the health system. Stakeholders both within and outside EPI were interviewed (see Table 1). Interviewees were purposively sampled and selected based on having senior positions in their organisations and on having been involved in the introduction of the vaccine. The interviews were semi-structured. An interview guide was designed around the study framework (see Table 2), including questions on topics such as governance, planning, financing and service delivery. Given that the vaccine was delivered in schools, seven senior school staff members (either the headmaster or person in charge) who were involved in the vaccination effort were also interviewed across seven of our nine study districts. Interviews typically lasted 45 minutes and were carried out by members of

the research team, both from the London School of Hygiene and Tropical Medicine (LSHTM) and from Rwanda. They took place in the interviewees' offices. The data collection team spoke English, French and Kinyarwanda. Interviewees and respondents were encouraged to participate in whichever language they felt most comfortable.

(2) Health facility questionnaires:

Researcher-administered questionnaires were completed with a staff member from each of the 27 health facilities included. Health facilities were tasked by the Ministry of Health to coordinate and carry out the vaccination campaigns and respondents were either in charge of the facility or directly involved with vaccination. The questionnaire was designed by the LSHTM research team and was adapted from the Post Introduction Evaluation (PIE) methodology used by WHO (19). It aimed to understand whether the introduction had brought about any changes at the facility-level, and included questions on topics such as service delivery, training, staffing, surveillance and other elements from the study framework (see Table 2).

(3) Routine health service data:

At the facility level, daily service use data were collected on two indicators: delivery of the third dose of the diphtheria-pertussis-tetanus-hepatitis B-*Haemophilus influenzae* type b combined vaccine ('pentavalent' vaccine) and antenatal care (ANC) visits. Data was collected on these indicators for a 90-day period (March 1 – May 31 2011) around the time of introduction (one month before the introduction of the HPV vaccine, during the month of introduction, and one month after). These two indicators were used as proxies to ascertain possible interruption of routine health services. Limitations to this approach are mentioned in the Discussion.

Interviews, questionnaire administration and service use data collection took place during August 2012, 16 months after the introduction of the vaccine. At the time of data collection one whole round of three doses of HPV vaccination had already taken place (in 2011).

Ethical approval was obtained from the LSHTM, the National Health Research Committee at the Ministry of Health of Rwanda and the Institutional Review Board of the Kigali University Teaching Hospital. Before interviews were carried out, the aims and methods of the study were explained to interviewees and facility respondents, written consent was obtained and, when agreed, interviews were recorded.

Interview recordings were transcribed and, where necessary (10/30), translated into English by an experienced translator in our team. When consent for recording was not obtained (2/30), notes were taken and typed up.

The analysis of the semi-structured interviews was carried out using the software 'Open Code' (20). An initial coding framework was created based on a preliminary assessment of the interview transcripts and the study framework (see Table 2). These codes were applied to all the interview transcripts and the data categorised under each code was analysed. Questionnaire data were analysed through descriptive statistics using SPSS 19 software. Routine health service data was entered and analysed in Microsoft Excel.

RESULTS

Key informants and facility respondents saw the HPV vaccine introduction positively and thought it had integrated smoothly into vaccination and health system activities.

The findings presented below have been broken down according to the study framework's six building blocks.

Sample description

The sizes of the facilities sampled varied: median number of staff members per facility was 22, ranging from seven to 36. On average three staff members worked on immunisations.

I) Service Delivery

Access and utilisation: Despite the potentially disruptive nature of a campaign-based delivery approach, nearly no changes in access or utilisation of routine services were reported during the HPV vaccine introduction. Routine health service data showed that 20/27 facilities conducted ANC visits on the same days as the vaccination campaigns. Respondents at 24/27 facilities stated that the introduction had no effect on the availability of routine vaccination services. In fact, routine health service records suggested that routine vaccination continued, as did some outreach activities, simultaneous to the delivery of the HPV vaccine; records showed that 15/27 facilities offered the third dose of the pentavalent vaccine (on-site or outreach) on one or more of the days when the HPV vaccination campaign was taking place. Of those 15 facilities, four carried out routine outreach vaccination services during those days. It is important to note that routine records reviewed showed that out of the 27 facilities, only nine carried out outreach activities for other vaccinations during the 90-day period observed. This is important because it suggests that the majority

of the facilities may have had to develop the logistical capacities to vaccinate outside the facility in preparation for the HPV vaccine introduction.

Delivery modalities: Respondents at 20/27 facilities stated that other services (which were previously not targeted at schools) were co-delivered during school vaccination sessions. The most commonly cited intervention was health promotion sessions (16/27) on topics such as vaccination, hygiene, sexual health and family planning. Seven facility respondents reported delivering de-worming drugs, mostly during the second year of the vaccination campaign. One facility reportedly promoted free voluntary medical circumcisions at a nearby health facility to male students. One key informant working on EPI at the national level stated that vitamin A had also been delivered, although this was not mentioned by facility respondents.

“It [the HPV campaign] is of great benefit for activities’ integration.

We decided that when we do a campaign [of HPV vaccination], we associate [it] with other health-related activities like de-worming, mebendazole, vitamin A, family planning. So it means it is complimentary.” [R_13, National-level interviewee]

“During the campaign, we gained also new information about other diseases that we didn’t know before.” [R_11, School staff interviewee]

Quality of care: No or minimal effects were reported.

Demand and acceptance: No change in the demand for routine childhood vaccination was reported by facility staff. Rumours of infertility caused by the new vaccine that arose in the early phase of the HPV vaccine introduction subsided

rapidly and no effect was reported on the acceptance of other vaccines. While demand for other health services was said to have remained unchanged, several respondents stated that the HPV vaccine introduction had led to an increase in demand for cervical cancer screenings. It is worth pointing out that communication around the new vaccine was framed around an anti-cancer message.

“Now people started to go to the screening. Before the HPV vaccine, people kept quiet. Now they started because of teaching on HPV vaccine, cervical cancer. That contributes to other health intervention.” [R_18, National-level interviewee]

“The main message [of the communication] was the impact of the HPV vaccination on students’ health, that the benefit is for them to prevent cervical cancer” [R_26, School staff interviewee]

Social mobilisation was carried out simultaneously through schools, health centres and with the community at large. Community health workers, who usually did not take part in vaccine-related activities, were engaged in the social mobilisation effort around the HPV vaccine.

II) Health Workforce

Availability and distribution of staff: In the first HPV vaccine round, workload increased during the days of the vaccination according to 17/27 facility respondents. The increase was explained by the reduced number of staff remaining at the health facilities during the days of school vaccination. Five facility staff members in the Eastern Region, stated that time spent on routine vaccination activities had

increased because of the extra time it took to educate the population about the new vaccine.

“It is understandable that ... those left in health centres were overloaded since they did their tasks and tasks of those who went in campaign.” [R_09, District-level interviewee]

Training and capacity of staff: Training related to the HPV vaccine took place at all levels of the health system. The majority of facility-level respondents (22/27) stated that training had helped strengthen their skills. Teachers and school staff involved in the vaccination effort were also trained in data collection. No disruptions of services were reported due to the trainings.

“Because we are used to trainings, when some staff is in trainings, others organise themselves so that activities carry on normally. So [there is] no negative impact.” [R_23, District-level interviewee]

Remuneration and satisfaction: Key informants identified the positive health effects of the vaccine on the population’s health as a strong motivating factor for the staff. Per diems (of a standard range) were given to health facility staff during the days spent HPV vaccine training or delivery activities. These were also seen as motivating.

Performance and supervision: HPV vaccine-specific supervisions were reported by 10/27 facilities and were said to have taken place over four consecutive days before and during vaccination. No changes to routine supervision were reported subsequent to following the HPV vaccine introduction.

III) Health Information System

Routine data collection and reporting: No or minimal effects were reported.

Surveillance: Key informants stated that strengthening adverse effects following immunisation (AEFIs) surveillance was emphasised during the planning process and it was included in the training of health facility workers. School staff members were reportedly instructed on how to monitor AEFIs among their students.

“We trained the medical staff about the AEFI related to the vaccine. The training was the same. The AEFI monitoring is not an isolated monitoring. It is an integrated monitoring...” [R_13, National-level interviewee]

IV) Medical Products, Vaccines and Technologies

Forecasting of vaccines and injections supplies: No or minimal effects were reported.

Procurement: No or minimal effects were reported.

Cold chain management and waste disposal: A cold chain inventory was carried out by EPI before the introduction of the HPV vaccine and concluded that the available capacity was sufficient. This is likely due to the fact that the pneumococcal conjugate vaccine (PCV) introduced in 2009 had initially been packaged in pre-filled syringes and cold chain capacity was expanded accordingly. However, PCV packaging was subsequently changed to vials, making more cold chain space available which was then used for the HPV vaccine. Respondents at 23/27 facilities confirmed that cold chain space had not changed. No effects on waste disposal were reported.

V) Financing and Sustainability

Affordability: There was general consensus among key informants that additional funds were made available to the districts for the introduction of the HPV vaccine to cover costs such as transportation, social mobilisation and training. Only three facilities out of 27 did not report receiving additional funding to pay for costs incurred by the new vaccine.

Financing: The Government of Rwanda financed the cost of vaccine consumables and vaccine delivery. According to key informants, a decision to introduce the HPV vaccine was made partly because it was seen as a potentially cost-saving activity in the longer term, not only because of costs savings of cancer treatments averted, but also in terms of the cost savings involved in the co-delivery of additional interventions.

VI) Leadership and Governance

Regulatory policy: No or minimal effects were reported.

Political commitment: Key informants reported that partnerships between different actors involved in the introduction were reinforced, particularly between members of the Ministry of Health and Ministry of Education.

“It had been long since we [Ministry of Education] last worked in collaboration with the Ministry of Health....it was a good opportunity for authorities, ministers to be aware of school-based activities. It has also awakened teachers, school directors that we can think again about the health of children....” [R_16, National-level interviewee]

Organisation, structure, reform, negotiation and stewardship: Key informants noted that an extensive amount of planning was carried out before the introduction.

Planning was facilitated by the Inter-Agency Coordination Committee (ICC), whose membership was reportedly extended to Ministry of Education officials. Several interviewees stated that relations between schools and health centres had been improved thanks to the new vaccine and that, as a result, schools had asked nurses to return to schools at later times to further discuss topics, such as hygiene. A strong emphasis on HPV vaccination days as an opportunity for health facility staff to check students' general health and hygiene was identified during key informant interviews.

“For HPV vaccine planning process... the process was very long because ... it was a school-based immunisation programme. When you go to the schools, we have to include the Ministry of Education. The planning process has to include all partners, to include advocacy, to mobilise internal resources, and external resources so that implementation can be easy.” [R_18, National-level interviewee]

DISCUSSION

The HPV vaccine introduction was generally well integrated into the EPI, with no or minor negative effects reported on most components of the health system. This is noteworthy given that the vaccine targeted a new age group and was based on a new school-based campaign delivery model. Particular findings of our study that deserve being highlighted include the decision to co-deliver other interventions at the school-level alongside the HPV vaccine, and the continuation of routine services during the delivery of the campaign.

Towards a more integrated service delivery model

Evidence suggests that school-based delivery in low- and middle-income countries is effective (9), and positively and statistically significantly associated with vaccine uptake rates (21). However, the introduction of HPV in Rwanda showed that the benefits of this delivery type could extend beyond vaccination itself. Adolescent and pre-adolescent uptake of preventive services is known to be low in low- and middle-income ones (22, 23). The HPV vaccine introduction in Rwanda presented a rare opportunity for the health service to interact with schools and provide new services. Indeed co-delivery was reported by the majority of facility respondents. It is worth noting that said co-delivery of interventions was not only aimed at the girls receiving the vaccine, but more broadly at the school community at large. The vaccination effort was perceived as a way for health facilities to generally monitor schools in terms of hygiene and students' health, and as an opportunity for people at the Ministry of Health and at the Ministry of Education to think jointly about adolescent health.

There is scope for further interventions delivered through the vehicle of school-based HPV vaccination. A range of effective health interventions that could be integrated into HPV vaccine delivery in low- and middle-income countries has been identified in recent years (24). Some of these co-delivered interventions have been shown to be welcomed by parents, young adolescents and teachers (25). Bringing information about health services into schools may also help to reduce the barriers young people face in accessing HIV prevention services (26) and, provided they are age-specific, broad sexual and reproductive health services. For example, introduction of voluntary medical male circumcision for adolescents (mentioned by one facility in our study) has been considered by other countries introducing the HPV vaccine (27).

In our study there were reports that the introduction of the HPV vaccine might have increased the public's awareness of, and demand for, cervical cancer screenings services. However, because of the limited scale of the existing pilot screening sites, it was unclear whether this translated into increased service utilisation. The Ministry of Health has plans in place to roll out more extensive screening services over the coming years (28).

Continuity of routine service during school-based HPV vaccine delivery

Other studies have shown that routine vaccination may be disrupted during campaigns during HPV vaccination delivery campaigns (29). However, the availability of routine vaccination services did not appear to have changed in most facilities (24/27). The fact that the majority of surveyed facilities (15/27) carried out routine vaccination activities at least once whilst the HPV vaccine campaign was taking place is significant, given that facilities were not required to hold daily routine vaccination services. This suggests an extensive amount of planning was carried out before the introduction to coordinate simultaneous HPV and routine vaccination activities. Normal continuation of vaccination activities is also likely to be the product of pre-existing strengths in the health system and the EPI. Rwanda's public health expenditure as a proportion of gross domestic product was 6.1% in 2012, which is more than double the average figure for countries in sub-Saharan Africa (2.9%) (30). Routine vaccination coverage is very high, with 97% coverage of pentavalent vaccine reported in 2010 (31). Rwanda benefits from stronger human resources for health than other countries in sub-Saharan Africa, with a higher number of nurses and midwives proportional to population (69 per 100,000) than the median for the region (59 per 100,000) (32). Finally, the vaccine targets a relatively small population

when compared to traditional campaigns, such as measles vaccination, which Rwanda has carried out on several occasions over the past decade (10).

Sustainability

The costs of routinely delivering a complex package of interventions through schools three times a year to a non-traditional population group have been acknowledged to be substantially higher than the costs of simply adding a routine vaccine to the EPI (33). The financial recurrent cost of delivering the HPV vaccine has been estimated at \$5.77 per girl fully immunised by a recent study undertaken in Tanzania (34), which is significantly below Gavi support of \$2.40 per girl fully immunised (35). The economic cost in Tanzania was estimated at \$12.40, a much higher level reflecting opportunity costs for staff and other resources (34). Although costs might be lower in Rwanda, the HPV vaccine remains a significant investment for a low-income sub-Saharan African country.

Limitations

The inherently positive perception of new vaccines may have made it difficult for respondents to report negative impacts (through either conscious or unconscious acquiescence bias). The vertical nature of EPI meant that many interviewees may have found it difficult to respond to questions about the broader health system while those outside of EPI often had little knowledge about vaccination activities. In some cases complete routine health service use data were not available in facilities. It is important to note that it is beyond the scope of this study to determine whether the number of children vaccinated with the pentavalent vaccine or the number of ANC visits changed due to the HPV vaccination campaign, although it is a worthwhile question for future research.

Although the findings of this study should be considered encouraging insofar as showing that low-income countries can introduce the HPV vaccine without major negative effects on the health system, there are questions around the extent to which they can be generalised to other countries. Although Rwanda is a low-income country it has a comparably strong health system and a high school enrolment, which made the task of locating the target group easier for health facilities. Furthermore, Rwanda's small size, high population density and adequate transportation infrastructure likely reduced the kinds of obstacles that other low-income countries in sub-Saharan Africa face when delivering similar interventions.

CONCLUSION

The HPV vaccine was well integrated into existing EPI activities and into the health system in general. Some opportunities were seized to maximise co-delivery of interventions. Rwanda's experience in introducing the HPV vaccine suggests that vaccination campaigns in low-income settings can be rolled out without major negative effects.

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Table 1: Summary of Data Collection Methods

I. KEY INFORMANT INTERVIEWS		
Health System Level and Type of Respondent	Data Collection Method	Number
National		
Expanded Program on Immunization, Ministry of Health	Interview	3
Other, Ministry of Health	Interview	4
Civil society and international agencies	Interview	2
Academics/other domestic agencies	Interview	3
District		
District head doctor and other staff involved in vaccination activities	Interview	11
School staff	Interview	7
Total		30
II. FACILITY QUESTIONNAIRE		
Health facility staff	Questionnaire	27
III. ROUTINE SERVICE DATA		
Health facility-level	Archival	27

Table 2: Study framework for assessing the health systems impacts of the HPV vaccine introduction in Rwanda

Health system building block	Vaccination-specific components
Service delivery	<ul style="list-style-type: none"> ▪ Access and utilisation ▪ Quality of care ▪ Delivery modalities ▪ Demand and acceptance
Health workforce	<ul style="list-style-type: none"> ▪ Availability and distribution of staff ▪ Training and capacity of staff ▪ Remuneration and satisfaction ▪ Performance and supervision
Health information system	<ul style="list-style-type: none"> ▪ Routine data collection and reporting ▪ Disease surveillance
Medical products, vaccines and technologies	<ul style="list-style-type: none"> ▪ Forecasting and procurement of vaccines and injection supplies ▪ Procurement ▪ Cold chain management and waste disposal
Financing and sustainability	<ul style="list-style-type: none"> ▪ Affordability ▪ Domestic financing ▪ External financing
Leadership/governance	<ul style="list-style-type: none"> ▪ Regulatory policy ▪ Political commitment ▪ Organisation, structure, reform, negotiation, stewardship